

Doctor 021

MICROBIOLOGY

Sheet no. 13



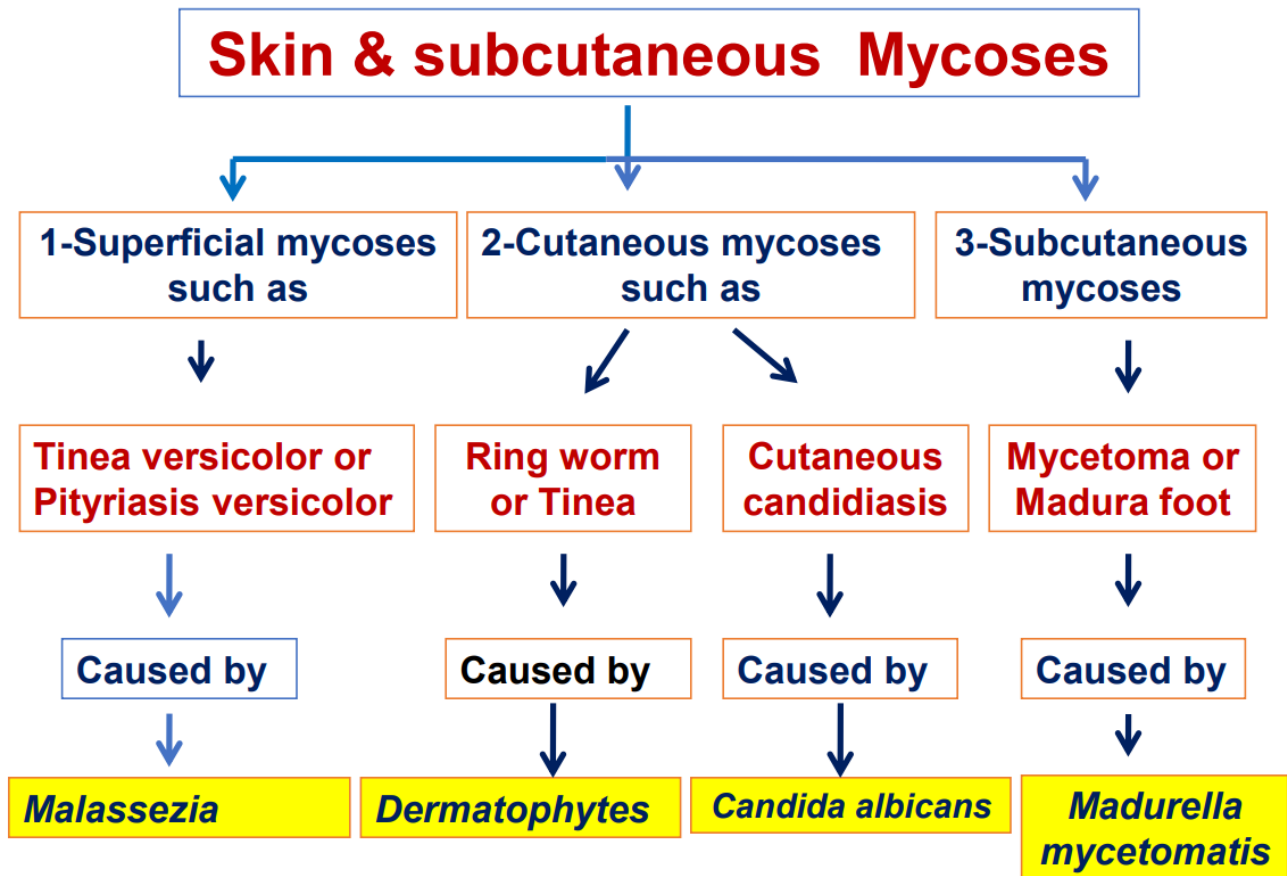
Writer : Ammar Ismail & Infection

Corrector : Abulrahman Abu Shaweesh
& Layan Al-Zoubi

Doctor : Nader Alaraideh

FUNGAL INFECTIONS

Note before studying the sheet: we tried to include everything that the doctor said -even names of bacteria, fungi and diseases- because as we have seen in the midterm exam, the doctor is not committed to the slides, and most importantly deciding what is important and what is not, is totally up to you. BEST OF LUCK.



SUPERFICIAL MALESSEZIA INFECTIONS:

PITYRIASIS (TINEA) VERSICOLOR

- **Lipophilic yeast round in shape.**
 - They're yeasts, but they can be hyphae.
 - Recall that dimorphic fungi are hyphae when they are non-pathogenic, and yeasts when they are pathogenic.
 - However, ***Malassezia*** can exist in either hyphae or yeast while being pathogenic or non-pathogenic inside human body.
 - Lipophilic because they mainly favor sebaceous glands that secrete fats (oil) which can nourish fungi.
 - They can be found on trunk, neck, and beard.
- **Normal commensals (flora) of skin.**
 - They can't be transmitted to others because they're normal flora.

- **Can cause skin infections and catheter associated infections.**

- They become pathogenic and infect skin due to gaining a virulence factor or being introduced to another abnormal site (in catheters).

- **Skin (stratum corneum) infection.**

- Only cosmetic reasons. No symptoms are present.

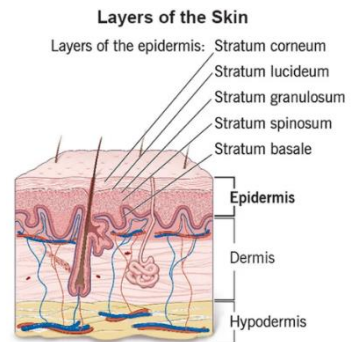
- **Trunk and proximal limbs**

- ***M. furfur*, *M. globose* and *M. sympodialis*.**

- **Common in tropics and precipitated by sun exposure.**

- When there are excessive humidity and sun exposure, the infection becomes severe.

- Versicolor means changing color. Therefore, when the patient is white, the infection causes **hyperpigmentation** (darkening of the skin), and when he's black, it is **hypopigmentation** (lightening of the skin). This effect is probably due to the carboxylic acid that is produced by yeast.



- **Carboxylic acid produced by the yeast causes the depigmentation.**

- **Clinically:**

- **Asymptomatic, non-itchy macules (بقعة) hypo or hyper pigmented.**

- **Can coalesce to form scaly plaques.**

- Look at the following picture, the patient has well-demarcated big white, brown macules, and they tend to merge together, and has some scales (قشور).



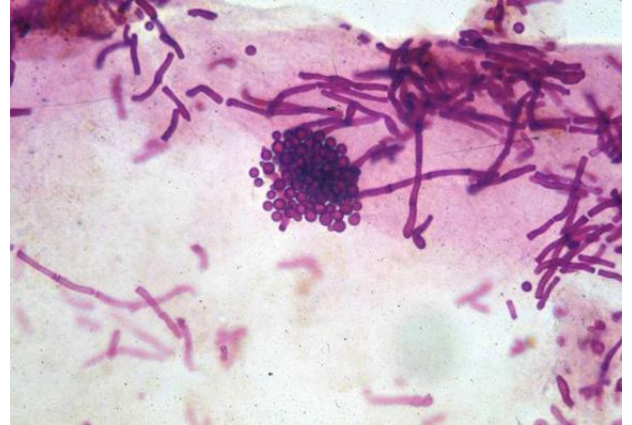
Caucasian (white) man with **hyperpigmentation**



Dark-skinned man with **hypopigmentation**

Diagnosis:

- **UV light: pale greenish colour under Wood's ultra-violet light.**
 - This device scans the lesion, and it shows orange-coppery (pale greenish) color in infected people.
- **Skin scraping then ink and KOH staining** (simply, using microscope, might be cultured sometimes).
- Look at the picture, they look under microscope as a **thick septate hyphae and clusters of budding yeast cells (spaghetti and meatballs)**.
 - Side note: **Acanthosis nigricans** may be confused with tinea versicolor. It is in the axilla and the back of the neck. It's a sign of insulin resistance and related to T2DM.



- **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.**
- **Seborrheic dermatitis:**
 - The relationship between *M. furfur* and this disease isn't well-established, because they don't follow Koch's postulates.
 - **Skin hyperproliferation with hair dandruff being the mildest manifestation.**
 - **Lesions are red and covered with greasy scales and itching is common in the scalp.**
 - ***M. furfur* has a hand in seborrheic dermatitis.**
 - **Azoles** and shampoo are of benefit when are given to seborrheic dermatitis patients.
- Pityriasis folliculitis and atopic dermatitis also have a relationship with *M. furfur*.

CUTANEOUS MYCOSES

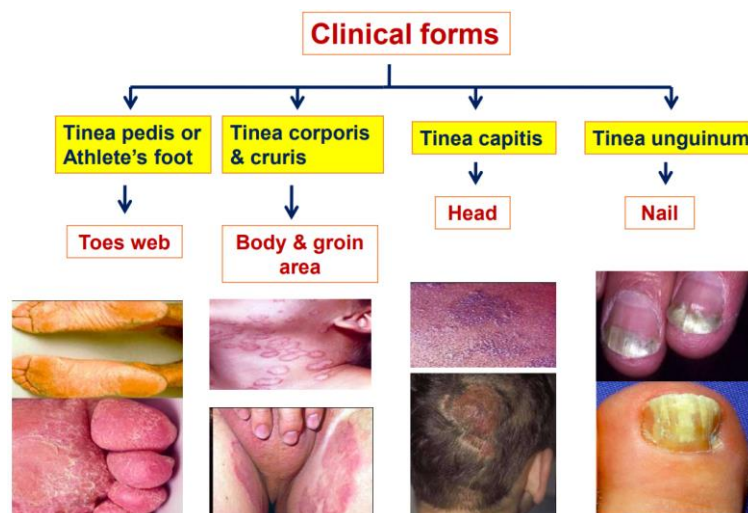
RING WORM OR TINEA

- Caused by dermatophytes (filamentous fungi/molds) which include 3 genera: *Microsporum*, *Trichophyton* & *Epidermophyton*.
- These fungi affect the keratinized tissues as skin, hair & nails (as well as the outer most layer).
 - Immunological response and symptoms (pruritus “itchy”) are present.
- Infection not spread to deeper tissues.



SOURCE OF INFECTION

1. Man to man by direct contact (Anthrophilic).
 - Usually chronic, high recurrence.
 2. From animals e.g., dogs and cats (Zoophilic).
 3. From the soil (Geophilic). (Sharing food, gym, clothes... etc.)
 - Zoophilic and geophilic are usually acute.
- The intact skin is an important barrier against infection.
 - Heat and humidity enhance the infection.



- Dermatophytes are named tinea + suffix (according to the infected site).
1. In the feet, **tinea pedis** or **athlete's foot**.
 2. Glabrous (hairless) skin, **tinea corporis**.
 - If it infects hairy skin, it's called **tinea barbae**.

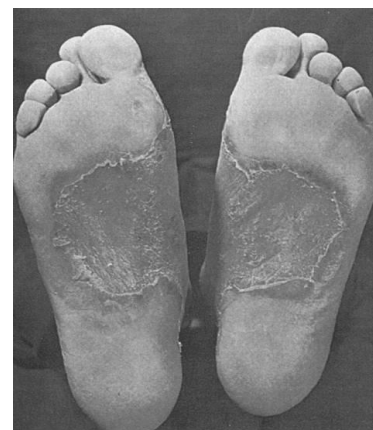
3. Proximal medial thighs, **tinea cruris**.
4. Scalps (head), **tinea capitis** (the most severe).
 - Permeant hair loss with black dots.
5. Nails, **tinea unguinum** (also called **onychomycosis**).
 - Yellow and brittle (easily breakable) nails. It's painless.

Clinical pictures:

- This is tinea corporis it's on the trunk.
- **Red, itchy scaly rash, ring like with raised more inflamed border on the body or groin.**
 - They're named ringworm because they appear like red rings with normal skin color in the center.
- **Scaling and hair loss leaving black dots.**
- **White and opaque / yellow, thickened & broken nails.**
- **DDX (differential diagnosis): Eczema, psoriasis, impetigo, alopecia, drug reactions.**



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



- **Dermatophytes of the soles**
 - Severe form, complete loss of tissue.

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.

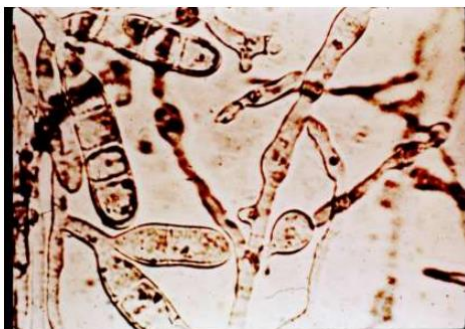
The arising colonies examined microscopically after staining with **lactophenol cotton blue stain**.

Treatment

Local antifungal cream as miconazole or oral terbinafine weeks to months

- To sum this up, we can diagnose dermatophytes infections in the first place by their ring structure, then we can confirm that by:
 - KOH and microscope method.
Note: KOH is the universal protocol for all fungal infection diagnosis.
 - Culture method by SDA then using lactophenol cotton blue stain.
- It affects hair and nails, so we can take them as specimens.

COMMON DERMATOPHYTES



Epidermophyton floccosum:

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



Microsporum:

Thick wall **spindle shape** multicellular



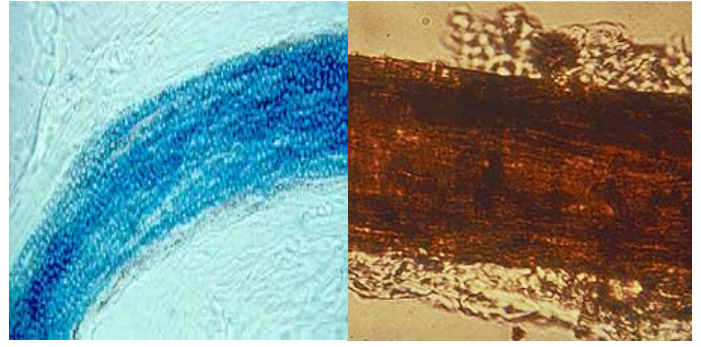
Trichophyton:

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

- Dermatophytid is the body's hypersensitivity reaction to circulating fungal antigen. Thus, symptoms now include erythema and macules in addition to ring lesions.

HAIR EXAMINATION

- The picture on the left is **endothrix**, it is a hair sample with fungal spores within the hair shaft.
- The picture on the right is **ectothrix**, the spores are outside the hair shaft.



SUBCUTANEOUS MYCOSES

MYCETOMA (MADURA FOOT)

- This infection is 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 lesion is firstly red and swollen, then it becomes like nodules (ball-shaped), then these nodules get fistula and sinuses (they start to ooze to form bridges between them), the sanguineous fluid that comes out contains granules, these granules are black in case of fungal infection.
- Usually, Madura foot doesn't invade deeper tissues, so can't be systemic. Thus, we can differentiate between it and actinomycetoma which spreads further.
- Madura foot is painless. Antifungal can't be enough to treat it; we need surgical debridement.
- The disease usually affects farmers.



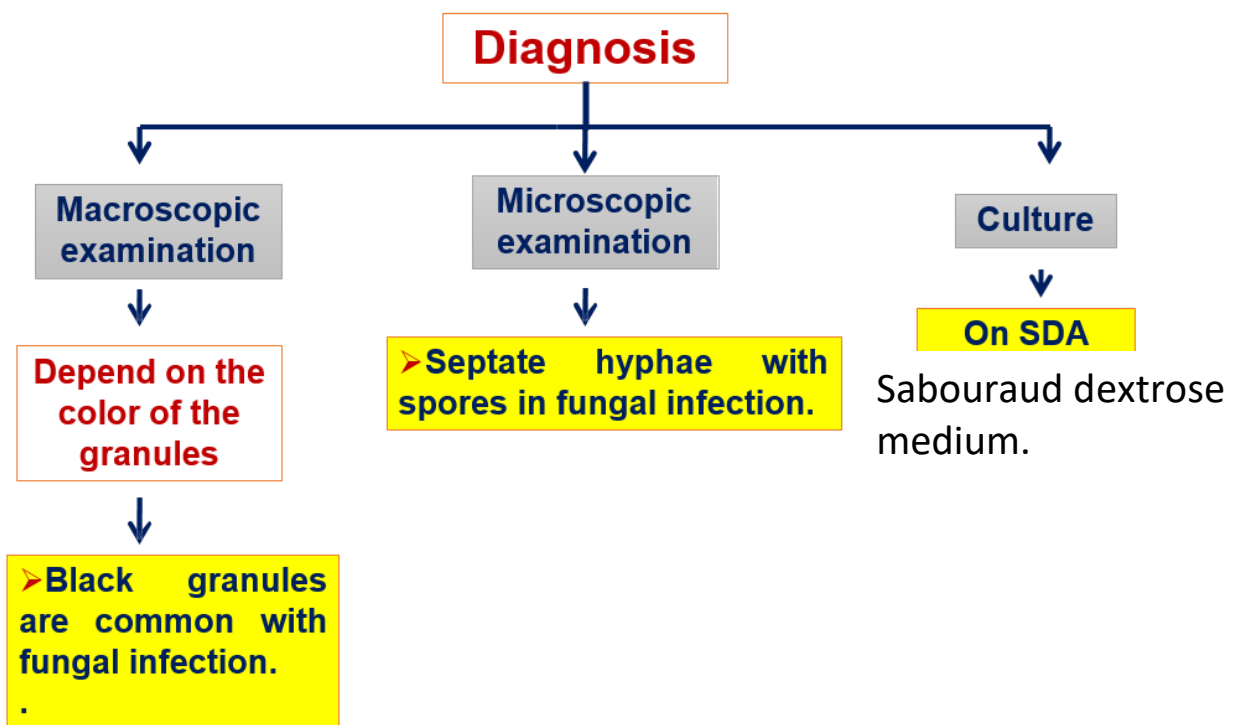
CAUSATIVE ORGANISM OF MYCETOMA

It can be divided to two types depending on the cause:

- 1 **Eumycetoma**: caused **by fungi** *Madurella mycetomatis* that have true septate hyphae.-it is painless and it contains black granules.
- 2 **Actinomycetoma**: caused by species of actinomycetes (filamentous aerobic **bacteria**) e.g: *Actinomyces Israelii*. -It is painful, also it disseminates deeper than eumycetoma -.

Clinical pictures:

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



You'll see under the microscope hyphae having Intercalary chlamyospore formation.



Madurella mycetomatis with intercalary chlamyospores

TREATMENT

1. Medical:

These are serious infections, so we need systemic antifungals such as:

- - ketoconazole
- - Itraconazole
- - Amphotericin B
- 2. Surgical:

you might need surgical intervention at any time, as patients usually come to you in late stages.

OPPORTUNISTIC MYCOSES

- 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.
- They can produce disease ranging from superficial skin or mucous membrane infections to systemic involvement of multiple organs

Patients at risk (immunocompromised patients.... Please note they can only cause disease in these patients and not immunocompetent ones) include: 1-those with hematologic dyscrasias-blood diseases- (eg, leukemia, neutropenia), 2-patients with HIV/AIDS with CD4 counts less than 100 cells/ μ L, 3- as well as those treated with immunosuppressive (eg, corticosteroid) or cytotoxic drugs.

Remember: Giving broad-spectrum antibiotics can lower our immunity by affecting commensal microorganisms in our body which normally help us defend against pathogens.

CANDIDIASIS

- *Candida albicans* is the most important of the species of candida (other species...). -such as: *candida krusei*, *candida tropicalis*-
- *Candida albicans* is oval gram positive budding yeast which produce pseudohyphae.
- It's a member of the normal flora (endogenous infection) which colonizes the mucous membranes of the upper respiratory, GIT & female genital tracts.

However, if it goes from the upper respiratory to the lungs -for example- it causes disease even with immunocompetent individuals.

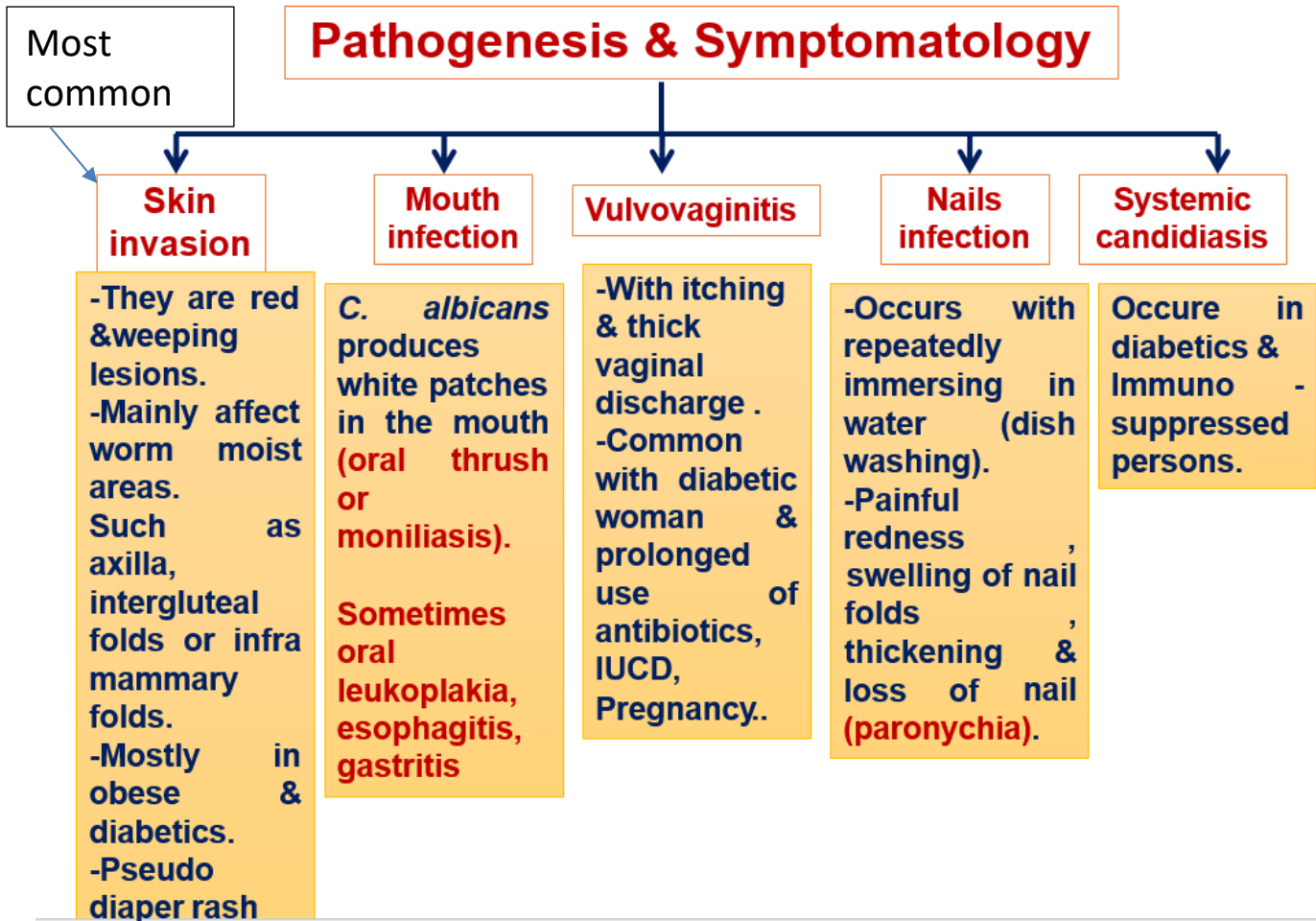
➤ **It causes superficial infections but can predominate with lowering in immunity causing infection so it is one of the opportunistic fungi.**

We have a range of candidiasis (severity) based on the localization, from cutaneous to oropharyngeal to vulvovaginitis –in females-, to systemic candidiasis which is the most severe form (candidemia: candida in blood) which can cause endocarditis –in the heart – and meningitis- in the meninges -.

PREDISPOSING FACTORS TO CANDIDA INFECTIONS

People at high risk of getting infected:

- 1- Diseases as AIDS & diabetes mellitus.**
- 2- Drugs: prolonged treatment with broad spectrum antibiotics & corticosteroids.**
- 3 - General debility (general weakness, e.g:patients in the ICU) .**
- 4 - Indwelling urinary catheters,- or vascularized catheters-.**
- 5- premature infants.**



weeping means: oozing or the fluid is inside the lesion is leaking.

IUCD: intrauterine contraceptive device *زي اللولب وما شابه*

Vulvovaginitis is characterized by the vaginal discharge which is called cotton cheese discharge

Paronychia: nail inflammation that may result from trauma, irritation or infection. It is painful and when you touch it, it will be tender.

Systemic: Candida is in the blood (Candidemia) and most probably will lead to endocarditis and meningitis.

These 2 are oral, the right one is more excessive, characterized by pseudo membrane (Dead epithelial cells+ Candida) formation



The left one is an infant infected in infragluteal fold called pseudo diaper rash, no hygiene when changing the diaper for example, the right one is around the mouth (لا يا شيببيخ)



This one is Paronychia; it is red, swollen and painful.



Candida finger web erosion : related to fatness, occupation etc.

another common type of candida infections, called candida finger web. It is most common among cooks and people who deal with hot water.

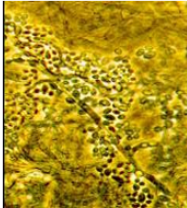


Laboratory diagnosis

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:**

a. **Germ tube test :** germ tube is formed when colonies incubated with human serum at 37 C for 30 min.

b. **Chlamyospore** formation on corn meal agar.

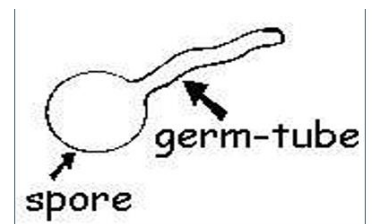
c. **Biochemical reactions:** *C.albicans* ferments glucose & maltose with acid & gas production.



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The differentiation tests in the culture are used for differentiation between the species of *Candida*.

*If this germ tube is formed, we can make sure that this is *C.albicans*.



Germ tube

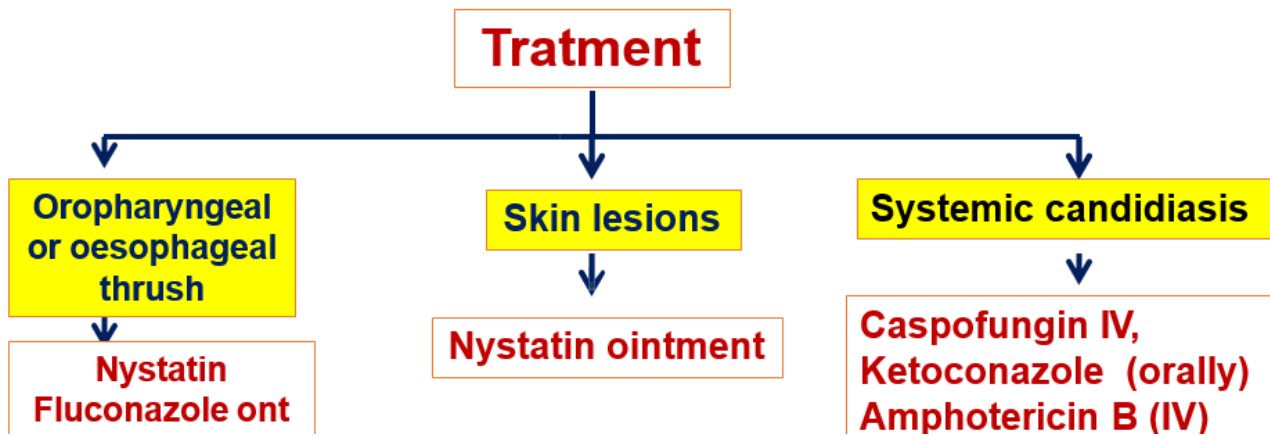
*You can see under the microscope chlamydo spores formation which are terminal (at the ends of hyphae).

This is a characteristic of *C.albicans*.

As you can see in cutaneous and the oropharyngeal topical and oral treatments are given, but systemic infections need systemic antifungals (aggressive).



Terminal Chlamydo spore & pseudohyphae



Okay we have finished our first opportunistic infection and keep in mind that it is endogenous, because the others are exogenous.

CRYPTOCOCCUS NEOFORMANS

- *Cryptococcus neoformans* –and *cryptococcus gattii*- causes cryptococcosis.
- A widespread encapsulated yeast that inhabits soil around pigeon roosts. -it is the only pathogenic yeast with a capsule-.
note: phagocytosis is the main defense mechanism against it.
-please check the last note in the correction page-
- Common infection of AIDS, cancer or diabetes patients
- Infection of lungs leads to chronic productive cough, fever, and lung nodules. –infection happens due to the inhalation of corresponding spores (or conidia)-
- Dissemination to meninges and brain can cause severe neurological disturbance and death. (It is neurotropic – prefers to migrate to neurons)

DIAGNOSIS

Microscopic

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

Cerebrospinal fluid sample, we add 'India ink stain' which stains the capsule. But it might miss up to 50% of the cases.

- **Extra explanation:** India ink is a negative stain, meaning that it stains the background, and the capsule stays unstained.

Culture

- Bird seed agar
- Routine blood culture
- PCR

ASPERGILLOSIS: DISEASES OF THE GENUS *ASPERGILLUS*

- Very common airborne soil fungus
- 600 species, 8 involved in human disease; *A. fumigatus* most commonly- it is the most common type and causes fungal allergies +infections -.
- Serious opportunistic threat to AIDS, leukemia, and transplant patients

The infection causes allergies, which can be in the form of Allergic rhinitis (inflammation of the inside of the nose) or bronchopulmonary constriction (asthma), **AND** it can affect the alveoli causing Extrinsic allergic alveolitis.

- Infection usually occurs in lungs (if the patient had cavities in the lungs for any reason, for example he had pneumonia which formed these cavities) – spores germinate in lungs and form fungal balls-also called aspergilloma-; can colonize sinuses, ear canals, eyelids, and conjunctiva- it colonizes cavities-.

Note : the doctor said that aspergilloma and fungal balls are invasive but google doesn't agree 😊.

- Bronchopulmonary allergy or Invasive aspergillosis in preformed cavities can produce necrotic pneumonia, and infection of brain, heart, and other organs.
- Surgery-to remove the cavities or you might need to remove the lobe of the lung-, **Amphotericin B(systemic) and nystatin.**

ZYGOMYCOSIS

- Zygomycota –also called zygomycetes or Mucoromycetes- are extremely abundant saprophytic- obtaining food by absorbing dissolved organic material- 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 (DKA) 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-The likely outcome or course of a disease; the chance of recovery-: **very poor**. - the patients don't live for a long time-

The doctor said it is very rare but they have seen some cases.

PNEUMOCYSTIS

- *Pneumocystis jirovecii*-also called *pneumocystis carinii*- is the cause of a lethal pneumonia (interstitial pneumonitis) in immunocompromised persons, particularly those with AIDS.
- Definite diagnosis of pneumocystosis depends on finding organisms of typical morphology in appropriate specimens (Sputum, BAL-bronchoalveolar lavage-)

BAL is used to collect a sample from the lungs for testing, when the patient cannot produce بلغم.

- The organism cannot be cultured. - it is an obligate extracellular-
- **TMP-SMX-Trimethoprim-sulfamethoxazole-** is treatment of choice

ENDEMIC MYCOSIS

They affect immunocompetent individuals. So of course they can effect immunocompromised individuals and in this case, they will be more severe.

- **Endemic mycosis is caused by a thermally dimorphic fungus (in the body they are yeast and outside it they are hyphae), and the infections are initiated in the lungs following inhalation of the respective conidia.**
- **Each of the four primary systemic mycoses—coccidioidomycosis -caused by coccidioides immitis, they have special spores called spherules-, histoplasmosis-caused by histoplasma capsulatum, it **doesn't** have a capsule-, blastomycosis – caused by blastomyces dermatitidis-, and paracoccidioidomycosis-caused by paracoccidioides brasiliensis-is geographically restricted to specific areas of endemicity.- north and south America and Mexico-**
- **Most infections are asymptomatic or mild and resolve without treatment. However, a small but significant number of patients develop pulmonary disease.**

They have a skin test like the one for TB but again it only shows the past exposure and we can't know when the individual got infected.

*The one who loves the journey,
will walk further than the one
who loves the destination.*

If you're still able to do more, don't forget to watch sketchy videos ;)

V2:

- **Page 15, extra explanation:** India ink is a negative stain, meaning that it stains the background, and the capsule stays unstained.

V3:

- **Page 2,** Recall that dimorphic fungi are hyphae when they are non-pathogenic (~~normal flora~~), and yeasts when they are pathogenic.
 - Delete normal flora, they can't be normal flora, whenever they get to the body, they're pathogenic.
- **Page 4,** The relationship between ~~these two diseases~~ isn't well-established, because they don't follow Koch's postulate.
 - It's "between *M. furfur* and seborrheic dermatitis".
- **Page 4,** Pityriasis folliculitis and atopic dermatitis also have a relationship with ~~tinea versicolor~~.
 - *M. furfur*.
- **Page 15,** note: phagocytosis is the main defense mechanism against *C. neoformans*.
 - The doctor might have meant it is the main defense mechanism against *histoplasma capsulatum* since it has no capsule. Furthermore, *C. neoformans* does have a capsule which aids in phagocytosis avoidance. However, it turned out it strongly induces complement activation resulting in deposition C3b on the capsule (it's an opsonin). So, it can be phagocytosed.