Shatt Al -Arab University

Faculty of science

Department of Pathological analysis science.

Medical Mycology

Lect-9- Aspergillosis

Prof.Dr. Mohammed A. Fayyadh

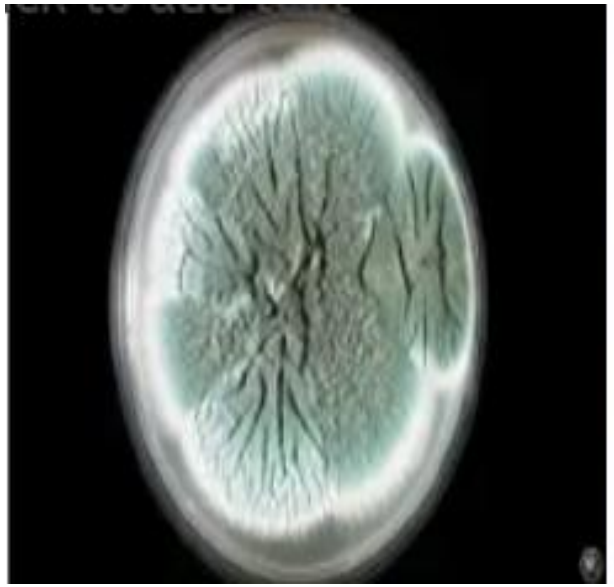
Aspergillosis

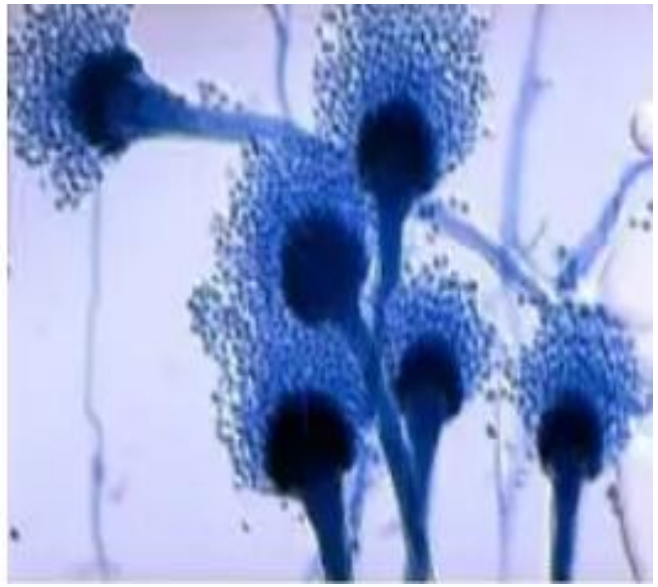
- Aspergillosis comprises a group of world wide human disease caused by about dozens of fungal species of the genus *Aspergillus*. About 185 different species has been identified.
- Since *Aspergillus* species are many and are widespread in soil, air, and decaying vegetable matter many people are heavily exposed to inhalation of spores.

Aspergillus

Is a genus consisting of hundred mold species found in various worldwide. Some species can cause infection in humans and other animals.

The most common pathogenic species are *A. fumigatus* and *A. flavus*, which produce aflatoxin which is both a toxin and a carcinogen.





Pathogenesis and clinical picture

- The spectrum of human disease caused by Aspergillus ranges from allergy to disseminated infection.
- Most of the disease processes are caused by the inhalation of conidia.
- ***Allergy:-*** Persons may develop IgE. against *Aspergillus* and present with allergic condition. Example, asthma
- ***Non-invasive colonization:-*** *Aspergillus* can colonize a pre-existing lung cavity e.g., tuberculosis, forming fungus ball or aspergilloma.

Invasive aspergillosis

- May occur in severely immunocompromised patients, organ transplant recipients.

- Patients under corticosteroid therapy and patients with leukaemia.

- ***Toxin production***
- ***e***.g. aflatoxin of *Aspergillus flavus* is
  - carcinogenic; cause liver cancer and necrosis. Can be found in spoiled legumes.

Predisposing factors

- Infections occur principally in individuals who have disease or predisposing abnormalities such as **cystic fibrosis**, **bronchietasis, chronic bronchitis, tuberculosis** etc. or who are immunosuppressed.

- *Aspergillus* species are not dimorphic; they are characterized by chains of conidia borne on conidiophore.

- Speciation is based on principally morphology; some 150 species are recognized.

- *Aspergillus fumigatus* is most commonly recovered from immunocompromised patients, and most often seen in clinical laboratories.
- *Aspergillus niger* and *A. flavus* are also recognized as significant cause of infection in immunocompromised patients.

Laboratory diagnosis

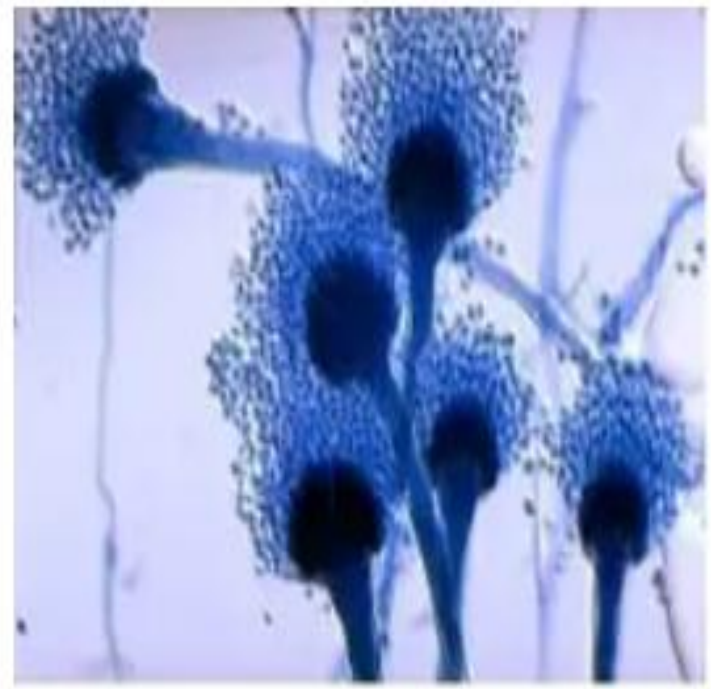
- The diagnosis of aspergillosis is difficult due to their wide spread in nature.
- ***Direct examination***
  - Microscopic examination of KOH preparations of sputum show characteristic branching hyphae filaments and may show the conidiophores attached to the spare head.
  - Demonstration of hyphal fragments in tissue biopsy is diagnostic of tissue invasion.

Gram stain of Aspergillus

Culture and identification

- *A. fumigatus* is rapidly growing mold (2 to 5 days) that produce a fluty to granular, white to blue- green colony, on blood enriched medium.

- Mature sporulating colonies most often exhibits the blue-green powdery appearance.



Serologic test

- Antibodies to Aspergillus extracts are detected in serum and positive skin testing in allergic *cases*.

Mucormycosis

- Mycormycosis is caused by several genera belonging to zygomycetes, e.g. *mucor*, *rhizopus*, and *Absiedia*.
- It is some what less common infection when compared with *Aspergillosis*; however it is a significant cause of morbidity and mortality in immunocompromised patients.
- Like *Aspergillus* species, members of the zygomycetes are common environmental molds of low intrinsic pathogencity.

- The disease occurs in debilitated persons, metabolic acidosis, malignancies, uremia, malnutrition, steroid therapy and hepatic failure.
- The organisms produce broad non septate hyphae, aerial mycelia, sporangia, sporangiospores and sexual zygospores; grow rapidly on routine media to produce profuse cottony colonies.

Pathogenesis and clinical picture

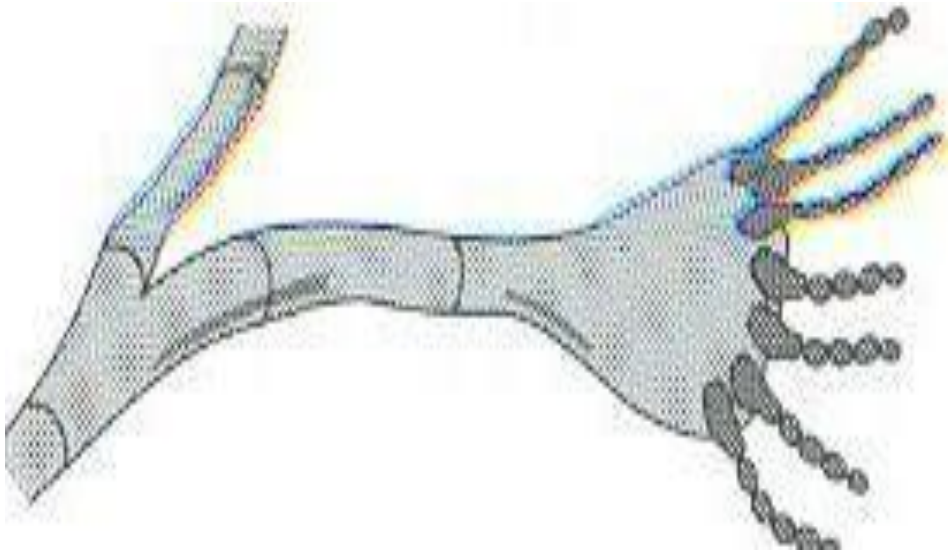
- One of the most common forms observed in the
- Rhinocerebral form in which the nasal mucosa, plate, Sinuses, orbit, face, and brain are involved; each shows massive necrosis with vascular invasion and infraction.
- Other types of infection involved the lungs and gastrointestinal tract; some patients develop disseminated infection.

- Organs including the liver, spleen, pancreas, and kidney may be involved.
- The hyphae usually invade the upper or lower respiratory tract or through burn wound of the skin.
- Lesion progression is usually rapid, spore do not form in vivo.

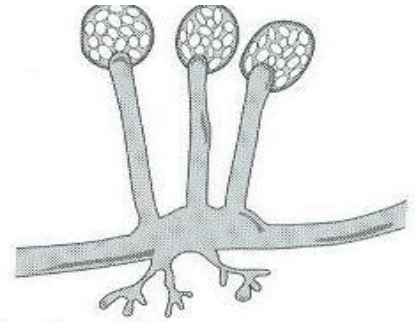
Laboratory diagnosis

- Is based on the demonstration of non- septate hyphae in smears and biopsy sections.
- Culture show sporangium containing sporangiospores

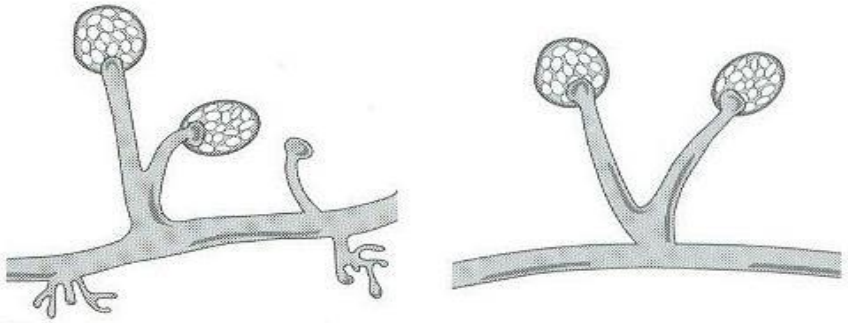
Morphology of frequently isolated opportunistic fungi



Aspergillus species

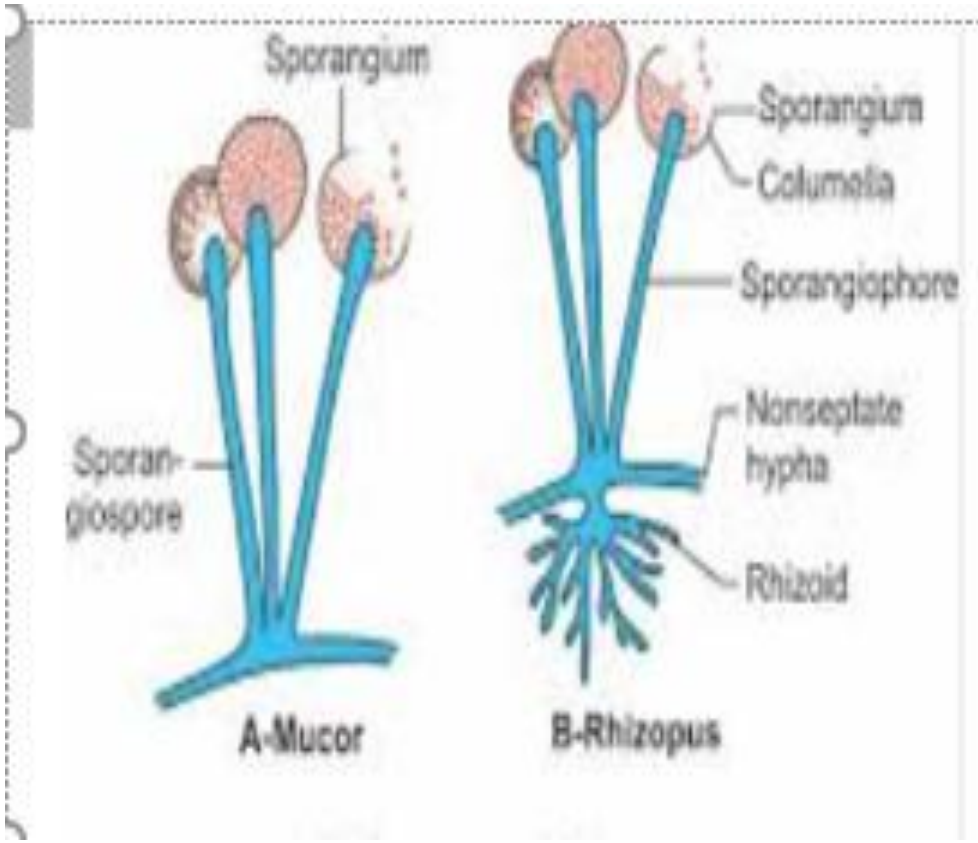


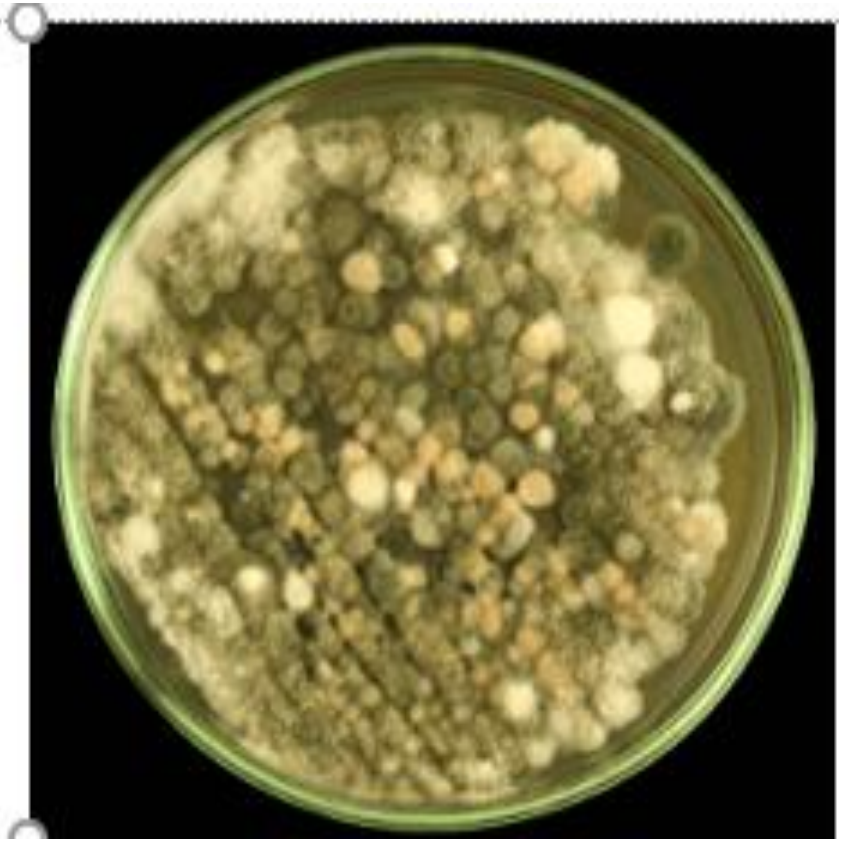
Absidia: similar to *Rhizopus;* however, sporangiophores arise between nodes from which rhizoids are formed.



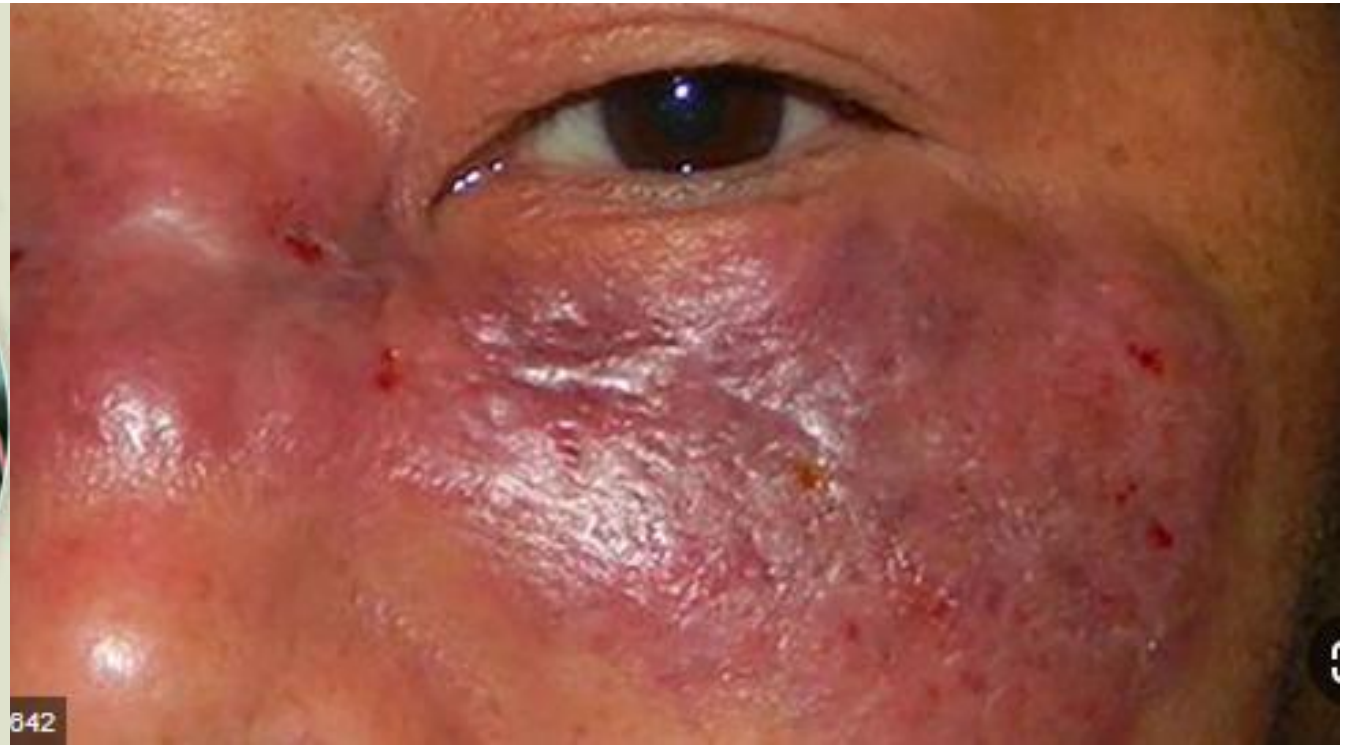
Mucor: no rhizoids

Zygomycetes


Sporangium
Sporan-
giospore
A-Mucor
Sporangium
Columella
Sporangiophore
Nonseptate
hypha
Rhizoid
B-Rhizopus



Mucormycosis symptoms



MCQ

1. Which of the following fungi most commonly causes opportunistic infections in immunocompromised patients?

A. Histoplasma capsulatum B. Candida albicans C. Blastomyces dermatitidis D. Paracoccidioides brasiliensis

2. Which condition most strongly predisposes a patient to opportunistic mycoses?

A. Hypertension B. Diabetes mellitus C. Immunosuppression
D. Hyperthyroidism

3- **"Black necrotic lesions in nasal cavity" are characteristic of which infection?**

A. Aspergillosis B. Candidiasis C. Mucormycosis D. Cryptococcosis

4- **Oral thrush is most commonly caused by:**

A. Cryptococcus B. Candida C. Aspergillus D. Histoplasma

5-**Which opportunistic fungal infection is associated with pigeon droppings?**

A. Histoplasmosis B. Cryptococcosis C. Aspergillosis D. Candidiasis

6. Which antifungal drug is commonly used for severe systemic opportunistic infections?

A. Griseofulvin B. Amphotericin B C. Fluconazole (only topical)
D. Nystatin

7- **Invasive aspergillosis most commonly affects which organ?**

A. Liver B. Skin C. Lungs D. Brain

8- **Which species is most commonly responsible for invasive aspergillosis?**

A. *Aspergillus niger* B. *Aspergillus flavus* C. *Aspergillus fumigatus*
D. *Aspergillus terreus*

Fill in the Blank Q

1. Opportunistic fungal infections mainly occur in _____ patients.
2. The most common cause of oral thrush is _____.

3-_____ neoformans commonly causes meningitis in AIDS patients

4-The most common species causing invasive aspergillosis is _____ fumigatus.

5-Mycormycosis is caused by several genera belonging to ---------- , ----------, and ----------

Q)List the Most important **opportunistic mycosis.**

Q) List the groups at highest risk for opportunistic fungal infections.

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Medical Mycology

Lect-3-Dermatophytes fungi

Prof.Dr. Mohammed A. Fayyadh

Dermatophytes fungi (Cutaneous mycoses)

Cutaneous Mycoses:

- Are infections that extend deeper into the epidermis. It invades hair and nails and causes diseases. The diseases are referred to as **ringworm** (**القوباء الحلقية**)or **tinea**, also called(**dermatophytes**) .Dermatophytes are keratinophilic - "keratin loving". Digest the keratin Which is found in the skin, nails and hair by their keratinase enzyme.
- The **dermatophytes**, are group of about 40 related fungi that belong to **three genera: Microsporum, Trichophyton, and Epidermophyton .**

- **Dermatophytes are probably restricted to the nonviable skin because most are unable to grow at 37 °C or in the presence of serum.**

&-Dermatophyte infections are common in HIV-infected children. The common name of these infection are **Tinea** or **(ringworm) infections**

They include: *Tinea pedis*, *Tinea corporis*, *Tinea unguium and Tinea capitis*

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&- Dermatophytoses are among the most prevalent infections in the world. Although they can be persistent and troublesome, they are not debilitating or life-threatening.

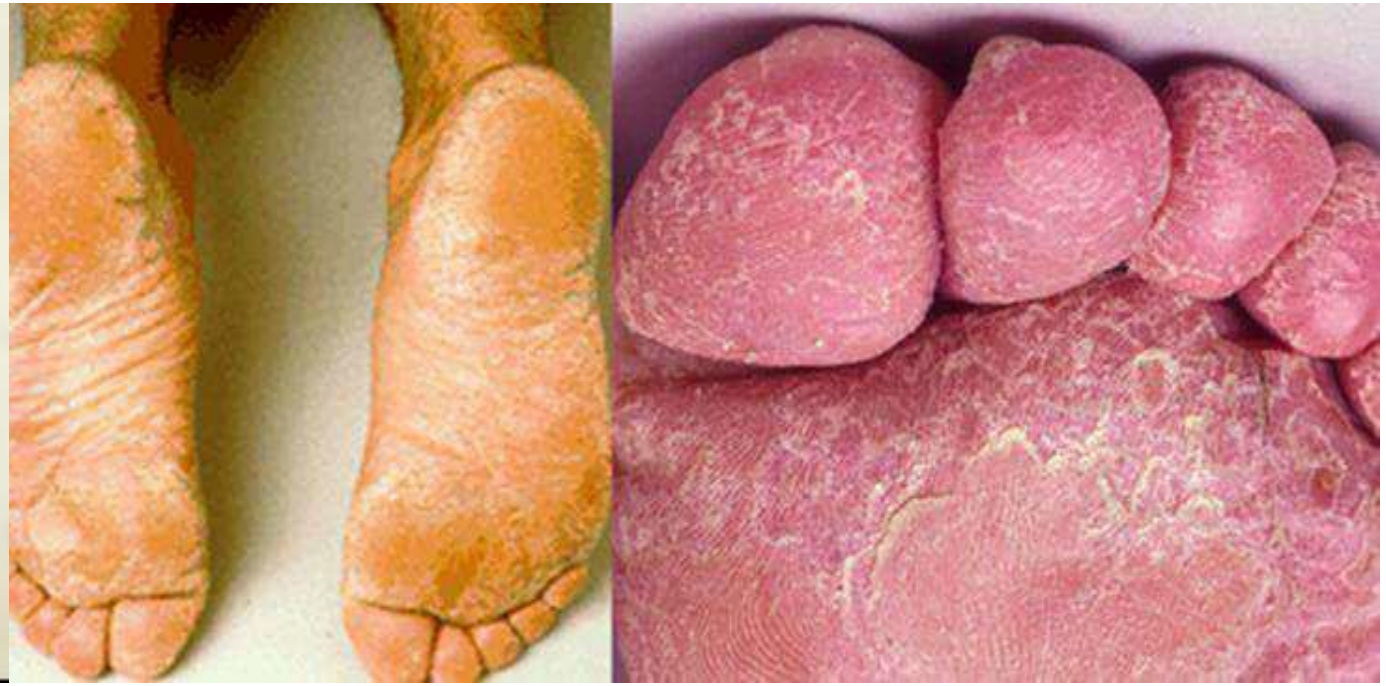
&- Dermatophytes are classified as **geophilic**, **zoophilic, or anthropophilic** depending on whether their usual habitat is soil, animals, or humans.

&- **Anthropophilic species, which cause the greatest number of human infections**, **cause relatively mild and chronic infections in humans, produce few conidia in culture**, and may be difficult to eradicate. Conversely, **geophilic and zoophilic dermatophytes, being less adapted to human hosts, produce more acute inflammatory infections that tend to resolve more quickly**. **Dermatophytes are acquired by contact with contaminated soil or with infected animals or humans.**

Tinea pedis(سعفة القدم)

Also known as Athlete’s foot is a dermatophyte infection of the skin of the foot . Symptoms include: itching or burning on the skin of the foot, peeling or flaking skin, dry skin, blisters or thick patches of dry red skin. Three species of fungi ,*Trichophyton rubrum, Trichophyton mentagrophytes*, and *Epidermophyton floccosum* are together responsible for the vast majority of cases of Tinea pedis throughout the world.

spores

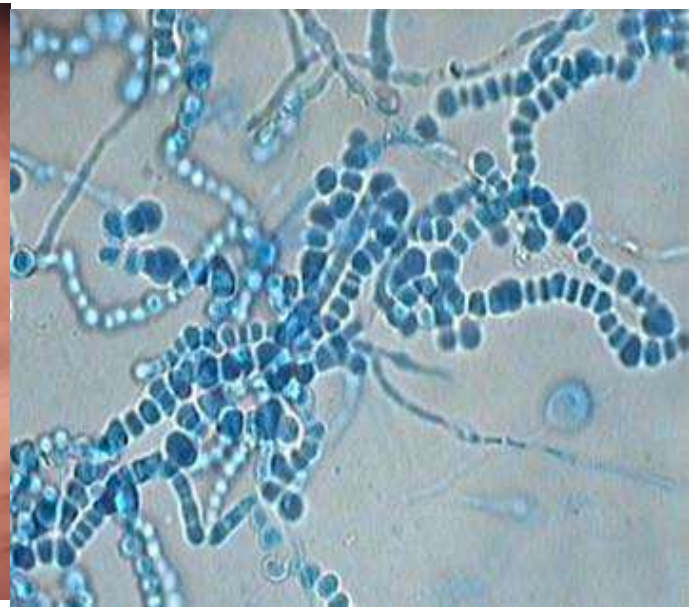


symptoms

Tinea pedis caused by *Epidermophyton* ***floccosum***

Tinea corporis(سعفة الجسم)

Dermatophytosis of the body (Tinea corporis) affects the glabrous skin(الجلد الاملس) and is commonly known as ringworm. Clinically, the lesions present as annular plaques(لويحات حلقية) with central clearing, leading scale, and a ring-shape appearance .They occur mainly on the trunk, limbs, and may be single or multiple, of varying sizes, and may coalesce .*Microsporum canis* is a frequent cause of human infection.


Tinea corporis: The lesions present as annular plaques and a ring-shape appearance and macroconidia of the fungus

Tinea cruris(سعفة الفخذ)

Tinea cruris is infection of the groin with a dermatophyte fungus. It is most often seen in adult men. Tinea cruris is commonly known as **jock itch**. *Trichophyton rubrum* and *Epidermophyton floccosum* are the most common causes. Symptoms of jock itch are mainly seen in the groin region, inner and upper thighs and on the male genitalia. Some of the symptoms of jock itch infection are: Red or pink ring shaped rash, Dry and roughened skin, Small blisters (formation).

Tinea of the groin and buttocks caused by *T. rubrum*

Tinea unguium(سعفة ألاظافر)

Onychomycosis a fungal infection of the nail, usually caused by a dermatophyte *Trichophyton rubrum* and *T. interdigitale*.

Tinea capitis(سعفة الرأس)

Is a fungal infection of the scalp, involving both the skin and hair. It is also known as scalp ringworm. Symptoms of Tinea capitis include hair loss, dry scaly areas , redness, and itch .Tinea capitis is caused by dermatophytic fungi capable of invading keratinized tissue, such as the hair and nails. *Trichophyton tonsurans* is an anthropophilic dermatophyte that is the most common cause of tinea capitis. Examples of other anthropophilic fungi that cause tinea capitis include: *T. soudanese*, *T. schoenleinii*, Microsporum. *audouinii*.

The infection occur following invasion of the keratinised stratum corneum of the scalp ,the fungus grows downwards into the hair follicle and the hair shaft. It penetrates the hair cuticle and typically invades the hair shaft in one of following ways:

-Ectothrix infection: the fungus grows within the hair follicle and covers the surface of the hair. Fungal spores are evident on the hair shaft and the cuticle is destroyed. *Microsporum . canis* is a cusal agent .

-Endothrix infection: The dermatophyte invades the hair shaft and grows inside the hair shaft, and the cuticle is not destroyed. *T. tonsurans* is an endothrix dermatophyte.

-Favus infection: a chronic dermatophyte infection caused by *T. schoenleinii* and characterized by clusters of hyphae at the base of the hairs, with air spaces in the hair shafts. Clinically there is yellow crusting around the hair shaft.

Ectothrix infection:

Endothrix infection:

Favus infection:

Tinea versicolor

Tinea versicolor (also called **pityriasis versicolor**) is a **common, harmless fungal skin condition**. It causes **patches of skin that are lighter or darker than the surrounding skin**, often on the **chest, back, neck, shoulders, or upper arms**.

- **The patches may:**
- Be white, pink, tan, or light brown
- Have fine scaling (dry, flaky skin)
- Sometimes itch slightly, especially when sweating

Tinea versicolor is caused by an **overgrowth of a yeast called** *Malassezia spp*
This yeast **normally lives on everyone's skin**, but under certain conditions it grows too much and affects skin color.

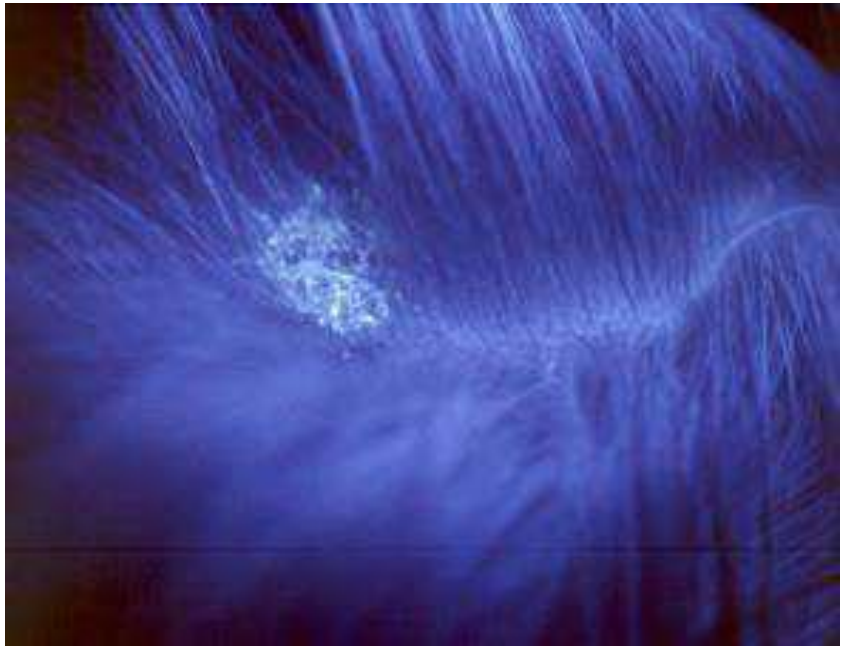
Tinea Versicolor Symptoms (النخالية المبرقشة)

Laboratory Diagnosis:

1-Direct Microscopy: Skin Scrapings, nail scrapings and epilated hairs should be examined using 10% KOH and Parker ink.

2-Culture: Specimens should be inoculated on to appropriate Media (Sabouraud's dextrose agar) containing **cycloheximide** (to inhibit bacterial growth)and incubated at 26-28˚C for 4 weeks. The growth of any dermatophyte is significant.

3-Wood lamp examination Wood lamp is diagnostic when hair fluorescence is seen, Bright green fluorescence of infected hairs is observed in tinea capitis caused by Microsporum species. A Wood lamp examination is a test that uses ultraviolet (UV) light to look at the skin closely.(**Microsporum** species show **bright green fluorescence under a Wood's lamp** because they produce **fluorescent metabolites called pteridines** during infection of hair.



Tinea capitis: Wood lamp fluorescence

MCQ

1-Dermatophytes infect which keratinized tissue?

a. Hair b. Skin c. Nails d. All of the above

2-**Which of the following genera does *not* belong to dermatophytes?**

a. Trichophyton b. Microsporum c. Epidermophyton d. Candida

3-**Which dermatophyte is most commonly associated with tinea pedis (athlete's foot)?**

a. Trichophyton rubrum b. *Microsporum canis* c. *Epidermophyton floccosum* d. *Trichophyton mentagrophytes*

4-**Ringworm" appearance in skin infections is mainly due to:**

a. Enzyme keratinase activity b. Immune reaction at the periphery c. Fungal pigment production d. Secondary bacterial infection

5-**Woods lamp fluorescence is positive in which dermatophyte infection?**

a. Trichophyton rubrum b. *Microsporum audouinii* c. *Epidermophyton floccosum* d. *Trichophyton tonsurans*

6-**The best initial diagnostic test for dermatophyte infection is:**

a. Blood culture b. KOH mount of skin scrapings c. PCR d. Chest X-ray

Fill in the blank

1-Dermatophytes are fungi that infect _____, _____, and _____ tissues.
2-The three main genera of dermatophytes are _____, _____, and _____.
3-Dermatophytes produce the enzyme _____ which allows them to digest keratin.
4-Infection of the scalp by dermatophytes is called Tinea _____.
5-Tinea pedis is commonly known as _____ _____.
4-The typical lesion of dermatophytosis is _____ shaped with central clearing.
5-Tinea cruris mainly affects the _____ region.
6-Dermatophytes are classified based on their natural habitat into _____, _____, and _____ types.
7-A common laboratory test used to diagnose dermatophytes is microscopic examination with _____ preparation.
8-Some species of Microsporum show fluorescence under _____ lamp.

Thank you for listening

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Medical Mycology

Lect-6- *Histoplasma* & Histoplasmosis

Prof.Dr. Mohammed A. Fayyadh

Histoplasmosis (Darling ‘s disease)

&- **Histoplasmosis** is the most common type of systemic fungal infection caused by *Histoplasma capsulatum* (classic or small form) and *Histoplasma duboissi* (African or large form).

&- ***Histoplasma capsulatum*** is a dimorphic fungus that grows as a mold in nature or on sabourauds agar at room temperature.

&- Hyphae bear both large and small spores, which are used for identification.

&-**Samuel Darling**, who discovered *H. capsulatum* in around 1900, so-named the organism because he mistook it for a capsulated animal parasite.

&-Since it is now known to be a non- capsulated saprophytic soil fungus, its present name is obviously inappropriate. Histoplasmosis, caused by *H. capsulatum*, shared many characteristics with **coccidioidomycosis.**

&- Both diseases extend over a spectrum from acute self-limited to chronic, granulomatous infection, and both are endemic in man. However, histoplasmosis occurs worldwide.

Clinical manifestations .

Histoplasmosis may be divided into the following types:

&-Primary pulmonary histoplasmosis

&-Progressive disseminated histoplasmosis

&-Primary cutaneous histoplasmosis

Source of infection

Histoplasmosis is acquired via inhalation of the infective fungal units from the environment; particularly soil enriched by dropping of certain **birds and bats** (that encourages the growth of *H. capsulatum*) that are deposited in the lungs.

Disease mechanism

- *H. capsulatum* grows in soil and material contaminated with bird or bat droppings.The fungus has been found in poultry house litter, caves, areas harboring bats, and in bird roosts (particularly those of starlings). The fungus is thermally dimorphic: in the environment it grows as a brownish mycelium, and at body temperature (37 °C in humans) it morphs into a yeast. Histoplasmosis is not contagious, but is contracted by inhalation of the spores from disturbed soil. The inoculum is represented principally by microconidia. These are inhaled and reach the alveoli. In the alveoli, macrophages ingest these microconidia. They survive inside the phagosome. As the fungus is thermally dimorphic, these microconidia are transformed into yeast. They grow and multiply inside the phagosome. The macrophages travel in lymphatic circulation and spread the disease to different organs.

Pathogenesis and clinical picture

&-Infection begins with small primary focus of lung infection much like the early lesions of tuberculosis.

&-The causative agents are ingested by alveolar macrophage in the lung.

&-These macrophages carry the fungi to nearby lymph nodes, usually the hilar nodes.

&- The fungi multiply within the node tissue and ultimately are released into a circulating blood, from which they go on to seed other organs or destroyed by the body defenses.

&-The initial lung infection is usually in apparent.

&-Clinical disease develops in some 5% of those infected.

&-The majority of the infections are either asymptomatic or mild, and the diagnosis is elusive cough fever, malaise, and chest X-ray findings of hilar adenopathy with or with out one or more areas of pneumonitis is typical features.

&-Chronic pulmonary histoplasmosis is characterized by a gradual onset (over weeks or months) of increasing productive cough, weight loss and some times night sweats.

&-Acute disseminated histoplasmosis may be mistaken milary tuberculosis.

&- Common findings include fever, hepatosplenomegaly, lymphadenopathy, Jaundice, anemia leukocytopenia and thrombocytopenia

&-In such individuals the infection may occur either as an acute disease, as a chronic cavitary disease or as a severe blood born disseminated disease

- Disseminated Histoplasmosis is commonly a generalized disease of the reticuloendothelial system that presents lesions in almost every organ of the body.
- It is rare, occurring mostly in individuals with patients of depressed cellular immune response (e.g. Patients with AIDS, T-cell defects, or lymphoma)
- In children younger than age one year who appear to have reticuloendothelial defect (fulminant disease of child hood).

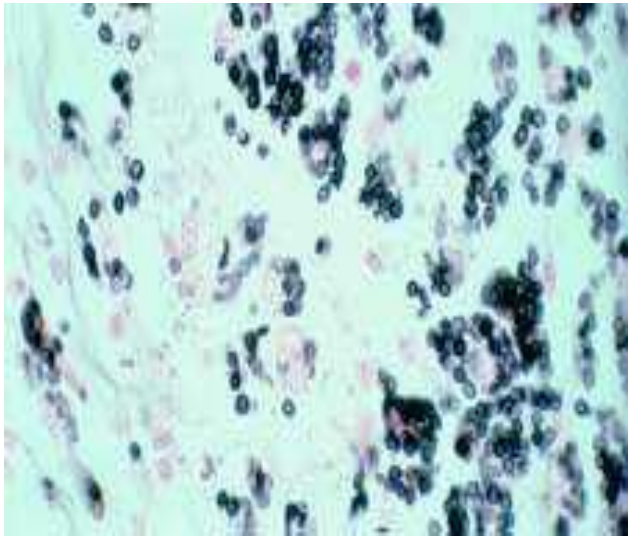
Laboratory diagnosis:

1-**Clinical material:** Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, bone marrow, urine and tissue biopsies from various visceral organs.

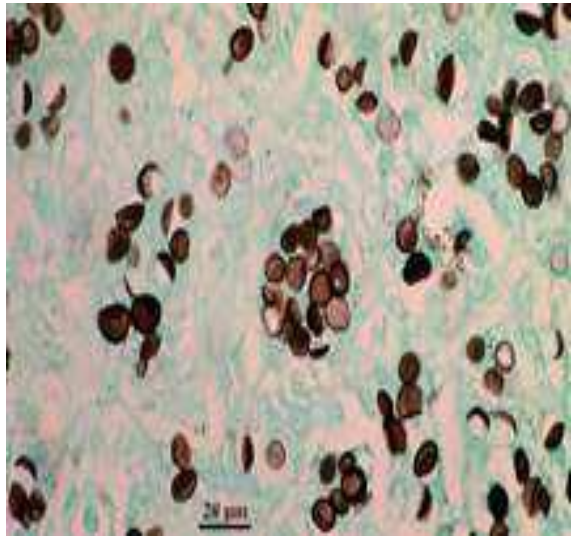
2-Direct Microscopy: (a) Skin scrapings should be examined using 10% KOH and Parker ink(Pi) or calcofluor white mounts(CWM); (b) Exudates and body fluids should be centrifuged and the sediment examined using either 10% KOH and (Pi)or (CWM), (c) Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

H. capsulatum (a)

H. duboisii (b)



b



a

3-Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood..

4 . **-Serology**: Immunodiffusion tests for the detection of antibody have proven to be useful in the diagnosis of Histoplasmosis.

Treatment . Typical treatment of severe disease first involves treatment with amphotericin B, followed by oral itraconazole.

Histoplasmosis: Cutaneous dissemination in a HIV-positive Female.

MCQ

1-The natural reservoir of *Histoplasma capsulatum* is associated with:

A. Soil contaminated with bird and bat droppings
B. Freshwater lakes C. Domestic animals D. Contaminated drinking water

2- **The usual route of infection in histoplasmosis is:**

A. Ingestion B. Skin penetration C. Inhalation of microconidia D. Blood transfusion

3- **In tissues, *Histoplasma capsulatum* appears as:**

A. Spherules with endospores B. Broad-based budding yeast C. Intracellular oval yeast within macrophages
D. Pseudohyphae with budding yeast

4- **Which population is MOST at risk for disseminated histoplasmosis?**

A. Healthy young adults B. Immunocompromised patients (e.g., AIDS) C. Pregnant women D. Children below 5 years

5- **A key laboratory finding in disseminated histoplasmosis is:**

A. Elevated eosinophils B. Decreased lymphocytes C. Pancytopenia D. Hypercalcemia

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Medical Mycology

Lect-10-Mycotoxin

Prof.Dr. Mohammed A. Fayyadh

Mycotoxicosis

The harmful effects of medicinal fungi are divided into two main categories:-

A- **-Mycoses are the diseases caused by fungi**

B--Mycotoxicosis : This term refers to the damage caused by toxic compounds**(Mycotoxins**) produced by fungi in the bodies of humans and other mammals when food contaminated with these compounds is consumed . The most important are **Aflatoxin** produced by *Aspergillus flavus.*

Mycotoxin

&- secondary metabolites produced by fungi. “Myco” means fungal (mold) and “toxin” represents poison .

&-They encompass a considerable variety of low molecular weight compounds with diverse chemical structures and biological activities.

Historical reports of Mycotoxins

&-Modern Mycotoxicology was not developed until the discovery of

Aflatoxins in the early 1960s as the causative agent in the peanut meal causing the **“Turkey X”** disease that killed more than 100,000 Turkeys fed with the contaminated meal.

&-Because Aflatoxins are a series of highly potent carcinogens produced by commonly occurring *Aspergillus flavus* and *A. parasiticus*, research has focused high attention on mycotoxins .

In the last 40 years, many new mycotoxins have been identified and characterized, and their biosynthetic origin in various fungi elucidated. It has been estimated that at least 25% of the world's agricultural product is contaminated with mycotoxins and certain diseases have been linked to ingestion of food contaminated with mycotoxins.

Classification of mycotoxins

Mycotoxins can be classified according to their action(site of action) in the human body in to :-

1-hepatotoxins: Aflatoxin

2-Nephrotoxins: Ochratoxins which is a potent nephrotoxin was first isolated from *Aspergillus ochraceous* in south Africa.

3-Reproductive system toxins: Zearalenon.

4-Muscular tissue toxins : Ergot alkaloids.

5- Teratotoxins and carcinogenic toxins: Sterigmatocystin, it's a precursor in the biosynthesis of aflatoxins.

6- Neurotoxin : Fumonisin B_1

Aflatoxins

&- At least 16 structurally related toxins in this group are produced by *Asparagillus flavus* and *A. parasiticus*.

&- Although **liver cancer** may be attributable to exposure to aflatoxin in parts in Africa ,the formation of an **epoxide** could well be key to both **acute and chronic** toxicity and those animals and human which fail to produce it are relatively **resistant** to both.

&- the epoxide will react with DNA and then react with the protein and cause sever toxicity.

&- Several studies have demonstrated that very young children may be exposed to aflatoxins even before they are weaned because mothers consuming aflatoxin in their food may secret aflatoxin M1 in their milk .

*Aflatoxin family include the following types (AFB1 ; AFB2 ; AfG1 ; AFG2 ; AFM1 ; AFM2)

*Aflatoxins are mutagenic, teratogenic, and hepatocarcinogenic.

* Aflatoxin B1 is one of the most potent naturally occurring carcinogen, extensive research was primarily done on this toxin. The main target organ of AF is the liver.

* AFB1 also affects other organs and tissues including the lungs and the entire respiratory system.

Ochratoxin A

&-Ochratoxin A,(Produced by Aspergillus and Penicillium genera.) the most toxic member of this group of mycotoxins, has been found to be a potent nephrotoxin causing kidney damage as well as liver necrosis and enteritis in human (a debilitating disease in man known as Belkan endemic nephropathy) and many animal species.

&-Formation of free radicals has been considered as one of the mechanisms for the carcinogenic/toxic effects of OA.

&-Exposure to the mycotoxin ochratoxin A (OTA) causes nephropathy .Humans are exposed to OTA by consuming foods made with contaminated cereal grains and other commodities.

Fumonisins

&-Fumonisins (Fm) are a group of toxic metabolites produced primarily by *Fusarium verticillioides*, *F. proliferatum* and other related species readily colonize corn all over the world.

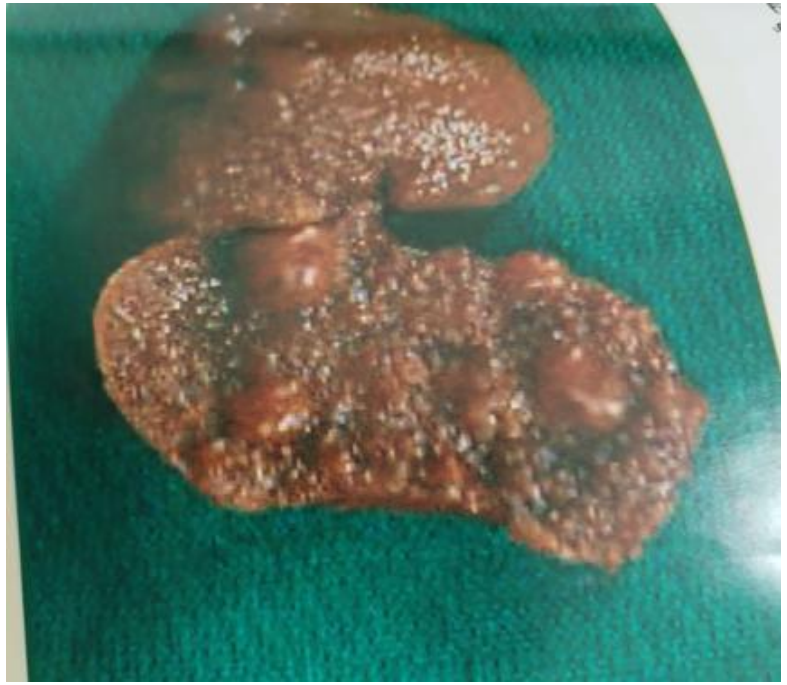
&-Fumonisins was Neurotoxin and associated with human esophageal cancer specially in south Africa .

Trichothecenes

&-Several species of Fusarium produce a variety of mycotoxins. The most important are Trichothecenes.

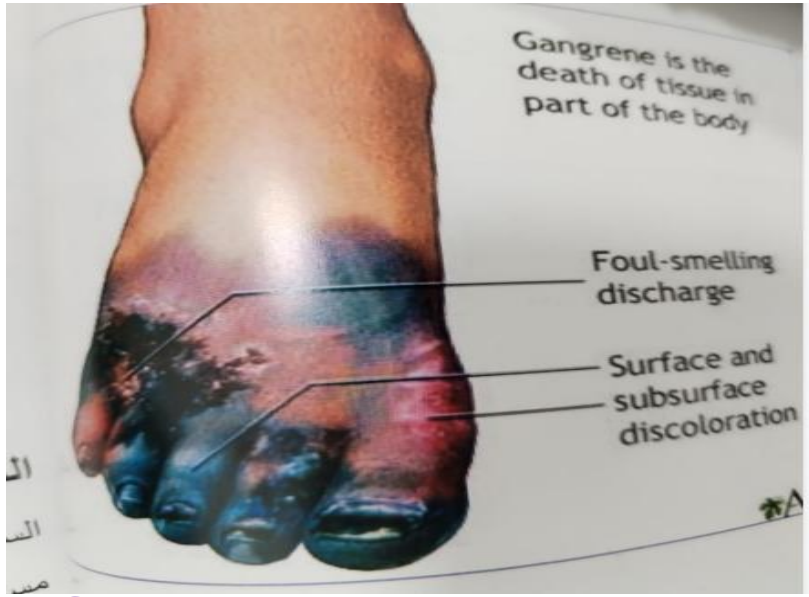
&-Trichothecenes produced by *Fusarium graminearum* and *F. culmorum*

&-Trichothecenes causes feed refusal and emesis.



Liver Cancer

Liver Cancer Symptoms



Gangrene

Brain damage

Thanks for your attention

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Medical Mycology

Lect-5-Systemic infection

Prof.Dr. Mohammed A. Fayyadh

Systemic mycoses

Introduction

- Systemic mycoses are fungal diseases that may affect internal organs and may disseminate to multiple sites of the body
- some times known as deep mycoses.
- Some times known as **Dimorphic Systemic Mycoses**
- They are difficult to eradicate and many patients with deep mycoses die in spite of extensive medical care especially when the central nervous system is involved.

Dimorphic Systemic Mycoses: These are fungal infections of the body caused by fungal pathogens which can overcome the physiological and cellular defenses of the normal human host by changing their morphological form. The primary site of infection is usually pulmonary, following the inhalation of conidia.

- **Systemic mycoses occur in three disease forms:**
  - **acute self limited pulmonary (asymptomatic to severe)**
  - **chronic (pulmonary or disseminated)**
  - **disseminated.**

The systemic fungi include :

- *Blastomyces dermatitidis* (blastomycosis).
- *Coccidioides immitis* (coccidioidomycosis).
- *Histoplasma capsulatum* (Histoplasmosis).
- *Paracoccidioides brasiliensis* (paracoccidioidomycosis).
- *Cryptococcus neoformans* (Cryptococcosis)

Coccidioidomycosis (Desert fever, valley fever, San Joaquin fever)

Definition

&- Coccidioidomycosisis, which is caused by *Coccidioides immitis* is also referred to as valleys fever , desert rheumatism or San Joaquin fever because of the geographic distribution of *C. immitis* and the associated area of occurrence of this disease.

&- It is seen often in the San Joaquin valley of California that it has gained the common name of “valley fever or San Joaquin Fever”.

Pathogenesis

Source of infection:

&-The infective fungal spore is found in the soil.

&-Patients with a history of exposure to soil acquire the disease by inhalation of wind borne arthrospores from dust generated when contaminated soil is agitated.

&-The infection may disseminate to different parts of the body, including bones, viscera, and the CNS(Central Nerve System)

&-however, the gastrointestinal tract is remarkably resistant to infection

&-The acute and most common forms of the disease resemble influenza.

&-Approximately 60% of the cases remain asymptomatic and self-limiting.

Disease Symptoms

&- The initial symptoms of pulmonary infection consist of cough, fever, and malaise.

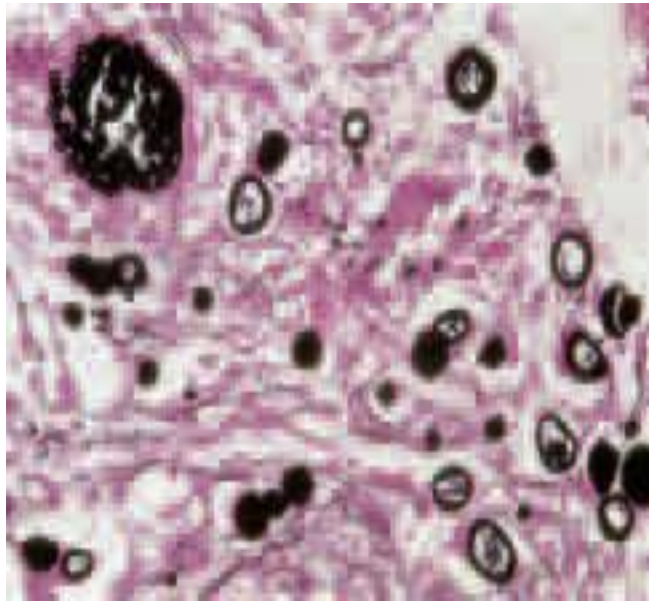
&- One to two weeks later, about 3 to 5% of patients develop complications attributable to a hypersensitivity reaction, the most frequent being skin lesions (erythema) or joint symptoms (desert rheumatism).

&- Chronic pulmonary Coccidiodomycosis cause cough, sputum production, variable degree of fever, and weight loss .

chlamydospore

Arthroconidia of Coccidioides

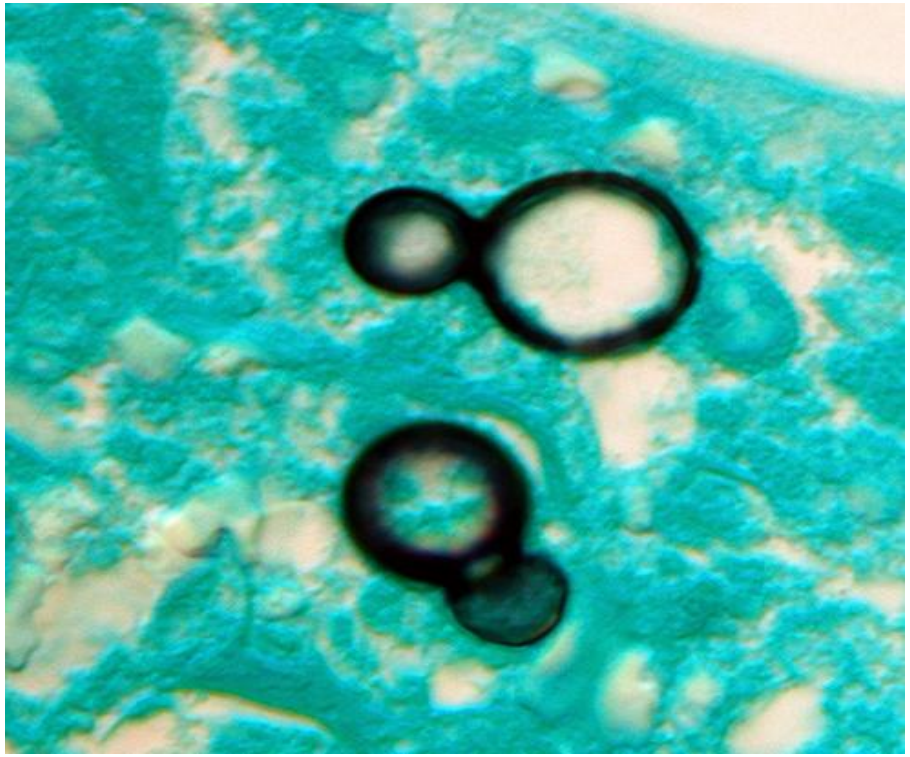
Coccidioides immitis colony



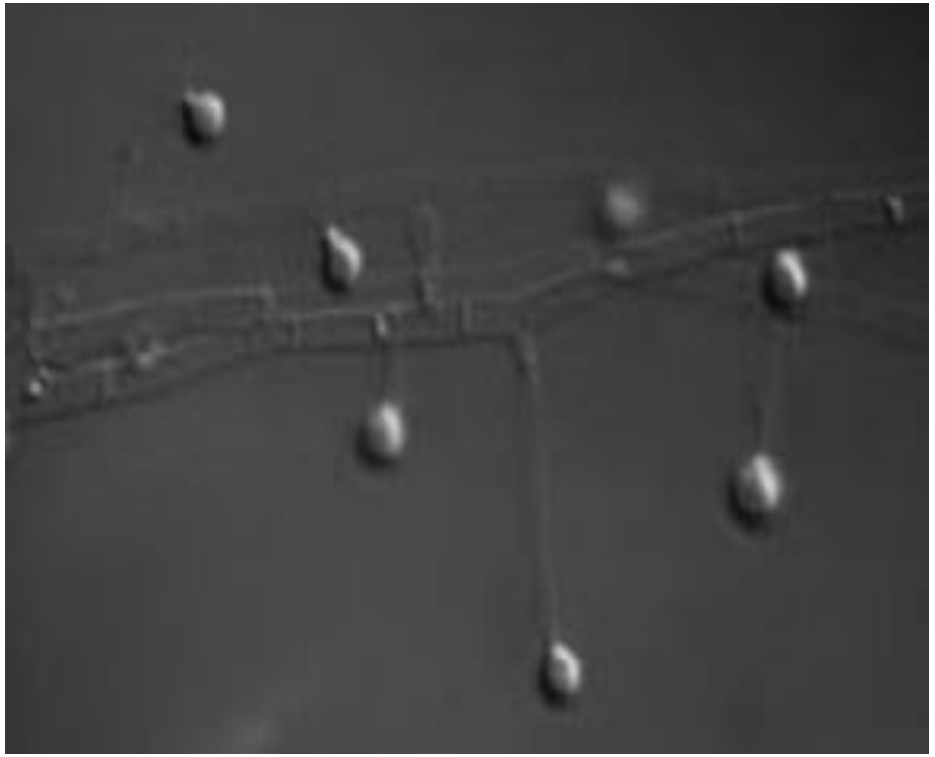
Coccidioidomycosis tissue section. Spherules of various sizes are stained black with GMS.

Blastomycosis

Blastomycosis is a severe systemic fungal disease due to *Blastomyces dermatitidis*, a spore-forming dimorphic saprophytic fungus that thrives in humid and acidic soil rich in decaying plant or animal waste ,organism grows as a mold in the environment and becomes yeast in host tissues .The fungus is a primary pulmonary pathogen in humans and outdoor or hunting dogs and can sporadically affect cats.



Blastomyces dermatitidis in a GMS-stained biopsy section from a human leg



***Blastomyces dermatitidis* — conidia found in the mold form**

Cryptococcus neoformans

-Most frequent cause of fungal meningitis in immunocompromised individuals (especially AIDS).

-Found in pigeon droppings(فضلات الحمام); infection occurs via inhalation.

Histoplasmosis (Darling ‘s disease)

&- **Histoplasmosis** is the most common type of systemic fungal infection caused by *Histoplasma capsulatum* (classic or small form) and *Histoplasma duboisii* (African or large form).

&- ***Histoplasma capsulatum*** is a dimorphic fungus that grows as a mold in nature or on sabourauds agar at room temperature.

&- Hyphae bear both large and small spores, which are used for identification.

&-**Samuel Darling**, who discovered *H. capsulatum* in around 1900, so-named the organism because he mistook it for a capsulated animal parasite.

Clinical manifestations

Histoplasmosis may be divided into the following types:

&-Primary pulmonary histoplasmosis

&-Progressive disseminated histoplasmosis

&-Primary cutaneous histoplasmosis

Source of infection

Histoplasmosis is acquired via inhalation of the infective fungal units from the environment; particularly soil enriched by dropping of certain **birds and bats** (that encourages the growth of *H. capsulatum*) that are deposited in the lungs.

Pathogenesis and clinical picture

&-Infection begins with small primary focus of lung infection much like the early lesions of tuberculosis.

&-The causative agents are ingested by alveolar macrophage in the lung.

&-These macrophages carry the fungi to nearby lymph nodes, usually the hilar nodes.(سرة الرئتين)

&- The fungi multiply within the node tissue and ultimately are released into a circulating blood, from which they go to other organs of the body.

&-Chronic pulmonary histoplasmosis is characterized by a gradual onset (weeks or months) of increasing cough, weight loss and some times night sweats.

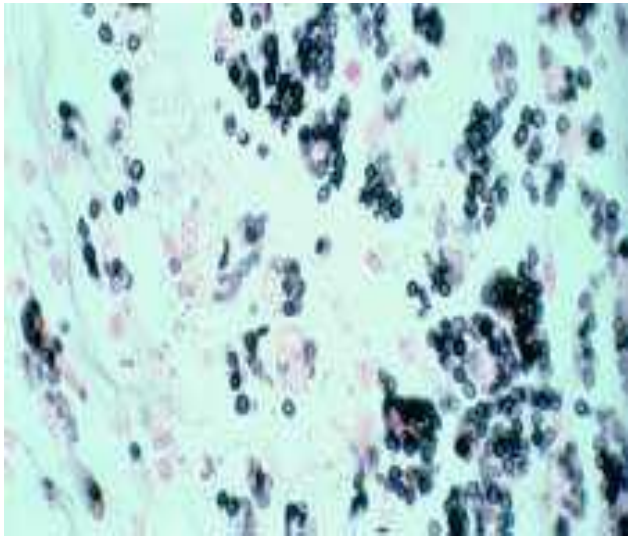
Laboratory diagnosis:

1-**Clinical material:** Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, *etal* .

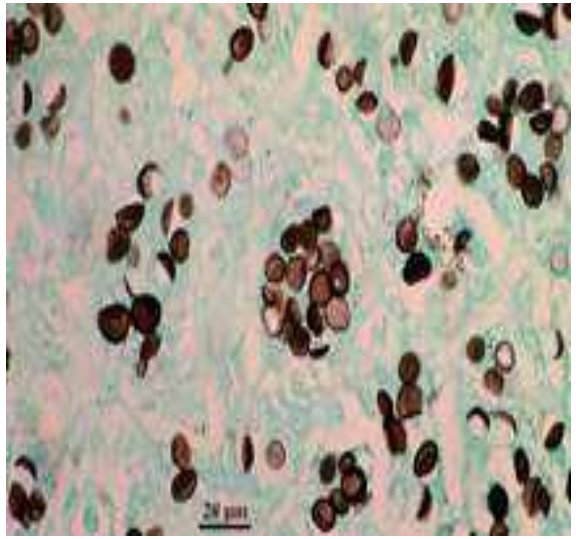
2-Direct Microscopy: (a) Skin scrapings examined with 10% KOH and Parker ink(Pi) or Calcofluor white mounts(CWM); (b) Exudates and body fluids should be centrifuged and the sediment examined using either 10% KOH and (Pi)or (CWM).

H. capsulatum (a)

H. duboisii (b)



b



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Treatment

Treatment .

Typical treatment of severe disease first involves treatment with amphotericin B, followed by oral itraconazole.

Histoplasmosis: Cutaneous dissemination in a HIV-positive Female. (Human Immunodeficiency Virus)

MCQ

1-Which fungus is the causative agent of histoplasmosis?

A. *Coccidioides immitis* B. *Histoplasma capsulatum*
C. *Blastomyces dermatitidis* D. *Paracoccidioides brasiliensis*

2-**The natural reservoir for *Histoplasma capsulatum* is commonly associated with:**

A. Bat and bird droppings B. Soil rich in keratin
C. Air-conditioning systems D. Contaminated water

3-**Which of the following fungi causes "desert rheumatism"?**

A. *Coccidioides immitis* B. *Cryptococcus neoformans*
C. *Candida albicans* D. *Aspergillus fumigatus*

4-**Which systemic fungal infection commonly causes meningitis in AIDS patients?**

A. Blastomycosis B. Coccidioidomycosis C. Cryptococcosis D. Sporotrichosi

5-***Coccidioides immitis* forms which of the following structures in tissue?**

A. Spherules containing endospores B. Arthroconidia C. Hyaline hyphae D. Pseudohyphae

6- **Which systemic fungal infection commonly causes meningitis in AIDS patients?**

A. Blastomycosis B. Coccidioidomycosis C. Cryptococcosis D. Sporotrichosis

7-The natural reservoir of *Histoplasma capsulatum* is associated with:

A. Soil contaminated with bird and bat droppings
B. Freshwater lakes C. Domestic animals D. Contaminated drinking water

8- **The usual route of infection in histoplasmosis is:**

A. Ingestion B. Skin penetration C. Inhalation of microconidia D. Blood transfusion

9- **In tissues, *Histoplasma capsulatum* appears as:**

A. Spherules with endospores B. Broad-based budding yeast C. Intracellular oval yeast within macrophages
D. Pseudohyphae with budding yeast

10- **Which population is MOST at risk for disseminated histoplasmosis?**

A. Healthy young adults B. Immunocompromised patients (e.g., AIDS) C. Pregnant women D. Children below 5 years

11- **A key laboratory finding in disseminated histoplasmosis is:**

A. Elevated eosinophils B. Decreased lymphocytes C. Pancytopenia D. Hypercalcemia

Thank You For Your Attention

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Medical Mycology

Lect-2-Types of Mycoses

Prof.Dr. Mohammed A. Fayyadh

Types of fungal infections(Mycoses)

1. Superficial mycoses:

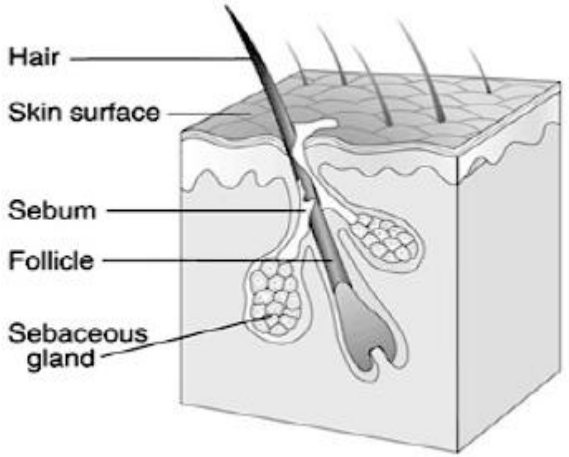
- Fungi causes infection of

outer surface of hair shafts , skin and nails.

- They are very rare

- E.g. Black Piedra (piedraia)

by the fungus *Piedraia hortae*



2. Cutaneous mycoses

- Also called dermatomycoses, ringworms, or tineas (القوباء الحلقية أو السعفة)
- most common fungal infections
- Infection occurs on the epidermal layer of skin and hair roots
- Three important genera **Epidermophyton , Microsporum , and Trichophyton**
- E.g. Tinea pedis (سعفة القدم)

3. Subcutaneous mycoses

- Cause infection of the subcutaneous layer of skin
- **Most are** Saprophytic species .
- unable to penetrate the skin, they enter tissue by a puncture contaminated with soil
- Nodules become ulcerated and protrude out containing drainage
- E.g. Chromoblastomycosis
- Mycetoma

4- Systemic infection

- Inhalation of fungal spores
(wind dispersed soil borne spores)
» lesion formation in lungs
» bursting of lesion » diffusion in blood
- Species are dimorphic i.e.
exist in 2 forms of parasitic
and saprophytic both
- E.g. Blastomycosis &
Coccidiodomycosis

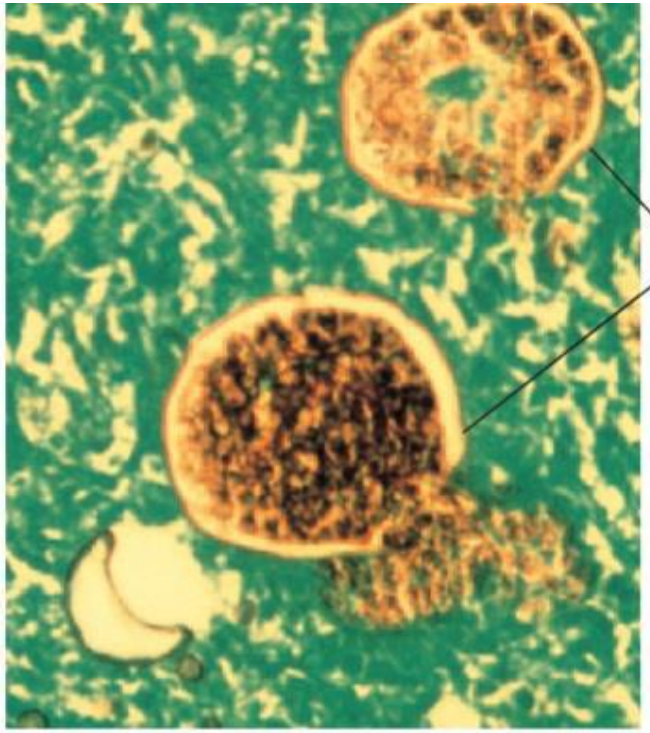


Figure 40.12 Systemic Mycosis: Coccidioidomycosis.
Coccidioides immitis mature spherules filled with endospores within a tissue section; light micrograph (×400).

1. Superficial mycoses:

- Superficial mycoses are usually confined to the dead outer layers of skin and it appendages (hair, feathers, horn, hooves, claws, nails) (الشعر،الريش، القرون، الحوافر،المخالب والاظافر)and do not invade living viable tissues.
- Dermatophytes, or more properly, keratinophilic fungi , produce extracellular enzymes **(keratinases)** which are capable of digesting keratin.
- Keratin is the primary structural protein of skin, nails ,feather , claw, horn ,hooves and hair. The digestion of keratin manifests as scaling of the skin, loss of hair, and crumbling of the skin.

Types of Superficial mycoses

Black and white Piedra

Piedra, meaning stone in Spanish, is limited to the hair shaft without involvement of the adjacent skin. Two varieties of piedra may be seen: black piedra and white piedra.

Etiology(causal agent):

The causative organism of black and white piedra are;-

Black Piedra

1- *Piedraia hortae*

White Piedra

1- *Trichosporon ovoides* **2-** ***T.*** *inkin* **3-** ***T.*** *asahii*

Epidemiology:

Black piedra occurs frequently in humid, wet tropical areas and is common in certain tropical areas of central South America and Southeast Asia, whereas white piedra occurs in semitropical and temperate countries(white piedra have a worldwide distribution). *P hortae* has been found on the hairs of animals, stagnant water, soil, and vegetables. *It has been suggested that for some native populations, black piedra may have cosmetic importance.*

The natural habitats of Trichosporon species(White piedra) are soil, lake water, and plants, and such fungi are occasionally seen as normal flora of the human skin and mouth.

White piedra has been found on animal hairs, including monkeys, horses, and lower mammals . Infection with piedra does not seem related to personal hygiene or exposure to an infected person.

Clinical manifestation

Black piedra is a condition that presents as **a stone-hard black** nodule on the scalp, beard, moustache, and pubic hair shaft. Brown-black hard nodules along the hair shaft characterize black piedra, with the fungal activity limited to the cuticle and with no penetration of the hair shaft. ***Black piedra*** *is more frequent and less sporadic(*consistently*) than white piedra*.

White piedra is characterized by **white-to-tan nodules** along the shafts of hair in the scalp, beard, eyebrows, eyelashes, and groin, genital and perigenital area. Numerous discrete, soft nodules that are barely visible to the naked eye are attached to the hair shaft, and produce a gritty sensation when palpated.

The nodules may be detached easily, and the affected hairs may be split or broken . *Trichosporon asahii* and *T. inkin* can behave as opportunistic pathogens, particularly in **immunosuppressed patients**, where they can cause serious and life-threatening symptoms .

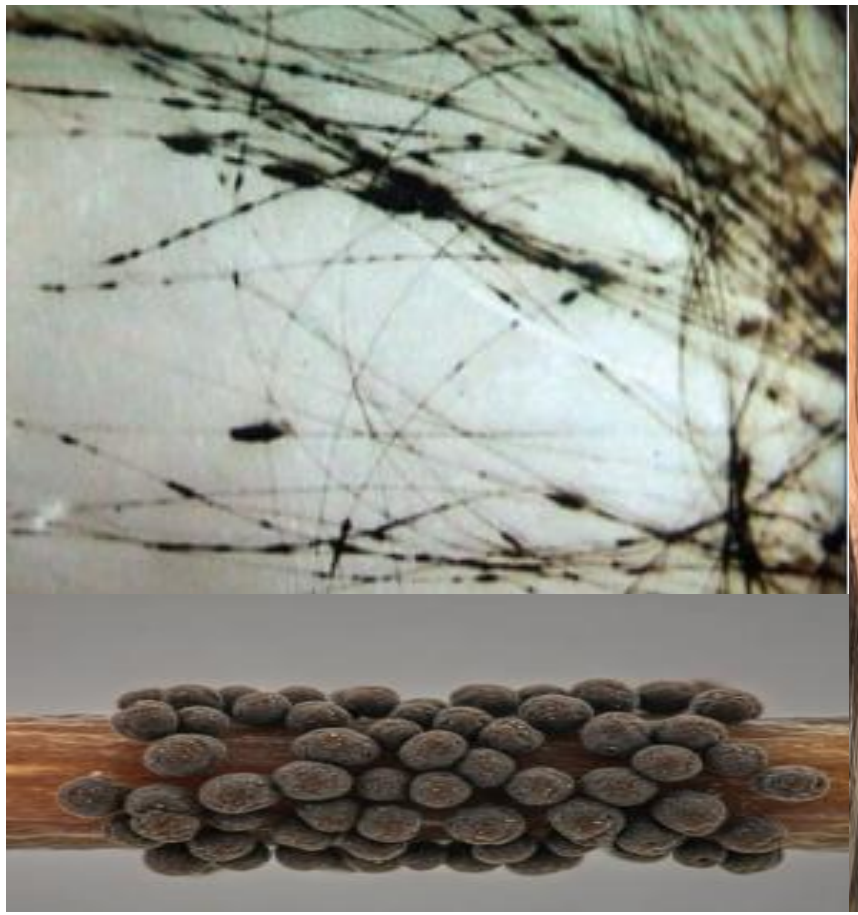
Clinically, many hair disorders can be confused with piedra . White and black piedra should be distinguished from each other and, hair casts, developmental defects of the hair shaft, and Trichomycosis axillaris. Infections can co-exist with dermatophyte or Candida infections, and erythrasma . White piedra should be differentiated from pediculosis.

Diagnosis and laboratory findings:

Infection with *Piedraia hortae* (**black piedra**) reveals tightly packed, darkly pigmented hyphae, *asci, and ascospores* attached to the hair shaft, whereas infection with Trichosporon species (**white piedra**) shows loosely arranged hyphae, *blastoconidia, and arthroconidia* attached to the hair shaft. Fungal cultures are performed on **Sabouraud's dextrose agar.** Some Trichosporon species involved in white piedra (eg, *T ovoides*) are inhibited by **cycloheximide**, which is found in dermatophyte test medium, **Mycosel, and Mycobiotic**.

Treatment

Shaving or clipping the infected hair is the treatment of choice for both types of piedra; however, this method may not be esthetically pleasing to all patients, especially women. Antifungal therapy may be initiated in conjunction with shaving. Black piedra may be treated with oral terbinafine. Effective therapies against white piedra **include imidazole's, ciclopirox olamine, 2% selenium sulfide, 6% precipitated sulfur in petrolatum, chlorhexidine solution, and zinc pyrithione.**



Black Piedra

White piedra

MCQ

1-**Which of the following is an example of a superficial mycosis?**

a. Dermatophytosis b. Tinea versicolor c. Histoplasmosis d. Aspergillosis

2-Dermatophytes typically cause which type of mycosis?

a. Systemic b. Subcutaneous c. Cutaneous d. Opportunistic

3-**Which of the following is considered a systemic (endemic) mycosis?**

a. Mycetoma b. Candidiasis c. Coccidioidomycosis d. Piedra

4-**Pityriasis versicolor is caused by *Malassezia* species and is classified as:**

a. Subcutaneous mycosis b. Cutaneous mycosis c. Superficial mycosis d. Opportunistic mycosis

5-**Mycetoma (Madura foot) is an example of which type of mycosis?**

a. Opportunistic b. Subcutaneous c. Superficial d. Systemic

6-**Black piedra affects which part of the body?**

a. Skin b. Nails c. Hair shaft d. Lungs

Home Work :-

What is the differences between White Piedra , erythrasma and pediculosis

Thanks for your attention

Shatt Al -Arab University

Faculty of science

Department of Pathological analysis science.

Medical Mycology

Lect-7- Opportunistic Mycoses

Prof.Dr. Mohammed A. Fayyadh

Objective

- Describe different cause of opportunistic Mycoses
- Explain the clinical manifestation of different opportunistic mycoses.
- Describe the different laboratory tests used to diagnose each opportunistic mycosis .

Introduction

- **The opportunistic mycoses**

+The opportunistic fungi usually cause infections in persons with impaired host defense, but do not cause disease in most of the immunocompetent hosts.

+The opportunistic mycoses can be fetal in people whose resistance has been lowered (immunocompromised patients).

* The highly susceptible groups for opportunistic fungal infection are

#-**AIDs patients,** #- **patients with leukemia**

#-**individuals on chemotherapy for treatment of cancer.** #- **alcoholics.**

Introduction cont'd…

- Many diabetic peoples are also susceptible to pulmonary infection by common saprophytic mold of genera *Rhizopus* and *mucor* (both Zygomycetes) and *Aspergillus* .
- Unless the predisposing conditions are corrected, many opportunistic mycosis can be fetal, even with antibiotic treatment.

- Many fungi previously considered non- pathogenic are now recognized as etiological agents of the opportunistic fungal infections.
- The laboratory must identify and report completely the presence of all fungi recovered from immunocompromised patient, since every organism is a potential pathogen.

- Although there is an ongoing list of opportunistic mycosis, some are seen more often and includes :

&- Candidiasis &- Cryptococcosis, &- Aspargillosis,

&-Zygomycosis &- Trichosporonosis

Candidiasis

Candidiasis is a fungal infection which is caused by a type of fungus called Candida. **Candida** is a type of yeast that lives in our mouth, throat, gut or vagina (incase of women), or on the skin. There are many species of the fungus candida causes of fungal infection.: *Candida albicans, Candida glabrata, Candida tropicalis, Candida parapsilosis*, but *Candida albicans* are the most that usually cause the infections.

Who is at increased risk?

- **Babies with a nappy rash**
- **People with a metabolic disorder (diabet….)**
- **Overweight people**
- **Pregnant woman, high dose contraceptive**
- **People who work in wet conditions**
- **Immunodeficiency (AIDS……)**

Clinical manifestations:

1- Oropharyngeal candidiasis: including thrush, glossitis, stomatitis and angular Cheilitis.

Oral candidiasis is the most common oral fungal infection. Oral candidiasis is considered an opportunistic infection, occurring more frequently in persons with impaired immunity. In thrush, white or yellow patches appear on the tongue, gums, lips, inner cheeks, and roof of the mouth. There is also redness and soreness in the mouth and throat. If the infection spreads to the throat, then there may be pain in swallowing too.

Symptoms of **Oral candidiasis**

2-**Cutaneous candidiasis: including intertrigo, diaper candidiasis, paronychia , onychomycosis and Vulvovaginal .**

- Candidiasis skin infection. is a common infection of the moist areas of the body, Candidiasis causes an itchy red rash Irritation Pain, Blisters Cracked skin those who have a compromised immune system are at an increased risk of developing a severe infection. candidiasis is most commonly seen in the axillae, groin, inter- and sub-mammary folds, interdigital spaces, and umbilicus. Moisture, heat, friction and maceration of the skin are the principle predisposing factors in the normal patient. Vaginal area can be effected with candida .

Symptoms of **intertrigo and paronychia candidiasis**

Lab diagnostic of candida

Ask some question !

- Occupation (work in wet condition)
- Age
- Underlying disease (metabolic disorder , immunodeficiency , vitamin deficiency .
- High dose broad spectrum antibiotics , corticosteroids chemotherapy.

Attention to the symptom

- **purple patches** on the skin like eczema
- **Itchy**, the itching in these patches is highest near the edge
- A small degree of **scalling**
- **Blister** resembling spots are often seen around the itchy patches

Patient preparation

&-3 days no washing prior sampling

&- No bacterial or fungal treatment during 7 days

&-Any ointments or other local applications present should first be removed with an alcohol wipe.

Sampling device

bone
curette

Sampling

* If **multiple lesions** are present **choose the most recent for scrapings** as old loose scale is often not satisfactory.

* The tops of any fresh vesicles should be removed as the **fungus is often plentiful in the roof of the vesicle**.

* **scrap the lesions with a bone curette or blunt scalpel** as for tinea .

* **scaly border should be scraped.**

NOTE: Following the collection of skin scales all scraped lesions should be firmly rubbed with a swab moistened in BHI broth.(Brain Heart Infusion broth)

Laboratory diagnosis of cutaneous candidiasis (direct exam & culture)

1 – direct exam

A. Skin scrapings:

- **Make a wet mount preparation in KOH 10% for direct microscopy**.
- Note a Calcofluor stained mount may also be necessary.

B. Skin swabs:

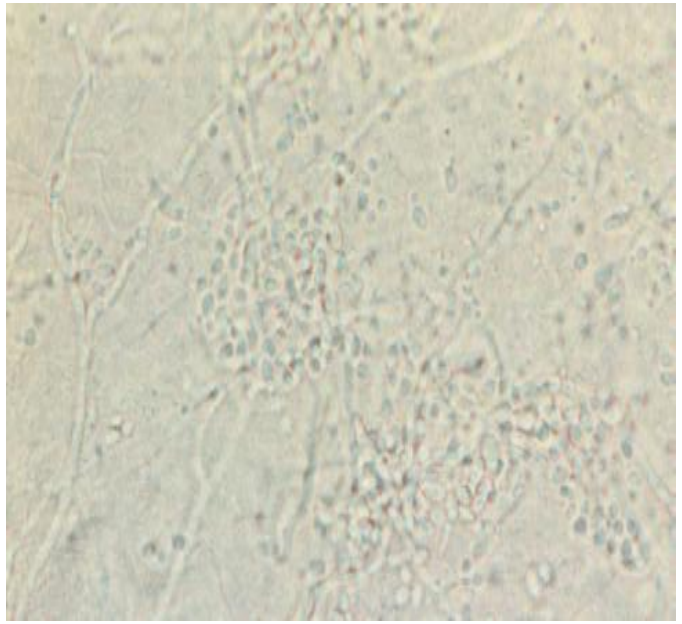
- **Smear swab onto heat sterilized glass slide for Gram stain**

2- Culture

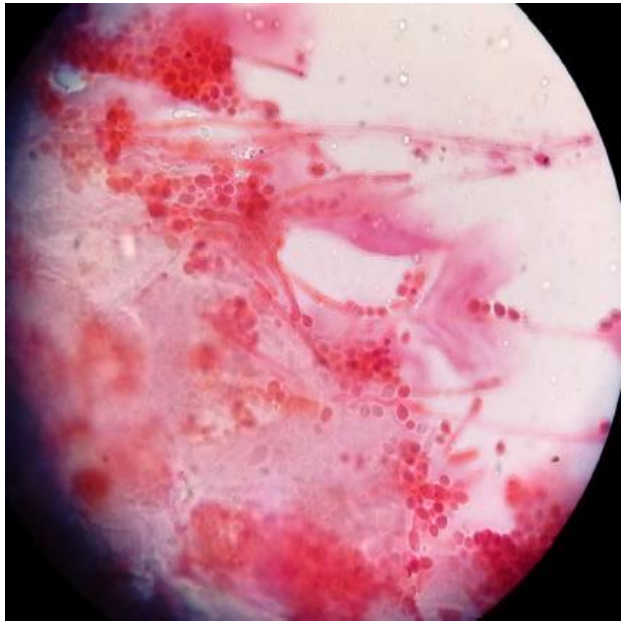
- **Sabouraud's dextrose agar** slopes containing **chloramphenicol and gentamicin**, but NO cycloheximide
- **Candida chrome agar**

3. incubate at 35C. Maintain cultures for 4 weeks

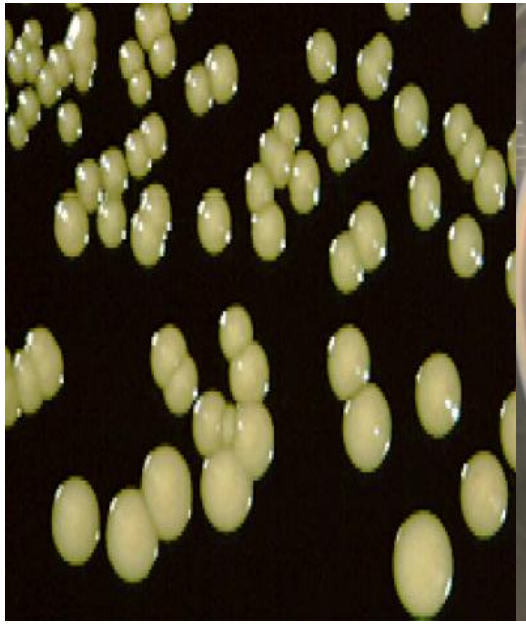
Sabouraud's dextrose agar



Candidiasis
(KOH 10% mount)



Gram staining

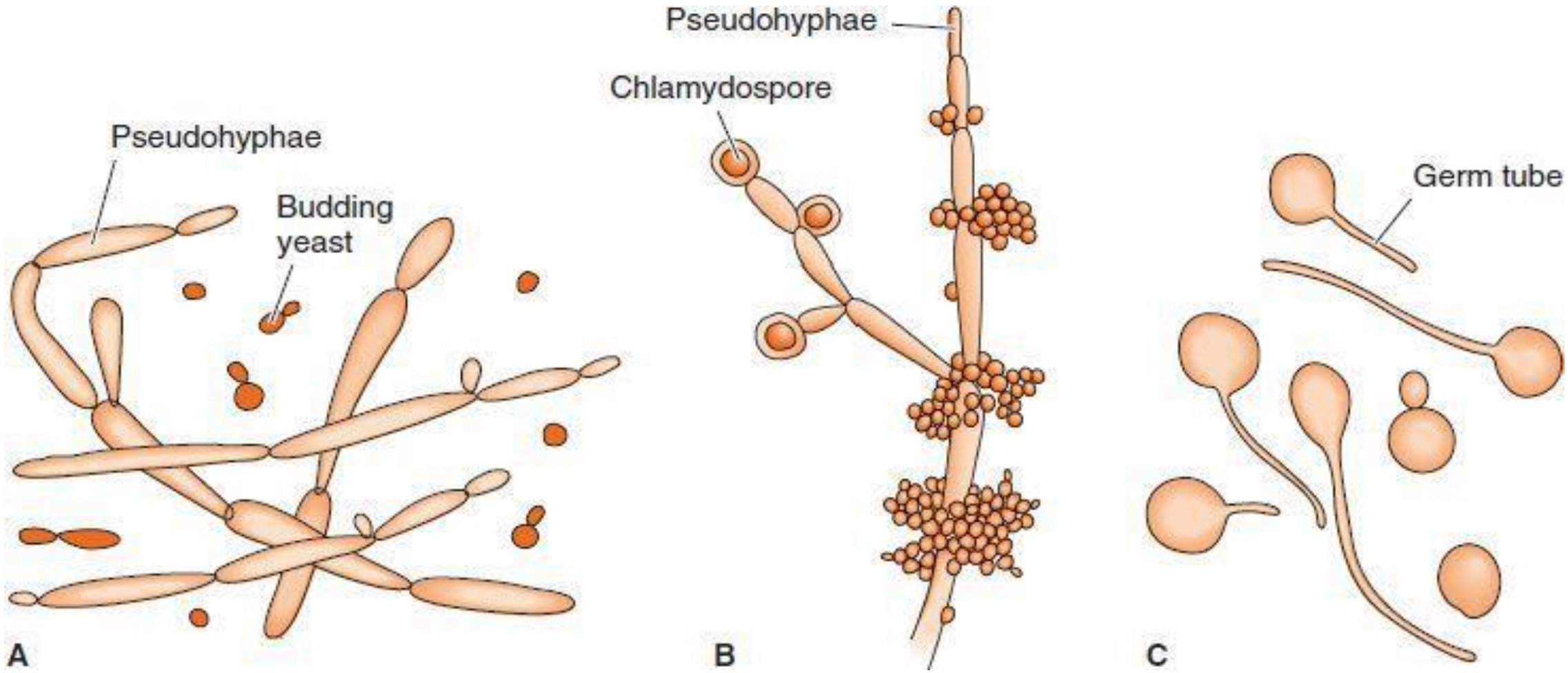


Sabouraud's dextrose agar

Candida chrome agar

Properties of **Candida albicans**

- *C. albicans* is ovoid or spherical yeast with a single bud.
- It is part of the normal flora of the mucous membrane of the gastrointestinal, genitourinary, and respiratory tract. It produces pseudohyphae in the cultures and in tissues. *Candida* grows readily on Sabouraud's dextrose agar produces creamy white, smooth colonies with a yeasty odor .
- It can be differentiated from other *Candida* species by carbohydrate fermentation reaction and by characteristic growth properties.
- Only *C. albicans* produces chlamydospores on cornmeal agar culture at 25°C.


Pseudohyphae
Budding yeast
A
Pseudohyphae
Chlamydospore
B
Germ tube
C

Thank you for your attention

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Faculty of science

Department of Pathological analysis science.

Medical Mycology

Lect-1-Introduction to Medical mycology

Prof.Dr. Mohammed A. Fayyadh

Medical Mycology

MYCOLOGY=

Myco = mykes (mushroom)-fungi

-logy = the study of--

Is the study of fungi, includes their genetic and biochemical properties, their taxonomy, and their use to humans as source for medicinal (e.g., penicillin), food (e.g., beer, wine, cheese, mushrooms …), as well as their dangers, such as poisoning or infection.

Medical mycology is a special of medical microbiology concerned with all aspects of diseases in humans and domestic animals caused by pathogenic fungi. **Mycoses** are diseases of humans and animals caused by pathogenic fungi.

What is Fungi

a- Eukaryotic cells contain membrane bound cell organelles including nuclei, mitochondria, Golgi apparatus, endoplasmic reticulum, lysosomes etc.

b- Heterotrophic - fungi lack chlorophyll and are therefore not autotrophic (photosynthetic) like plants and algae; rather they are heterotrophic absorptive organisms that are either saprophytes (living on dead organic matter) or parasites (utilizing living tissue).

c- Contains rigid cell walls(Chitin &glucan) and are therefore non-motile, a feature which separates them from animals.

Morphology of Fungi

1. Filamentous fungi (molds)

2. Yeasts

3. Yeast-like fungi

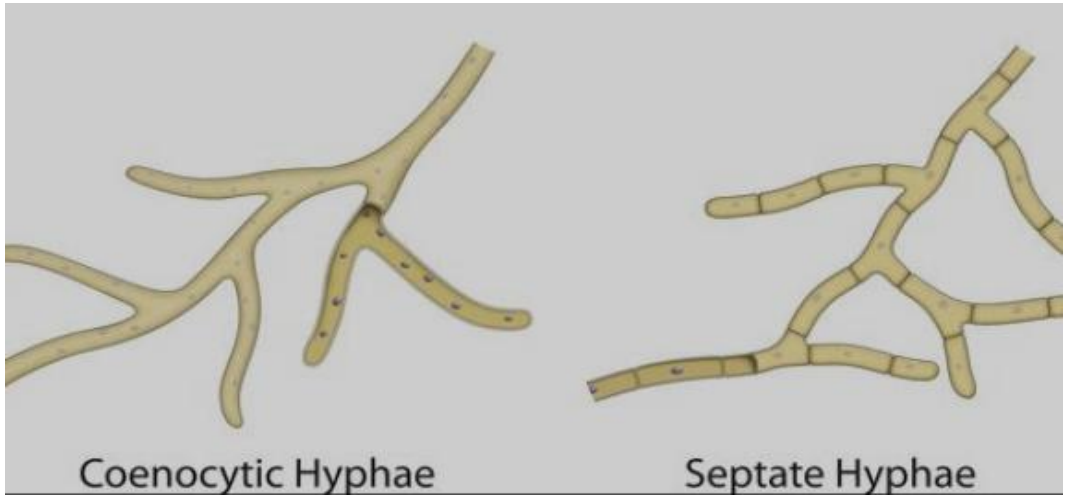
4. Dimorphic fungi

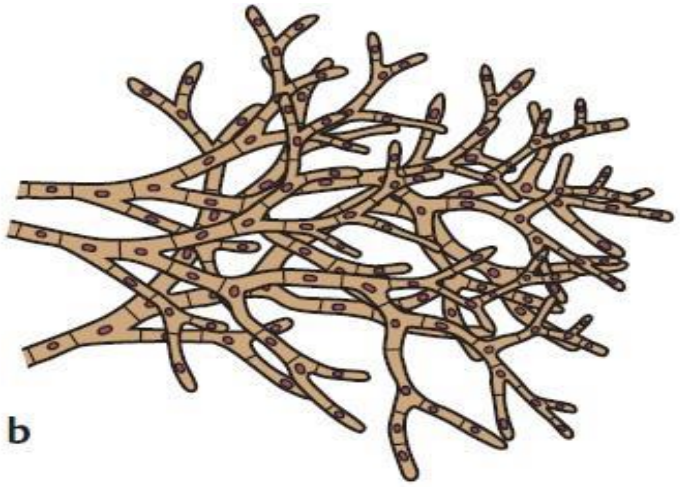
a

(a) A filamentous or mold form which is a vegetative growth of

Filaments fungi. consist simply of a number of filaments packed tightly together , and reproduction is by spores or conidia. Fungal filaments are known as **hyphae** and a mass of hyphae collectively make up the **mycelium**. There are two kinds of hyphae; non-septate (coenocytic) and septate.

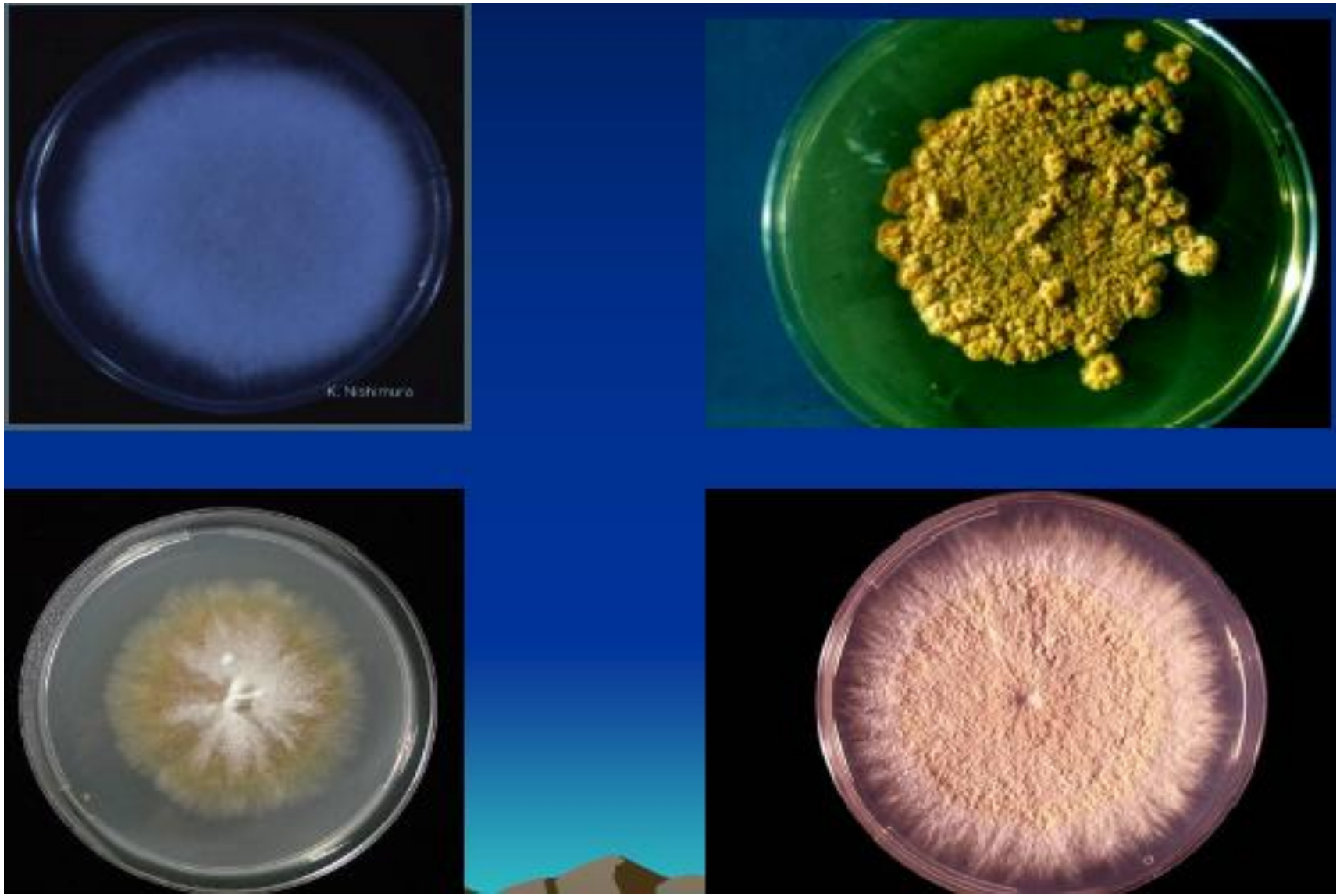
a





Colonies of fungi are strongly adherent to the medium and unlike most bacterial colonies cannot be emulsified in water. The surface of these colonies may be velvety, powdery, or may show a cottony aerial mycelium. And Pigmentation of the colony itself and of the underlying medium is frequently present.

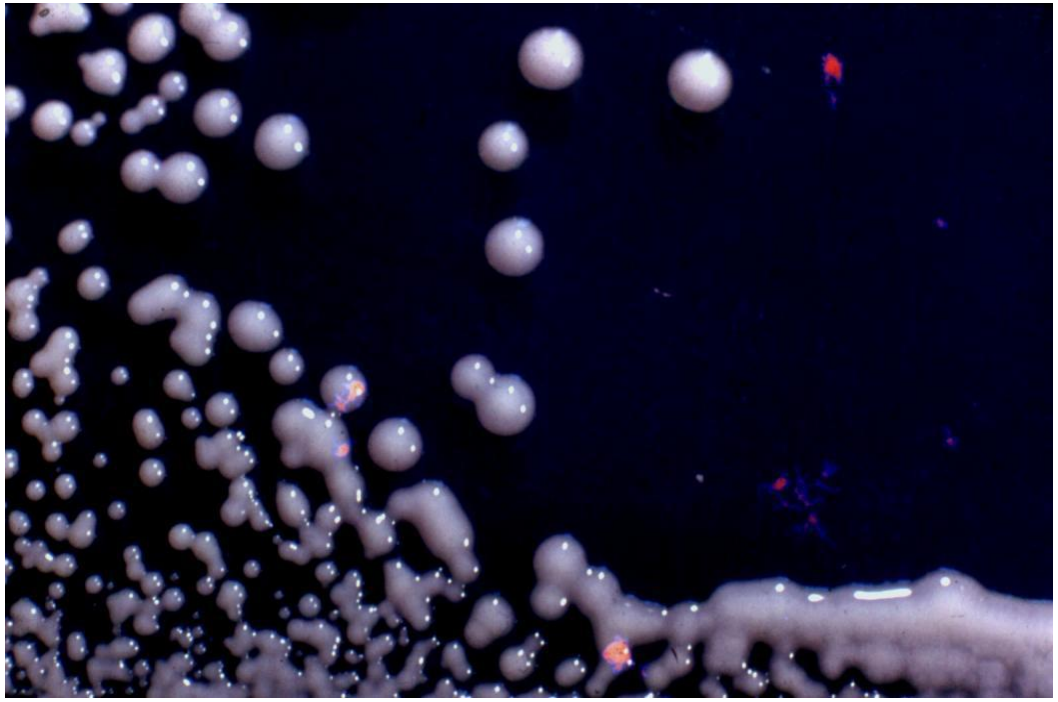
Colony Morphology

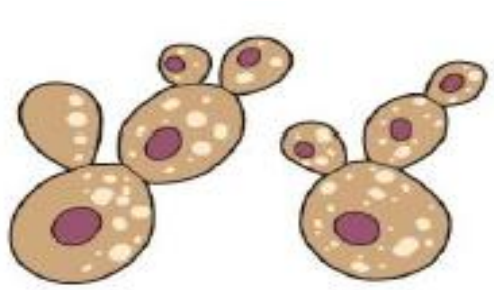


(b) A yeast or unicellular form which is defined morphologically, as a single-celled fungus that reproduces by simple budding to form Blastoconidia . round to oval and 3-10 um in diameter. yeast cells chained together and resembling true hyphae are called pseudohyphae . **Yeasts colonies resemble bacterial colonies in appearance and in consistency.**

The only pathogenic yeast in medical mycology is *Cryptococcus neoformans.*

Yeast Colonies



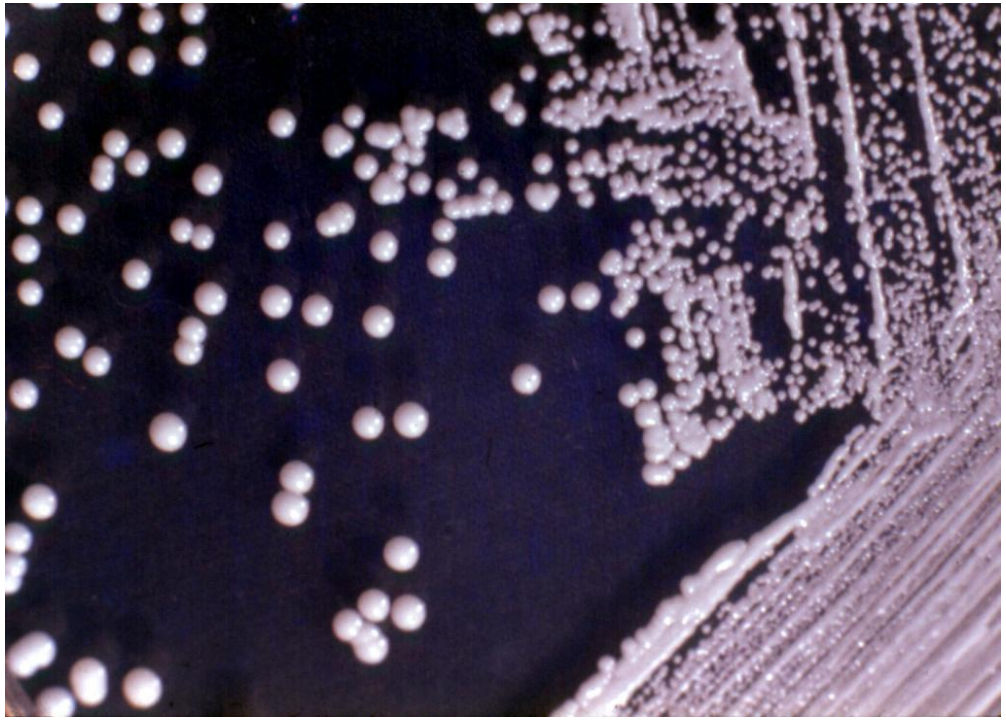


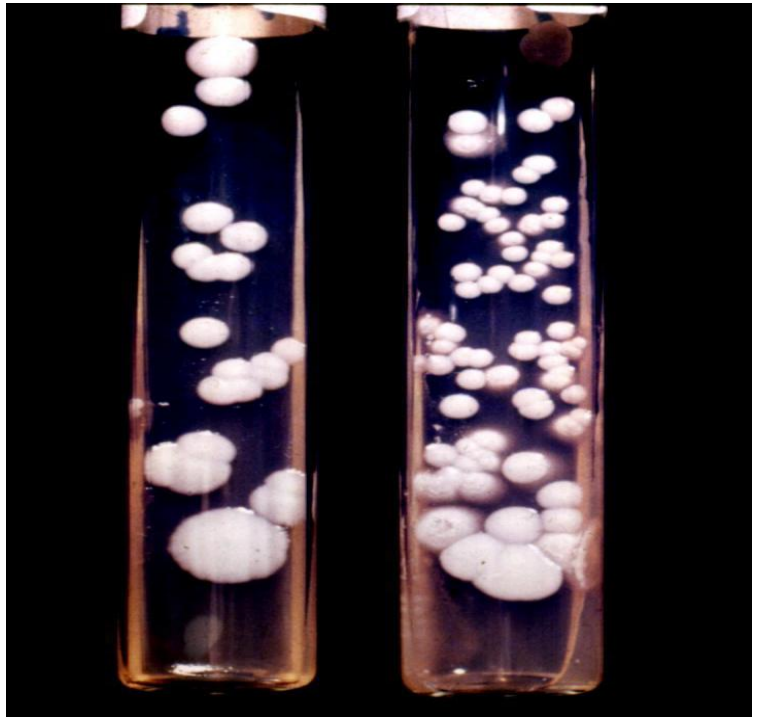
C-Yeast-like fungi

-These are fungi which occur in the form of budding yeast-like cells and as chains of elongated unbranched filamentous cells which present the appearance of broad septate hyphae. these hyphae intertwine to form a pseudomycelium.

- The yeast like fungi are grouped together in the genus **Candida**.

Candida Colonies





D- DIMORPHIC FUNGI:

• This class of fungi is characterized by two forms of growth:

1. Growth as **a mold** with septate hyphae in their natural reservoir (e.g. soil) or when incubated at 25° C. on conventional fungal media (Sabouraud dextrose or potato dextrose agars).

2. Growth as **a yeast** in the tissues of an animal/person or when incubated at 37° on enriched media (Brain heart infusion agar).e.g

Histoplasma capsulatum

Fungal cell wall

Fungi (yeast& molds) are eukaryotic organisms whereas bacteria are prokaryotic. Fungi differ from bacteria in some characteristics, as

Feature	Fungi	Bacteria
Cell Type	Eukaryotic	Prokaryotic
Cell Wall	Chitin	Peptidoglycan
Nucleus	Present	Absent
Organelles	Present	Absent
Structure	Mostly multicellular (e.g., mushrooms) or unicellular (e.g., yeast)	Unicellular
Reproduction	Asexual or sexual (e.g., spore formation)	Asexual (binary fission)
Mobility	Immobile	Motile via flagella (some)

Fungal cell wall

Consists of **chitin** not **peptidoglycan** like bacteria.

Thus fungi are **insensitive** to antibiotics as **penicillin's**.

Chitin is a polysaccharide composed of long chain of n-acetyleglucasamine.

•Also the fungal cell wall contain other Polysaccharide (β-glucan)

, which is the site of action of some antifungal drugs.

Fungal cell membrane

- Consist of Ergosterol rather than cholesterol like bacterial cell membrane
- **Ergosterol** is the site of action of antifungal drugs, amphotericin B & Azole group

Atmospheric & carbon source requirements of fungi

-Most fungi are obligatory aerobes, some are facultative anaerobes but none are obligatory anaerobes.

-All fungi require a performed organic source of carbon –association with decaying matter.

Medical mycology

Medical mycology: is the study of mycoses of man and their etiologic agents.

-Mycoses are the diseases caused by fungi. Of the several thousands of species of fungi that are known, less than 100 species are pathogenic to man. The most important are Candida , Histoplasma , Trichophyton etc--

-Mycotoxicoses : This term refers to the damage caused by toxic compounds produced by fungi in the bodies of humans and other mammals when food contaminated with these compounds is consumed . The most important are **Aflatoxin** produced by *Aspergillus flavus.*

In addition to those species which are generally recognized as pathogenic to man it is firmly established that under unusual circumstances of abnormal susceptibility of patient, or the traumatic implantation of the fungus, other fungi are capable of causing lesions. Those are called (Opportunistic Fungi.)

These circumstances may be :

1. A debilitating condition of the host, as Diabetes.

2. A concurrent disease such as leukaemia.

3. Prolonged treatment with corticosteroids.

4.Immunosuppressive drugs or an antibiotic for long duration.

MCQ

1-**Fungi differ from bacteria mainly because fungi:**

A. Are prokaryotic B. Contain peptidoglycan in their cell wall
C. Are eukaryotic organisms D. Cannot reproduce sexually

2-**The major component of the fungal cell wall is:**

A. Cellulose B. Chitin C. Peptidoglycan D. Lipopolysaccharide

3-**Yeasts reproduce primarily by:**

A. Binary fission B. Fragmentation C. Budding D. Spore formation only

4-**A fungus that can exist as both a yeast and a mold depending on temperature is called:**

A. Dermatophyte B. Opportunistic fungus C. Dimorphic fungus D. Zygomycete

5-**The most common method for microscopic detection of fungi in clinical samples is:**

A. Gram stain B. KOH (potassium hydroxide) preparation C. Ziehl–Neelsen stain D. India ink only

6-**Dermatophytes typically infect:**

A. Blood and lymphatic tissues B. Hair, skin, and nails C. Lung tissue only D. The gastrointestinal tract

Q2) What is **Opportunistic Fungi**

Q3)Classify fungi according to their Morphology

Never stop learning

Shatt Al -Arab University

Faculty of science

Department of Pathological analysis science.

Medical Mycology

Lect-4-Subcutaneous mycoses

Prof.Dr. Mohammed A. Fayyadh

Subcutaneous mycoses

Subcutaneous mycoses include a heterogeneous group of fungal infections that develop at the site of transcutaneous trauma. The main subcutaneous fungal infections include **Sporotrichosis ,Chromoblastomycosis ,Mycetoma , lobomycosis , Phaeohyphomycosis.**

Chromoblastomycosis (Verrucous dermatitis)

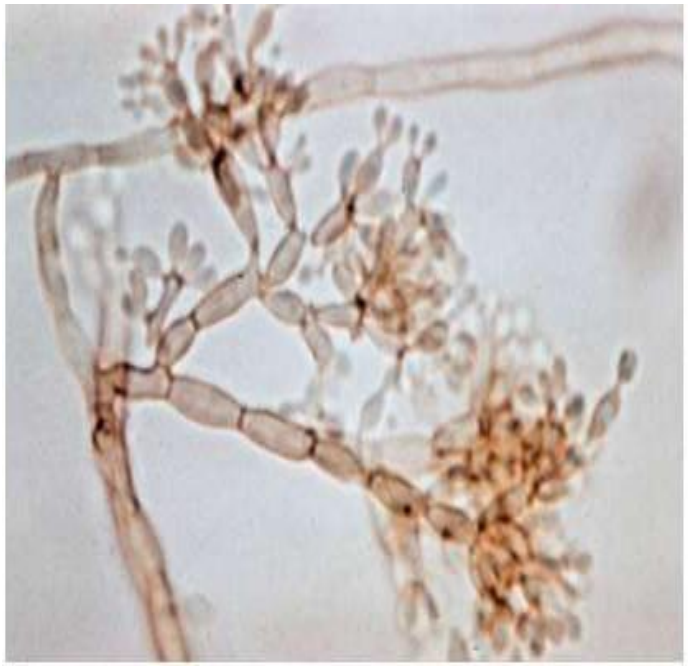
التهاب الجلد الثؤلولي

Aetiological agents include various dematiaceous hyphomycetes associated with soil, especially *Phialophora verrucosa*.

Lesions of **chromoblastomycosis** are most often found on exposed parts of the body and usually start a **small scaly papules or nodules** which are **painless** but may be **itchy**. lesions may gradually arise and as the disease develops rash-like areas enlarge and become raised irregular plaques that are often scaly or verrucose . In long standing infections, lesions may become **tumorous and even cauliflower-like in appearance**. Other prominent features include epithelial **hyperplasia**, **fibrosis and microabscess** formation in the epidermis.

Chromoblastomycosis on the toes, foot

Histological sample stained with hematoxylin



Phialophora verrucosa

Laboratory diagnosis:

1.Clinical Material: Skin scrapings and/or biopsy.

2.Direct Microscopy: Skin scrapings from a patient with chromoblastomycosis mounted in 10% KOH and Parker ink solution showing characteristic brown pigmented, planate-dividing, rounded sclerotic bodies(Medlar bodies) .

3. Culture: Clinical specimens should be inoculated on to primary isolation media, like Sabouraud's dextrose agar .

Management: The treatment of chromoblastomycosis has been exceedingly difficult. Successful surgical excision requires the removal of a margin of uninfected tissue to prevent local dissemination. both *itraconazole [400 mg/day] and terbinafine [500 mg/ day] for 6 to 12 months have been used successfully for the treatment of chromoblastomycosis* .

Lobomycosis

Aetiological agents . *Lacazia loboi*. The disease has been found in humans and dolphins .

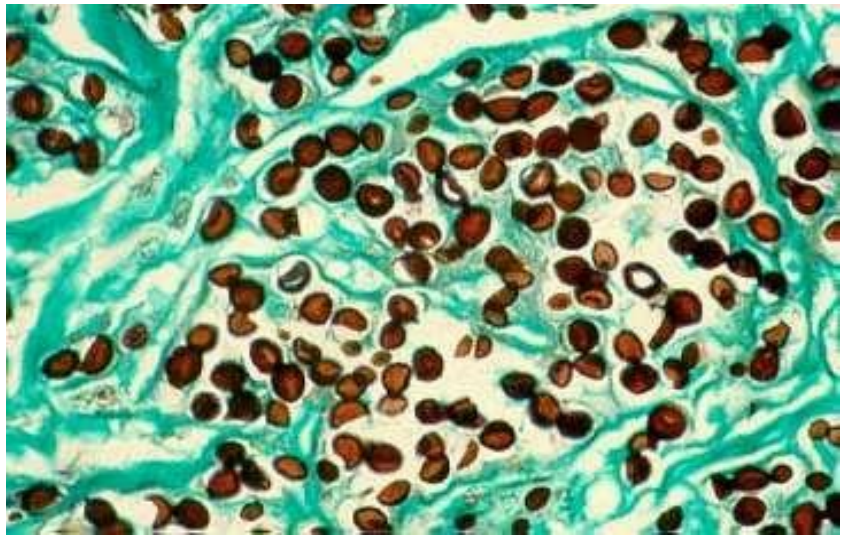
Clinical manifestations: The initial infection is thought to be caused by traumatic implantation such as an arthropod sting, snake bite, or wound acquired while cutting vegetation. The lesions begin as small, hard nodules and may spread slowly in the dermis and continue to develop over a period of many years. Older lesions become verrucoid and may ulcerate. The disease may be transferred to other areas of the skin by further trauma or autoinoculation. Lesions are usually found on the arms, legs, face or ears as keloid-like lesions

Lobomycosis showing extensive verrucoid lesions on the legs.

- **Laboratory diagnosis:**

1. Clinical material: Tissue sample obtained by curettage or surgical biopsy.

2. Direct Microscopy: (a) Tissue can be macerated and mounted in 10% KOH and Parker ink (b) Tissue sections should be stained using Grocott's methenamine silver (GMS) or Gram stains.



Darkly pigmented yeast-like cells, of the fungus

Management: The most successful treatment is for wide **surgical excision** of the affected area, however care must be taken to prevent contamination of surgical wounds, as relapse is common. Clofazimine at 100-200 mg/day has been used with varying results .

Mycetoma(worse than the thorn itself!!)

A mycotic infection of humans and animals Mycetoma are caused by 2 totally different groups of organisms: the first are moulds, and the second are filamentous bacteria in the order Actinomycetales. In the first case they are referred to as **Eumycetomas**, in the second as **Actinomycetomas** characterized by draining sinuses, granules and tumefaction.

Aetiological agents include *Madurella spp . Nocardia asteroides and Streptomyces somaliensis etc.*

Clinical manifestations:

Mycetoma is more common in men than women, particularly those aged 20 to 50. It generally presents as a single lesion on an exposed site and may persist for years. Two thirds arise on the foot.

- It starts as a small hard painless lump under the skin.

- It grows slowly but eventually involves underlying muscles and bones.
- The middle of the lesion caves in, ulcerates and discharges pus, which contains grains.
- granules which vary in size, colour and degree of hardness, depending on the aetiologic species. These grains are the hallmark of mycetoma.



Different symptoms of Mycetoma

Laboratory diagnosis:

1. Clinical Material: Tissue biopsy or excised sinus, fluid containing the granules which vary in size, colour and degree of hardness. depending on the aetiologic species.

2. Direct Microscopy: fluid containing the granules should be examined using either 10% KOH and Parker ink or tissue sections should be stained using Grocott's methenamine silver (GMS). The colour of the grains may suggest the likely diagnosis; black grains suggest a fungal infection, Microscopy using potassium hydroxide (KOH) confirms the diagnosis and type of mycetoma.

3. Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and incubated at 25-37 C . for six weeks.

Treatment of mycetoma :

- **Actinomycetoma** ….Streptomycin injections

-Eumycetoma **…**is more difficult to treat.

Itraconazole

ketoconazole

Phaeohyphomycosis infection

Exophiala jeanselmei

Sporotrichosis

Sporothrix schenckii

1-Chromoblastomycosis is characterized by which diagnostic microscopic feature?

A. Broad-based budding yeast B. Spherules with endospores
C. Sclerotic bodies (Medlar bodies) D. Hyaline septate hyphae

2- **Which organism is MOST commonly associated with black-grain eumycetoma?**

A. *Madurella mycetomatis* B. *Nocardia brasiliensis*
C. *Scedosporium apiospermum* D. *Exophiala jeanselmei*

3- **Mycetoma typically presents with which triad?**

A. Fever, lymphadenopathy, vesicles B. Nodules, ulceration, necrosis C. Tumefaction, draining sinuses, granules
D. Macules, papules, telangiectasia

4- **Which subcutaneous mycosis is most likely to cause cauliflower-like verrucous lesions?**

A. Mycetoma B. Sporotrichosis C. Phaeohyphomycosis D. Chromoblastomycosis

5- **The following are dematiaceous fungi EXCEPT:**

A. *Fonsecaea pedrosoi* B. *Cladosporium carrionii* C. *Madurella mycetomatis* D. *Histoplasma capsulatum*

Fill in the Blank

1-Subcutaneous mycoses are infections of the _____ and _____ tissues usually following traumatic implantation.

2-Chromoblastomycosis is characterized by the presence of _____ bodies in tissue.
2-The common causative fungi of chromoblastomycosis is _____,
3-Mycetoma can be caused by fungi (_____ mycetoma) or bacteria (_____ mycetoma).
4-The classical triad of mycetoma is swelling, sinus formation, and discharge of _____.
5-Lobomycosis is caused by _____.
6-Subcutaneous mycoses are usually acquired through _____ of fungal spores into the skin.

Thanks for your attention