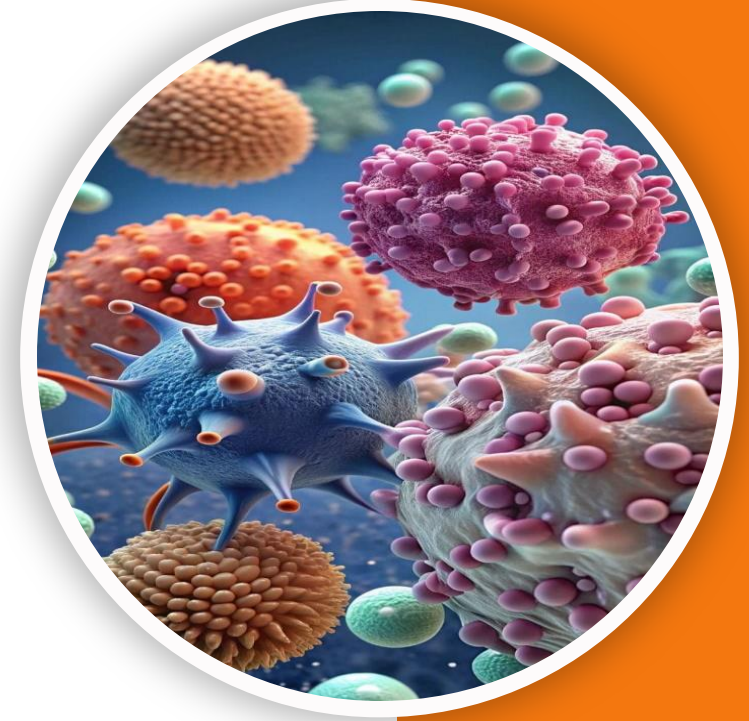


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(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



Microbiology | Lecture #2

Fungal Infections



Written by : Rama Ejueidi
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Fungal infections

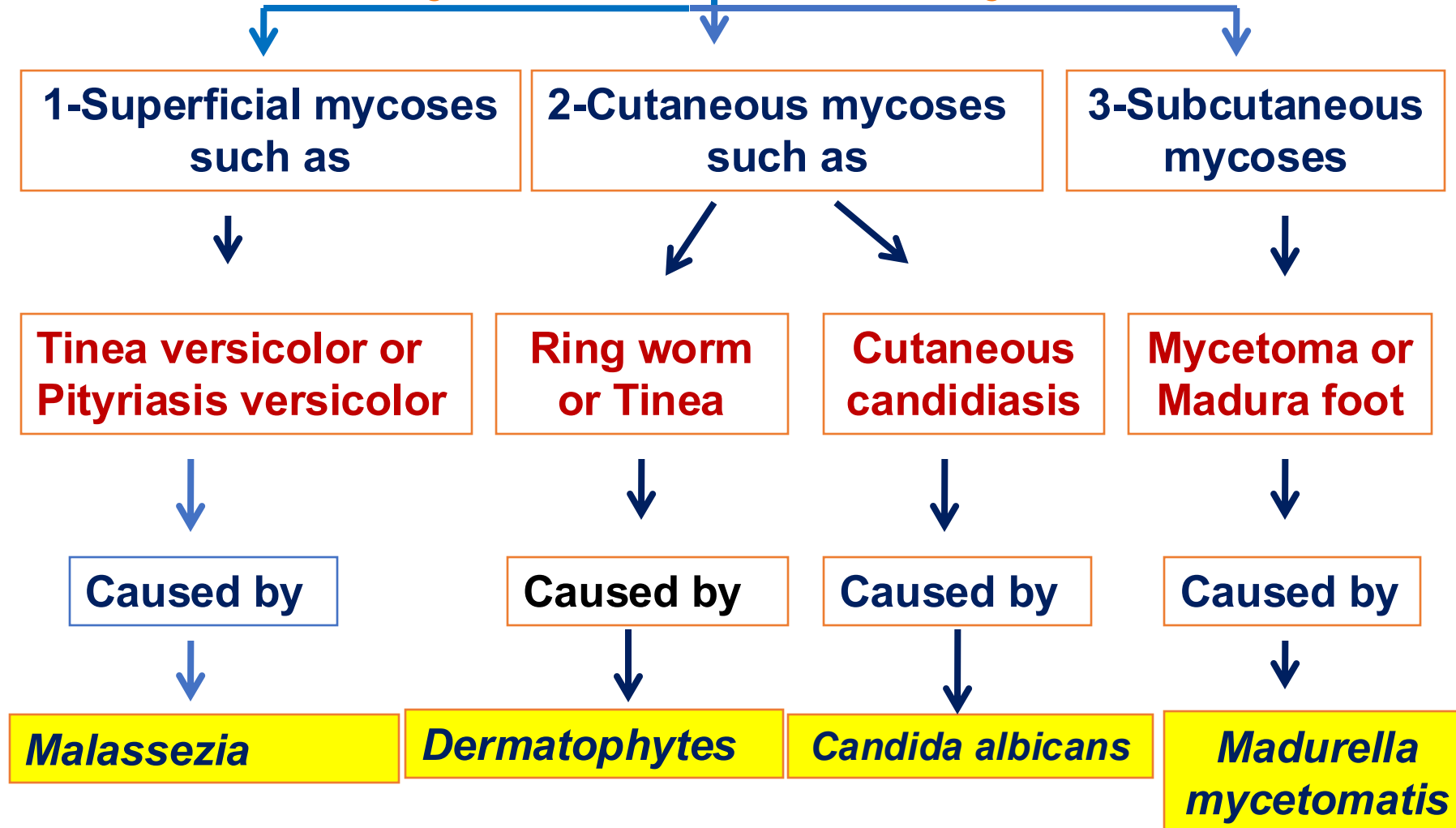
Mycotic infections

There are over 300,000 known species of fungi, but only about 10–15 of them are pathogenic and capable of causing diseases in humans.

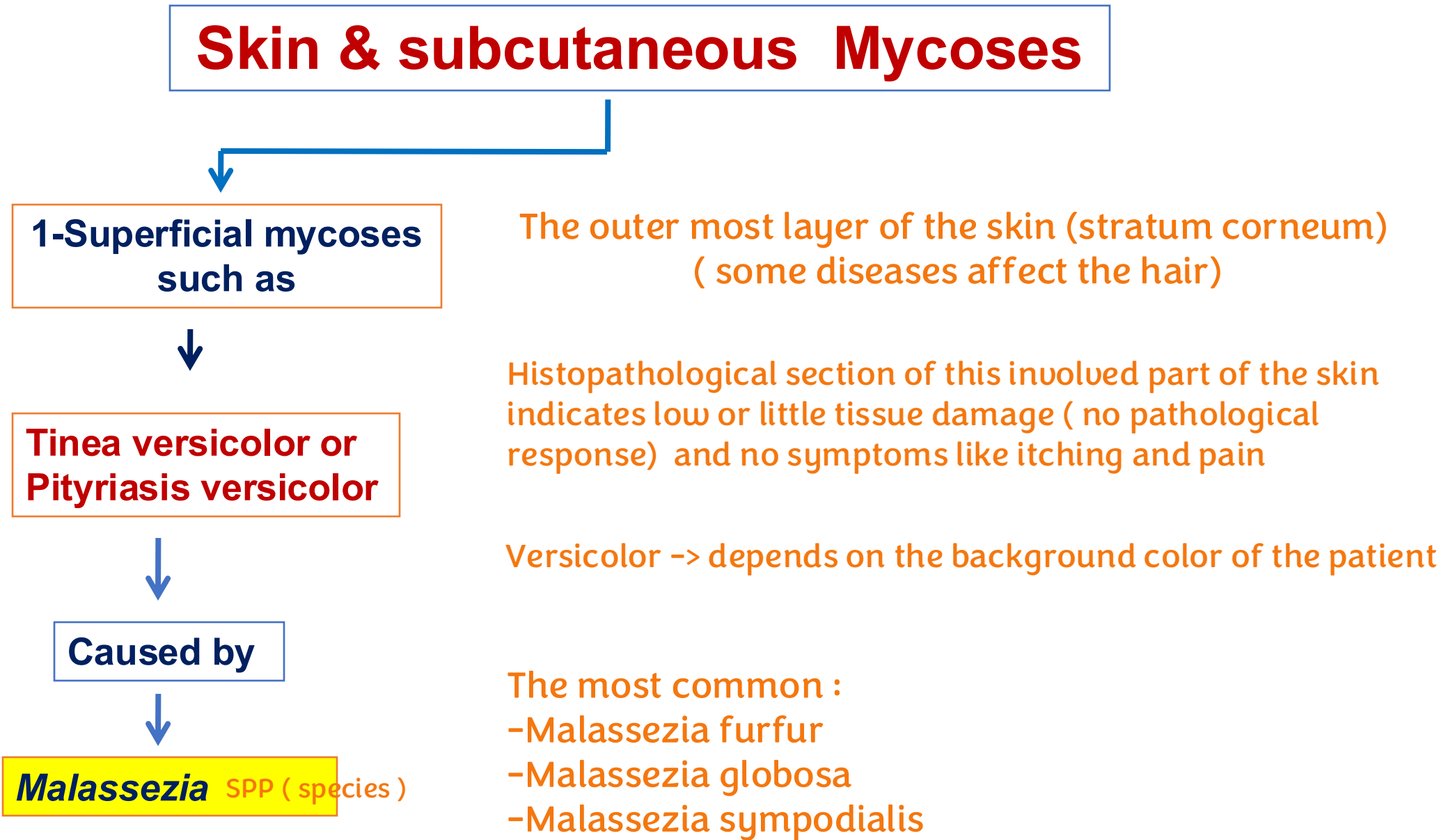
By: Nader Alaridah MD,PhD

Skin & subcutaneous Mycoses

Divided according to the anatomical / histological localization into:



Skin & subcutaneous Mycoses



```
graph TD; A[Skin & subcutaneous Mycoses] --> B[1-Superficial mycoses such as]; B --> C[Tinea versicolor or Pityriasis versicolor]; C --> D[Caused by]; D --> E[Malassezia SPP (species)];
```

**1-Superficial mycoses
such as**

The outer most layer of the skin (stratum corneum)
(some diseases affect the hair)

**Tinea versicolor or
Pityriasis versicolor**

Histopathological section of this involved part of the skin
indicates low or little tissue damage (no pathological
response) and no symptoms like itching and pain

Versicolor -> depends on the background color of the patient

Caused by

Malassezia SPP (species)

The most common :

- Malassezia furfur
- Malassezia globosa
- Malassezia sympodialis

Skin & subcutaneous Mycoses

Affect the keratinized (dead cells filled up with keratin) layer of the skin.

Affect nails and hair

Ring worm disease is the most commonly encountered

Important note:

Tinea in ring worm disease is followed by a suffix indicates which body part is affected

Three classes of Dermatophytes species:

- 1.Trichophyton
- 2.Microsporum
3. Epidermophyton

**2-Cutaneous mycoses
such as**

Histopathological section of this involved part of the skin indicates little to moderate pathological response and a patient shows symptoms like itching and pain

**Ring worm
or Tinea**

**Cutaneous
candidiasis**

The clinical spectrum of the candida is wide ,it includes skin , organs and systemic candidiasis (will be mentioned again in the opportunistic fungal infections)

Caused by

Caused by

Dermatophytes

Candida albicans

Skin & subcutaneous Mycoses

Include infections on the deeper layer of the dermis, fascia, muscles, eyes and cornea.

In this type of mycoses the physical barriers like intact skin barrier must be broken for the fungi to reach the subcutaneous tissues

Other examples: Chromoblastomycosis
Sporotrichosis (Rose gardener disease)

Chromoblastomycosis caused by (Fonsecaea, phialophora, cladophialophora) they are called dematiaceous fungi (naturally pigmented fungi)

Tinea nigra in the superficial mycoses is also caused by a dematiaceous fungus

3-Subcutaneous mycoses

Mycetoma or Madura foot

(Farmer foot disease)

Caused by

Madurella mycetomatis

Superficial Malassezia infections:

- Lipophilic yeast round in shape
- Normal commensals of skin (organisms that live in a relationship where one species benefits while the other is neither harmed nor helped)
• Part of a human normal flora found in the skin
- Can cause skin infections and catheter associated infections
- infections that occur as a result of a catheter (a medical tube) inserted into the body

The carriage rate of *Malassezia* SPP varies depending on many factors like age , geographical location and even mode of delivery (carriage rate is the percentage of individuals in a population who harbor a particular microorganism without showing signs or symptoms of infection.)

Generally, 80-90% of the population are colonized by (a microbe is present inside a host without causing disease) the *Malassezia* species

People in their late teens and early twenties have the highest carriage rate because of the excessive sebaceous gland secretions which enhance the lipophilic yeast growth

Patients admitted to the hospital have higher carriage rate to the *Malassezia furfur* which is in addition to causing Pityriasis versicolor in most cases , it is a part of the normal flora of the skin so if you want to insert a catheter , central line, or a needle to draws venous blood of a patient, and you don't work under aseptic conditions (ظروف معقمة) you might introduce fungemia (The presence of fungi in the bloodstream)

Malassezia furfur causes fungemia of premature infants; because of the central line that give them total parenteral nutrition (غذاء كامل) that includes lipids supplements (favorite environment for *malassezia furfur*)

Superficial Malassezia infections

Pityriasis versicolor:

:

- Skin (stratum corneum) infection
- Trunk and proximal limbs Usually they affect trunk and chest and less common on the shoulders and the least common on neck and face
- M. furfur and M. globosa
- Common in tropics and precipitated by sun exposure
- Carboxylic acid produced by the yeast causes the depigmentation Distribute melanin synthesis -> affect the pigmentation of the skin

The yeast (pityriasis species) also produce a chemical called pityrialacton (will be discussed later)

Superficial Malassezia infections

Pityriasis versicolor:

:

Clinically:

- Asymptomatic Non itchy macules hypo or hyper pigmented
- Can coalesce to form scaly plaques

In advanced cases there will be scales at the edges of the lesions (furfuraceous scales)

Can be precipitated by sun exposure; fungi favour heat and humidity

Dark skin patient show hypopigmentation

Well demarcated pink to white separate lesions , small lesions often merge together, creating a larger single patch.



Caucasian patients show
Hyperpigmentation



Superficial Malessezia infections

Pityriasis versicolor:

:

Diagnosis:

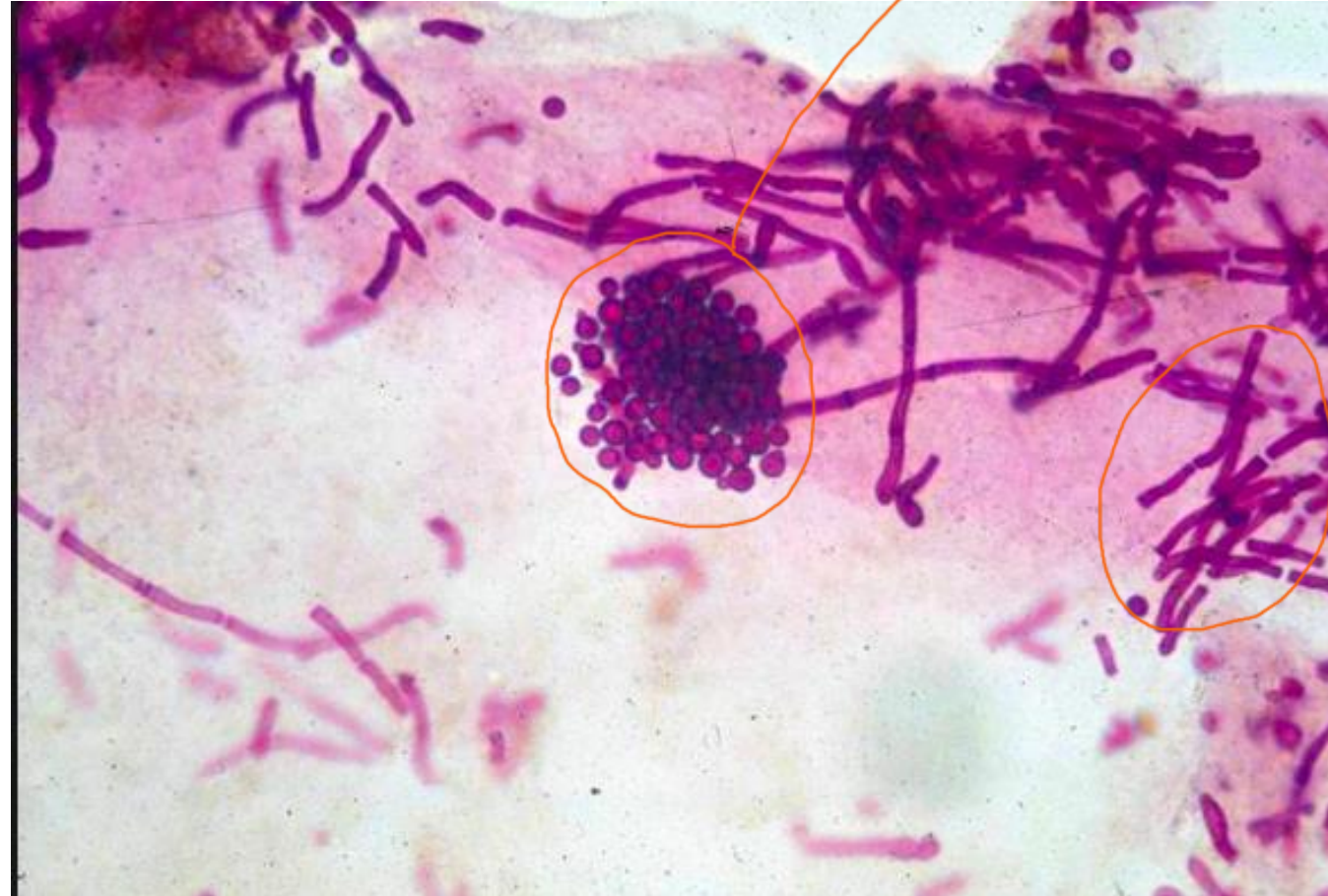
- UV light: pale greenish colour under **Wood's ultra-violet light**
- Skin scraping then Ink and KOH staining
 - thick septate hyphae and clusters of budding yeast cells (Spaghetti and meatballs)

Pityrialacton is a chemical substance produced by Pityriasis versicolor species. In dermatology clinics, clinicians darken the room and use a UV light source directed at the lesions. The color changes to green or coppery-orange because the UV light is absorbed by the Pityriasis versicolor species, which then emit Pityrialacton – a fluorescent substance that glows in this color.

Malassezia versicolor species are yeast—> form a single cell

Spherical cells and unbranched hypha called spaghetti and meat ball appearance

A specimen from a normal person or a normal flora appears as spherical cells but once they start to be pathological the specimen appears like this picture



Spherical cells

unbranched hyphae

Treatment —> Selenium disulfide

Superficial Malassezia infections

It is an endogenous infection non-contagious (from your own flora)

Treatment if needed is for cosmetic reasons:

- Some resolve spontaneously
 - Topical azoles cream/ shampoo for 2 weeks or in severe cases use oral azoles
 - Recurrence is common
- High recurrence rate because the same patient might face the same conditions like immunocompromising status , environmental factors

Hair dandruff (**Seborrheic dermatitis**): (one of the theories of the hair dandruff is the malassiza furfur overgrowth on the scalp)

Skin hyperproliferation with dandruff being the mildest manifestation.

Lesions are red and covered with greasy scales and itching is common in the scalp.

After using ketoconazole shampoo the symptoms disappear this might support the theory

Examples of uncommon fungal infections;

M. furfur

Azoles

- Tinea nigra → black macules (lesions are flat at the same level of the skin) usually on the back of the hand
- White and black piedra → black or white nodules appear on hair

Cutaneous Mycoses

Ring worm or tinea

- Caused by dermatophytes (filamentous fungi / moulds) which include 3 genera: *Microsporum*, *Trichophyton* & *Epidermophyton*.
- These fungi affect the keratinized tissues as skin, hair & nails.
- Infection not spread to deeper tissues.



Mild inflammatory response, high recurrence rate, repeated treatment

Source of infection

It is contagious(معدِي)

1- Man to man by direct contact (Anthrophilic)

Acute inflammatory response, recurrence rate almost zero, one treatment course is enough

2- From animals e.g. dogs and cats (Zoophilic)

3- From the soil (Geophilic).

Indirectly through shared objects(carpet ,same clothes ,same wardrobe ,gym , swimming pool)

Because they have scales , and these scales remain viable and infectious for years and months

N.B.

➤ The intact skin is an important barrier against infection.

➤ Heat and humidity enhance the infection.

Tinea cruris: it affects perineum and scrotum(inner thigh) another name is jock itch.

For hairless skin ,Yet if the person was bearded it's called Tinea barium

Clinical forms

Tinea capitis affects the hair scalp. The infected individuals usually experience hair loss
In the severe form, called tinea favosa, it causes permanent hair loss, where the hair does not grow back and the scalp becomes covered with black dots.

Tinea pedis or Athlete's foot

Tinea corporis & cruris

Tinea capitis

Tinea unguinum

Toes web

Body & groin area

Head

Nail



Extremely white or yellow and brittle (easily broken)

For differentiation it's not painful nor tender

Tinea corporis

❖ Clinical pictures:

- Red, itchy scaly rash, ring like with raised more inflamed border on the body or groin.
- Scaling and hair loss leaving black dots.
- White and opaque / yellow , thickened & broken nails.
- DDX: Eczema, psoriasis, impetigo, alopecia, drug reactions.



The rings are raised compared to the skin, in the center it is normal skin (clearance of inflammation) therefore called rings.

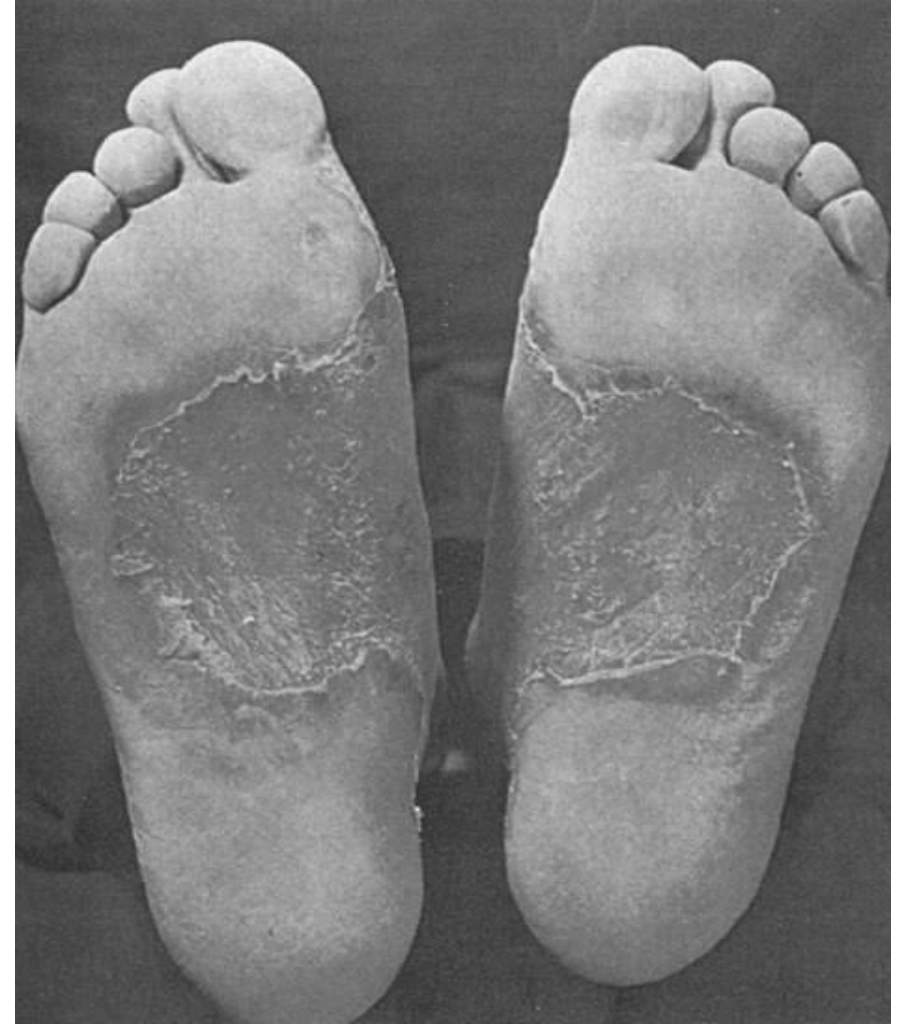
Ring like lesion

Mild



- Tinea pedis showing interdigital scalping
- *T. mentagrophytes*

Severe



Dermatophytos of the soles

Diagnosis

Microscopic examination

❖ Skin scales, nail & hair are examined microscopically after digestion using 10% KOH.

➤ Branching hyphae are detected among epithelial cells of skin & nails.

➤ Hyphae or spores are detected in the hair. Spores either detected inside the hair (**endothrix**) or outside the hair (**ectothrix**).

Culture

❖ Culture on **Sabouraud's dextrose agar (SDA)**:

❖ The agar incubated at room temperature for 4 ws. The arising colonies examined microscopically after staining with **lactophenol cotton blue stain**.

Treatment

Local antifungal cream as miconazole or **oral terbinafine** weeks to months

Common Dermatophytes



Epidermophyton floccosum:

Bifurcated hyphae with multiple, smooth, club shaped macroconidia (2-4 cells)



Microsporum:

Thick wall spindle shape multicellular

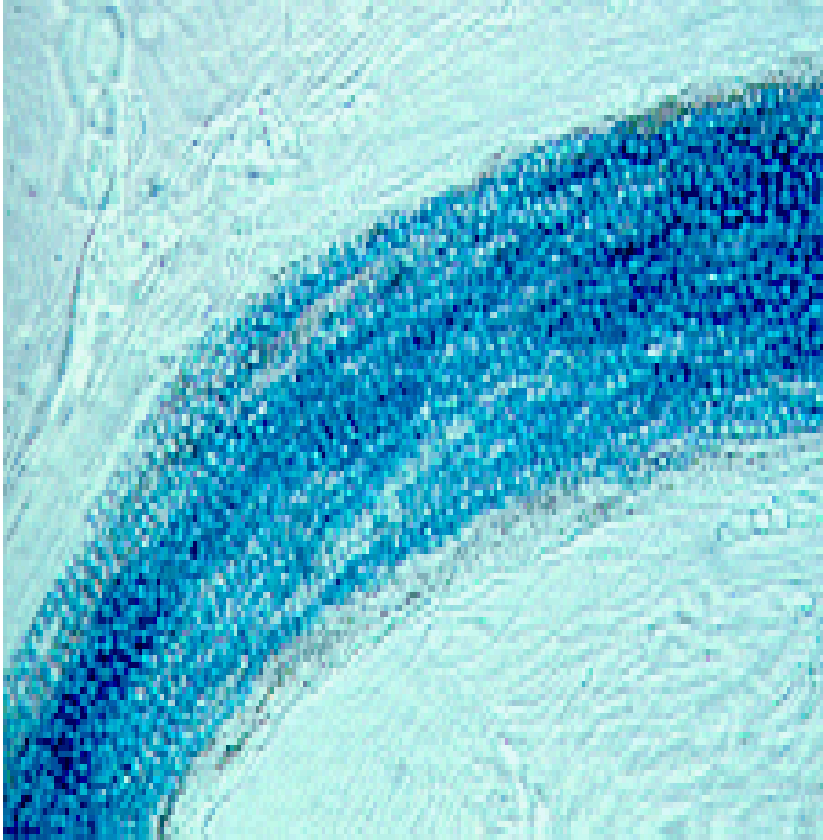


Trichophyton:

Large, smooth, thin wall, septate, pencil-shaped

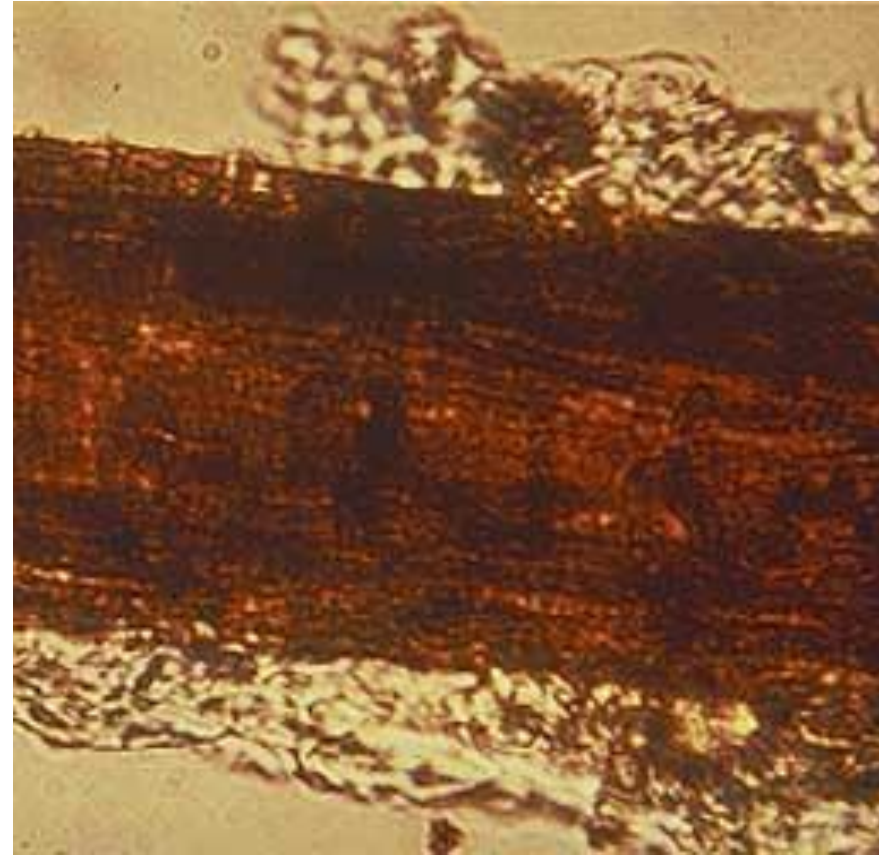
Hair examination

Many spores inside



Endothrix

Many spores outside



Ectothrix

Deeper

Subcutaneous mycoses

Mycetoma (Madura foot)

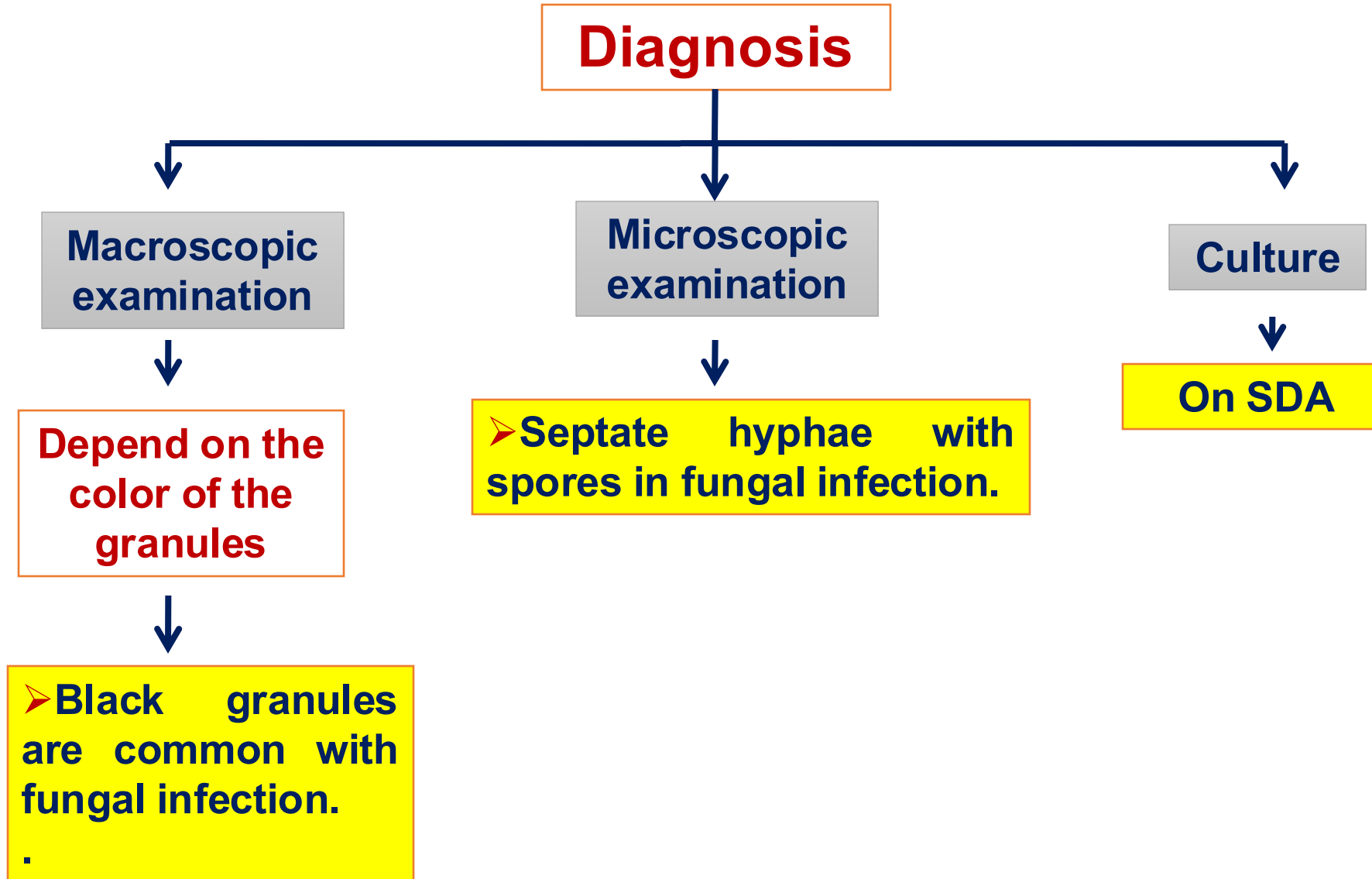
- These infection caused by fungi that grow in soil & on decaying vegetations.
- The fungi introduced into subcutaneous tissues through trauma.
- Mycetoma is a **chronic granulomatous infection** usually affects the lower limbs and hands
- The disease usually affects **farmers**. Due to walking bare foot

Causative organism of mycetoma

- 1- Eumycetoma: caused by fungi *Madurella mycetomatis* which having true septate hyphae.
- 2- Actinomycetoma: caused by species of **actinomycetes** (filamentous aerobic bacteria).

Clinical pictures

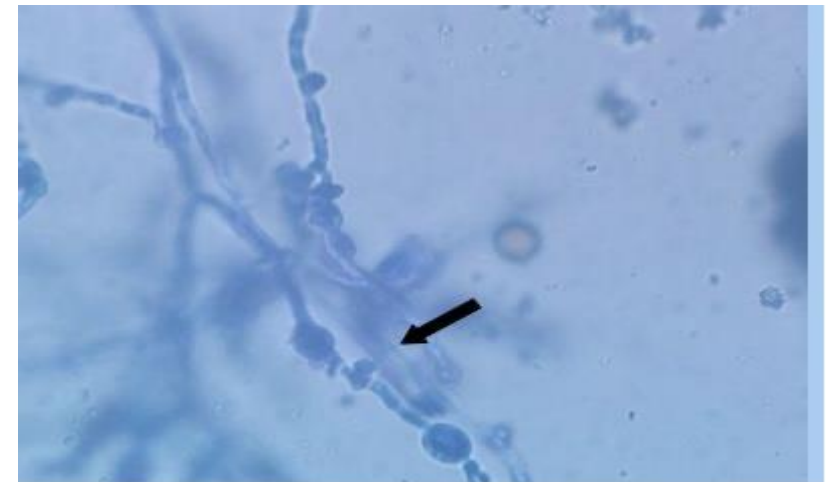
Swelling following trauma, purplish discolouration & multiple sinuses that drain pus containing yellow, white, red or black granules.





Madura foot

Painless



***Madurella mycetomatis* with
intercalary chlamydospores**

Treatment

1. Medical:

- - ketoconazole
- - Itraconazole
- - Amphotericin B For more severe cases
- 2. Surgical.

OPPORTUNISTIC MYCOSES

هم خمسة انتهازيين بدهم الفرصة المناسبة

like when the immune status of the host get compromised or they acquire new virulence factors

إذا بدنا نحكي عن المعادلة من طرفين المعتدي والمعتدي عليه

- Opportunistic mycoses are caused by globally distributed fungi that are either members of the human microbiota, such a *Candida* species, or environmental yeasts and molds.

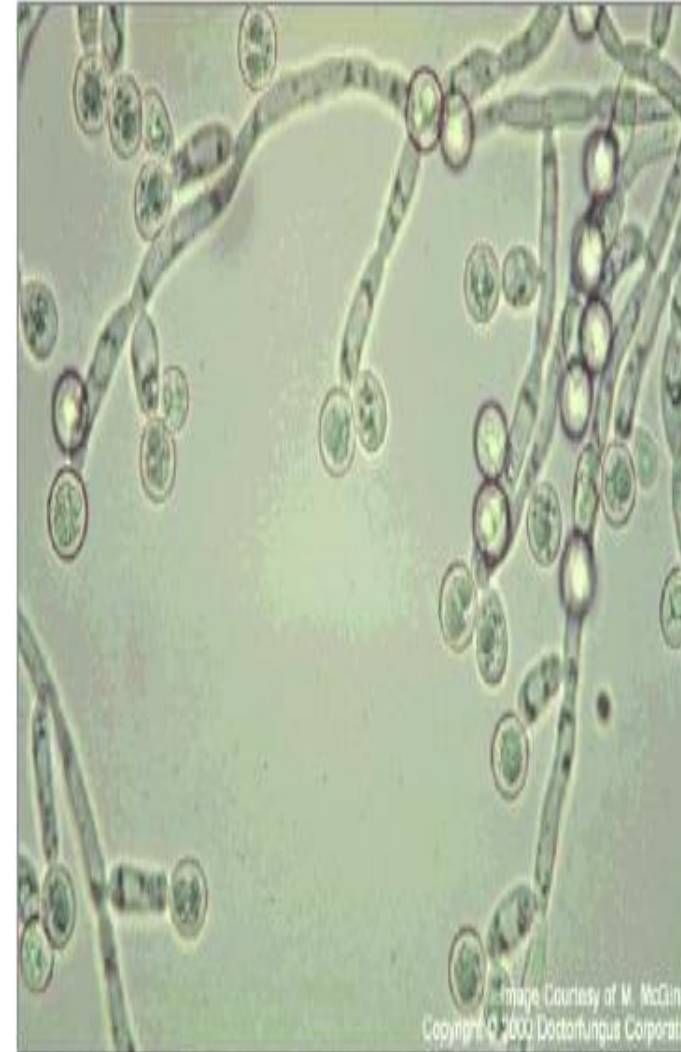
Cancer, HIV, cortisone, antibiotics patients and who takes immunosuppressant like organ transplantation patients are more susceptible to infection, so regardless of your specialty, you may see them, because usually after they are admitted to the hospital, they develop such infection.

- They can produce disease ranging from superficial skin or mucous membrane infections to systemic involvement of multiple organs
- Patients at risk include those with hematologic dyscrasias (eg, leukemia, neutropenia), patients with HIV/AIDS with CD4 counts less than 100 cells/ μ L, as well as those treated with immunosuppressive (eg, corticosteroid) or cytotoxic drugs

Most famous are the candida Disease called candidiasis collectively have wide spectrum , have more than one species so we write candida spp, most common are candida albicans followed by tropicalis, then auris, then parapsilosis... What makes candida special it can be part of the normal flora in upper respiratory tract , upper gastrointestinal tract, skin, and in the genital tract in the female

Candidiasis

- ***Candida albicans*** is the most important species of candida (other species...).
- ***Candida albicans*** is oval gram positive budding yeast which produce pseudohyphae.
- It colonises the mucous membranes of the **upper respiratory, GIT & female genital tracts**.
- It causes superficial infections but can predominate with lowering in immunity causing infection so it is one of **the opportunistic fungi**.



Risk factors for
the patients
who are
immune
compromised
and have
general debility

قليلين الحركة الي
بنضطر ندخلهم على
ال(ICU)
او بدك تحطلمهم
prosthetics

Predisposing factors to *Candida* infections

- 1- Diseases as AIDS & diabetes mellitus.
- 2- Drugs: prolonged treatment with broad spectrum antibiotics & corticosteroids.
- 3- General debility.
- 4- Indwelling urinary catheters.

Pathogenesis & Symptomatology

IUCD (Intrauterine contraceptive device) T-shaped device that is inserted into the uterus to prevent pregnancy

Skin invasion

-They are red & weeping lesions.
-Mainly affect warm moist areas. Such as axilla, intergluteal folds or inframammary folds.
-Mostly in & obese diabetics.
-Pseudo diaper rash

Weeping (بسيط)
They are oozing they release a fluid, they infect obese people, found in skin to skin fold like axilla, inframammary, gluteal fold and finger web they also infect diabetes patients

diaper rash is a kind of contact dermatitis but pseudo diaper rash is a fungal infection.

Mouth infection

C. albicans produces white patches in the mouth (oral thrush or moniliasis).

Sometimes oral leukoplakia, esophagitis, gastritis

AIDS patients through their curing procedure even if its under control they should under go at least 1 episode of moniliasis (oral thrush)

Vulvovaginitis

-With itching & thick vaginal discharge.
-Common with diabetic woman & prolonged use of antibiotics, IUCD, Pregnancy..

Under certain conditions specially during pregnancy specially females with IUCD or who takes broad spectrum antibiotics as it changes the microbial flora in vagina. Are characterized by extreme itching and pruritus + vaginal discharge (curd-like) زي الحليب المتخثر

Nails infection

-Occurs with repeatedly immersing in water (dish washing).
-Painful redness, swelling of nail folds, thickening & loss of nail (paronychia).

Systemic candidiasis

Occure in diabetics & Immuno-suppressed persons.

Nails infection called paronychia one of the difference between paronychia and onychomycosis (tinea unguium) is that paronychia is painful (swelling and redness is noticed), while onychomycosis is not



Oral candidiasis

leukoplakia

Moniliasis there is something called pseudo membrane as if the membrane عبارة عن بياض
 Consists of candida + epithelial cells
 It can reach the tongue called **leukoplakia**
 If it reach deeper areas like esophagus and the stomach it will cause **esophagitis, gastritis**



paronychia

Swelling, redness
 ,painful, thickening in
 the nail bed or nail fold

If you raise this skin fold
 you will find lesions we
 find this in candidiasis and
 not in contact dermatitis of
 the diaper rash that's why
 its called pseudo. So in
 diaper rash this area is
 clear its has no lesions as it
 does not touch the diaper
 directly

نفس البيبي صار عندو
oral candidiasis
result of bad
hygiene

Pseudo diaper rash

Its called diaper rash or
 napkin dermatitis as its
 contact dermatitis

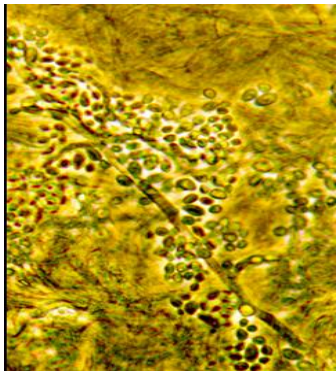


Candida fingerweb erosion: related to fatness , occupation etc.

Toes web or athlete foot in tinea pedis in candidiasis it causes something called finger web this fungal infection is common among housewives and people who frequently wash dishes and vegetables or wear gloves for long periods the picture shows a type of mild candidiasis



Candidiasis is yeast, pseudohyphae, true hyphae have severest form which is systemic candidemia. While diagnosis you will see either yeast form or pseudohyphae form under the microscope



Laboratory diagnosis

Direct microscopic examination

- Specimens from skin, vaginal discharge or exudates from mucous surfaces are examined.
- *C. albicans* is oval gram positive budding yeast cell with pseudohyphae.

Culture

On nutrient agar, corn meal agar & SDA. Colonies are creamy in color & identified by:

1- **Morphology:** oval budding gram +ve yeast cells.

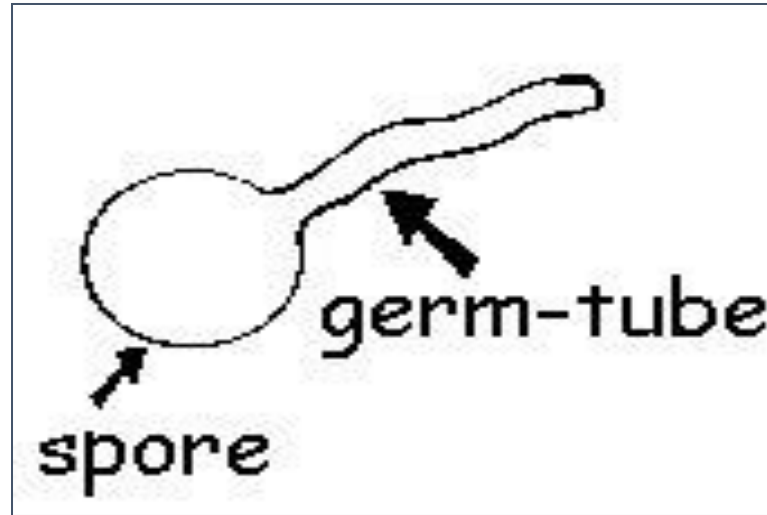
2- **Differentiation tests:**

- Germ tube test :** germ tube is formed when colonies incubated with human serum at 37 C for 30 min.
- Chlamydospore formation** on corn meal agar.
- Biochemical reactions:** *C.albicans* ferments glucose & maltose with acid & gas production.



When diagnosing candidiasis using a culture, using the sabouraud dextrose agar (SDA) white, creamy, globose, waxy colonies appear. To identify the species we have more than one test.³⁵

- To identify the different species we either use germ tube formation test or we culture them on a different agar called corn meal agar after 4 weeks we look at the agar under the microscope we will observe the chlamydospores formation.
- The germ tube test we take a colony and incubate it in the lab with serum from the healthy individual blood and incubate for half an hour at 37 C ,each spore will start to form a tube.
- Corn meal agar and the germ tube test can be replaced by chromogenic agar, different species produce different colony colors, allowing rapid identification.
- *Candida albicans* (albicans means white) it forms a green colony when using the chromogenic agar.



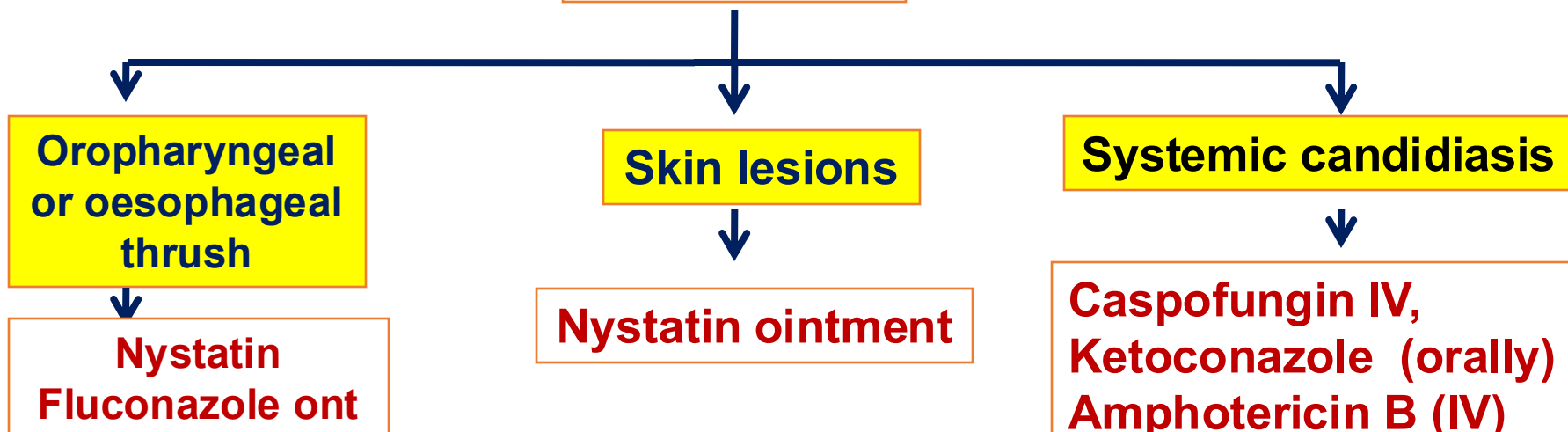
Germ tube



Corn meal agar

Terminal Chlamydospore & pseudohyphae

Treatment



- Treatment – of course, it depends. If we are dealing with cutaneous candidiasis we use nystatin (polyene) if we are dealing with oropharyngeal azoles or even nystatin can work, and if we are talking about systemic infections, you need to use something stronger like the ones mentioned the previous slide.

Cryptococcosis disease is caused by *Cryptococcus neoformans* or *Cryptococcus gatii*, cryptococcosis is a type of meningoencephalitis that infects the meninges and the brain. It is an oxygenous infection always pathogenic and is often present in soil contaminated with bird droppings; pigeon breeders are at higher risk of exposure to *Cryptococcus*. It enters the pulmonary system then it reaches the brain. This is the difference between prokaryotes and fungi. Fungi are non-motile.

They are neurotropic, meaning they infect the CNS, and of course, the immune-compromised individuals are at higher risk to develop cryptococcosis. It's a very severe disease.

Cryptococcus neoformans

- *Cryptococcus neoformans* causes cryptococcosis.
- A widespread **encapsulated yeast** that inhabits soil around pigeon roosts
- Common infection of **AIDS, cancer** or **diabetes patients**
- Infection of **lungs** leads to cough, fever, and lung nodules
- **Dissemination to meninges** and brain can cause severe neurological disturbance and death.

Diagnosis

Microscopic

- India Ink for capsule stain (50-80% + CSF)

Culture

- Bird seed agar
- Routine blood culture

PCR

It's the only capsulated fungi note that the dimorphic fungi *histoplasma capsulatum* doesn't have a capsule. In diagnosis, we rely on detecting the capsule. India ink stain delineates the capsule of the cryptococcus, using a specimen from neurotropic CFS(cerebrospinal fluid) the problem is that it might miss up to 50% of the cases. Therefore, we rely a lot on PCR, DNA probe cryptococcal antigen

Aspergillosis is caused by mainly *Aspergillus fumigatus* it's an allergic reactions (allergic rhinitis, asthma, extrinsic allergic alveolitis) some species go deeper they invade the lung tissue causing cavitory lung lesions. Cavitory means loss of lung volume

بصير في فراغ فاضي وبعبي
هاد الفراغ بكرة من العفن
Called fungal ball or aspergilloma it require surgery in order to be treated. Once they enter the pulmonary tract, they can colonize the ears, eyes, and sinuses.

Aspergillosis: Diseases of the Genus *Aspergillus*

- Very common airborne soil fungus
- 600 species, 8 involved in human disease; *A. fumigatus* most commonly
- Serious opportunistic threat to **AIDS, leukemia, and transplant patients**
- Infection usually occurs in **lungs** – spores germinate in lungs and form **fungal balls**; can colonize **sinuses, ear canals, eyelids, and conjunctiva**
- **Bronchopulmonary allergy or Invasive aspergillosis in preformed cavitis** can produce **necrotic pneumonia, and infection of brain, heart, and other organs.**
- Surgery , Amphotericin B and nystatin

Zygomycota have another name which is mucorales. 3 species which cause zygomycosis other name rhinocerebral mucormycosis. This disease is found in the sinuses and brain

Diabetes patients are the most susceptible who reach the DKA (diabetic ketoacidosis)+ immune compromised patients cancer and AID pateints

Zygomycosis

- Zygomycota are extremely abundant saprophytic fungi found in soil, water, organic debris, and food.
- Genera most often involved are ***Rhizopus, Absidia, and Mucor.***
- Usually harmless air contaminants invade the membranes of the **nose, eyes, heart, and brain** of people (Rhinocerebral mucormycosis) with **diabetes** and malnutrition, with severe consequences.
- **main host defense is phagocytosis**

Diagnosis is made by direct smear and by isolation of molds from respiratory secretions or biopsy specimens.

Treatment:

Control Diabetes ,surgery &
amphotericin B

Prognosis: very poor

PNEUMOCYSTIS

Opportunistic fungal infection have 2 name pneumocystis jirovecii and pneumocystis carinii it causes pneumonia PCP (pneumocystis carinii pneumonia) one-third of AIDS patients die from pneumonia. 2 things to know its obligate extracellular fungi, was previously thought to be parasite, it lives on the surfactant above the alveolar cells, cant be cultured in the lab, diagnosis relies on a lung biopsy, then it is stained by silver stain giving a honey comb appearance. On the CT it shows a ground-glass appearance. Treatment is very simple if the infection was diagnosed treated by TMP-SMX(trimethoprim-sulfamethoxazole)

- Pneumocystis jirovecii is the cause of a lethal pneumonia in immunocompromised persons, particularly those with AIDS.
- Definite diagnosis of pneumocystosis depends on finding organisms of typical morphology in appropriate specimens (Sputum, BAL)
- The organism has not been grown in culture
- TMP-SMX is treatment of choice

They are 4, called endemic because they have certain geographical distribution. All 4 caused by dimorphic fungi, they all start by inhaling the corresponding spores or conidia, they cause acute infection in the respiratory tract then they might spread to other body organs

Endemic mycosis

- Endemic mycosis is caused by a thermally dimorphic fungus, and the infections are initiated in the lungs following inhalation of the respective conidia.
- Each of the four primary systemic mycoses—coccidioidomycosis, histoplasmosis, blastomycosis, and paracoccidioidomycosis—is geographically restricted to specific areas of endemicity.
- Most infections are asymptomatic or mild and resolve without treatment. However, a small but significant number of patients develop pulmonary disease.

The End

رسالة من الفريق العلمي:

لا إِلَهَ إِلَّا اللَّهُ الْعَظِيمُ الْحَلِيمُ،
لا إِلَهَ إِلَّا اللَّهُ رَبُّ الْعَرْشِ الْعَظِيمِ،
لا إِلَهَ إِلَّا اللَّهُ رَبُّ السَّمَوَاتِ
وَرَبُّ الْأَرْضِ، وَرَبُّ الْعَرْشِ الْكَرِيمِ

For any feedback, scan the code or click on it.



Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	10+11	Dark people show hyperpigmentation while caucasians show hypopigmentation	Dark people show hypopigmentation while caucasians show hyperpigmentation
	14	Back of the hand	Palm of the hand
	31	pseudo diaper rash kind of contact dermatitis	diaper rash is a kind of contact dermatitis but pseudo diaper rash is a fungal infection.
V1 → V2			