Sheet n. 13

Doctor 22

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Fungal Infections

As we've mentioned in the last lecture, besides fungal allergies and fungal toxins, fungal infections (mycoses) are the most medically important type of fungal diseases in humans.

Skin & Subcutaneous Mycoses

Fungal infections are categorized according to the type of tissue involved and the site of infection. Superficial and cutaneous mycoses affect the skin and dermis whereas subcutaneous mycoses may affect fascia and the muscle.

1- **Superficial mycoses affect the outermost layer of the skin, also known as the stratum corneum, with no living tissue invasion and therefore no or little tissue destruction. A consequence of this is the lack of an immune response to these infections, and patients mainly desire treatment for cosmetic purposes.**

   An example on superficial fungal infections is Tinea versicolor also known as Pityriasis versicolor. The causative agents in this type of infection are known as the Malassezia complex. This complex includes several species of Malassezia, most notably *Malassezia furfur*, *Malassezia globosa*, and *Malassezia sympodialis*.

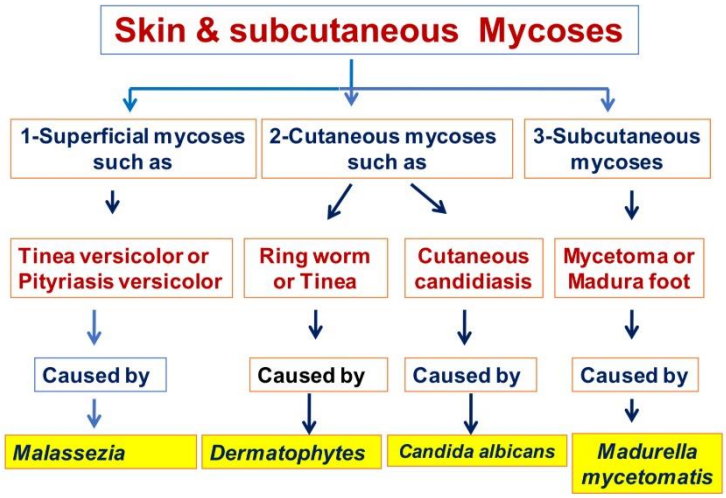
   Other examples on superficial mycotic infections are Tinea nigra and black and white piedra (both of which are not essential to know at our current level).

2- **In contrast to Superficial mycoses, Cutaneous fungal infections actually result in tissue damage and trigger an immune response (inflammation of the infected lesions) which results in obvious symptoms including itching (pruritus) and even pain in some conditions.**

   Examples on cutaneous mycotic infections include Ringworm infections caused by Dermatophytes (consist of three genera: Epidermophyton, Microsporum, and Trichophyton) and another example is Cutaneous candidiasis caused by *Candida albicans*.

3- **Subcutaneous mycoses also result in tissue damage, which in turn triggers the body's immune system, resulting in inflammation and the symptoms that accompany it. As mentioned previously, in order for these infections to reach subcutaneous tissue layers, traumatic implantation is required, which may be due to skin cuts, abrasions, maceration (softening and breakdown of the skin due to prolonged exposure to moisture), and even burns.**

Subcutaneous mycoses includes Chromoblastomycosis as well as Sporotrichosis (also known as rose gardener's/handler's disease) which is caused by Sporothrix as mentioned in the previous lecture. In this lecture we will focus on another type of subcutaneous mycoses known as Eumycetoma or Madura foot, caused by Madurella mycetomatis.



Superficial Malassezia Infections

-They are lipophilic yeast, round in shape, and are normal commensals of the skin (part of the normal skin microflora) in both humans and animals. This means that they are non-contagious infectious agents that originate from one's normal microbiota (as opposed to dermatophytes which are communicable).

As long as they are part of the normal flora, they appear to be in their nonpathogenic yeast shape, as single oval cells. As soon as they become pathogenic however, they are presented in their short angular hyphal form (spaghetti and meatballs appearance).

-They can cause skin infections (Tinea versicolor) and catheter associated infections, especially in patients that undergo intravenous administration of lipids in the ICU. Malassezia can also cause fungemia especially in premature infant hosts.

***Note: Their transformation from single cell yeast to hyphae once they become pathogenic isn't a sign of thermal dimorphism, which is distinguished as being heat induced transformation (even at body temperature, Malassezia may be in the yeast form if they aren't pathogenic).**

Pityriasis versicolor:

-Pityriasis versicolor is an infection that only affects the stratum corneum (the outmost layer of the epidermis) especially in the trunk region -including the chest, abdomen, back, and even parts of the neck and face- as well as proximal limb surfaces.

-The causative agents responsible for Pityriasis versicolor are species of the Malassezia genus, such as Malassezia furfur.

M. furfur, M. globosa, M. sympodialis, M. obtusa, and M. restricta are all species part of the Malassezia complex that most commonly cause Pityriasis versicolor in humans.

-This condition is more common in tropical regions where there are elevated humidity levels. Malassezia is also precipitated by more sun exposure.

-It is believed that the production of carboxylic acid by the Malassezia species is responsible for the depigmentation of the lesions that result from this condition.
These lesions are characterized by discoloration (either hyperpigmentation in individuals with light skin tones or hypopigmentation in individuals with darker skin tones).

Clinical observations:

- Clinically, patients with Tinea versicolor are asymptomatic with non-itchy hypo or hyper pigmented macules (discolored patches of the skin).
Due to their lack of symptoms, people with Pityriasis versicolor usually don't realize that they are affected unless they themselves notice the macules or other people inform them.

The clinical description of the observed skin lesions is that they are well demarcated, yellow/white/pink lesions.

-These lesions often tend to coalesce (gather) to form scaly plaques / fine scales.

(If a sample of these scales is taken, treated with potassium hydroxide, and observed under the microscope, Malassezia would be seen in the shape of hyphae with what is known as the spaghetti and meatballs appearance.)

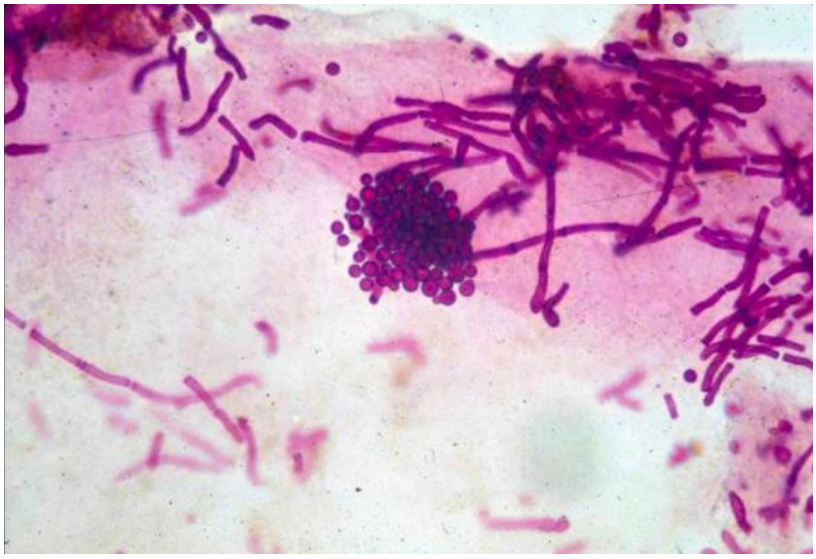
The discoloration usually occurs according to the background pigment of patient. Caucasians will usually be affected by hyperpigmentation, as opposed to people with darker skin tones, which will usually be affected by hypopigmentation. This discoloration is where the name versicolor (changeable in color) comes from.

Diagnosis:

Diagnosis of Pityriasis versicolor is usually very simple as clinical inspection of the skin lesions may only be required.

-UV light may also be used, revealing a pale greenish color under Wood's ultra-violet light or even showing a coppery orange tone.

-For more specific diagnosis, shallow scale samples are taken via skin scraping and are treated with ink staining and potassium hydroxide to be viewed under the microscope. Under the microscope, clusters of budding yeast cells are seen along with short angular hyphae that tend not to be septate (this indicates that some have turned pathogenic). This is referred to as the spaghetti and meatballs appearance.



Treatment:

-Some of these infections tend to resolve spontaneously without any extra treatment.

-If needed, treatment is done for cosmetic reasons, and is usually done by topical administration of azole containing creams/shampoos for 2 weeks, and in severe cases, oral azoles are prescribed.

-Although their treatment is usually simple with no complications, these skin lesions have a high reoccurrence rate (usually within 1 year after treatment) because their causative agent is part of the skin microflora.

*Currently not required

Tinea nigra which causes black macules on the palms and soles of the infected person and black and white piedra (black piedra results in black dots on the hair of the scalp while white piedra results in white dots on the rest of the body's hairs) are both other types of superficial mycotic infections but are out of the scope of this course.

Another type of superficial mycotic infection worth mentioning is Seborrheic dermatitis:

-Skin hyperproliferation with dandruff is the mildest manifestation of this infection.
-Lesions are red and covered with greasy scales and itching is common in the scalp.

It is theorized that Malassezia furfur is a contributing factor to the pathogenesis of this condition (it is associated with Seborrheic dermatitis and dandruff but isn't its causative agent).

This is the reason why azole compounds present in shampoos (such as in Nizoral anti dandruff shampoo) help in relieving their symptoms.

Cutaneous Mycoses

They cause tissue destruction and as a result trigger an immune response. They may involve hair and nail infections.

Examples on Cutaneous mycoses are Ringworm infections and Cutaneous candidiasis.

Ringworm or Tinea:

-Caused by Dermatophytes (filamentous fungi/molds, not yeasts) which include 3 genera: Epidermophyton, Microsporum, & Trichophyton.

-These fungi affect keratinized tissues such as skin, hair, & nails.

Infections by these fungi are characterized by ring shaped inflamed lesions and hence the name: Ringworm infections (although they aren't caused by parasites or worms).

The ring shaped lesions have red and inflamed margins that become clearer towards the center of the ring (central diminution/clearance). They are usually itchy (cause pruritus) but are not painful.

Patients suffering from a Dermatophyte infection may also show symptoms other than ring shaped lesions. Such symptoms include fluid filled blisters on their fingers and on the palm of their hands. These blisters are a result of what is known as Dermatophyte ID reactions. Dermatophtid reactions are systemic responses that occur due to circulating dermatophyte antigens.

-Infection does not spread to deeper tissues.

Source of infection:

1- Man to man by direct contact (Anthrophilic).

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

3- From the soil (Geophilic).

*Note:

It has been observed that Ringworm infections that result from Anthrophilic transmission tend to be chronic with mild symptoms but with relatively high reoccurrence rates, in contrast to infections that result from Zoophilic and Geophilic transmission.

Geophilic transmission of Dermatophytes usually results in acute and severe infections.

*Important Notes:

-Intact skin is an important barrier against infection.

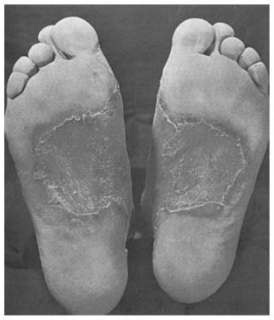
-Heat and humidity enhance the infection (increase the precipitation of Dermatophyte lesions).

Clinical forms:

Ringworm infections can also be referred to as: Tinea + a suffix that matches the site of the fungal infection (which is also the contact site where transmission occurred):

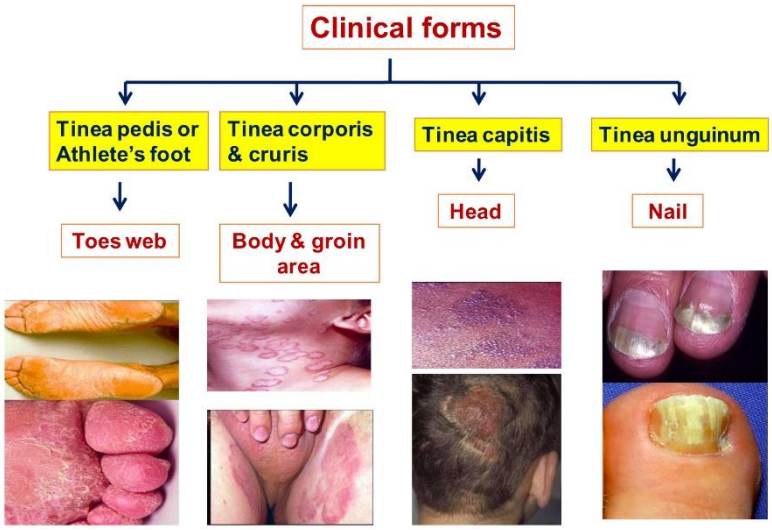
- **Tinea pedis or Athlete's foot: the infection occurs in the feet of the patient and is likely due to Geophilic and indirect transmission routes. Its most common type is Toe web.**
  Tinea pedis infection has different levels of severity which may vary from mild interdigital scalping (تسلُّخات بين أصابع القدم) to severe maceration and loss of volume of the foot.

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



Dermatophytos of the soles

- **Tinea corporis: occurs in hairless blubberous areas of the skin (may occur in any area of the body that lacks hair other than the feet, groin area, and nails).**
- **Tinea cruris: occurs in the groin and proximal thigh area, near the perineum.**
- **Tinea capitis: occurs in the scalp and affects hair follicles. Its most severe form, known as Tinea favosa, results in permanent balding and hair loss along with black dots in the area of infection.**
- **Tinea unguinum: affects nails, resulting in extremely white, opaque, or yellow nails that are very brittle and easily broken. Dermatophyte infection of nails is painless, even with all the other effects it has on the nails (unlike candida infection of nails, which results in painful inflammation and will be discussed later on in the lecture).**
- **Tinea barbae: also known as Beard Ringworm which affects hair of the beard and the neck.**



Clinical pictures:

-The clinical description of these infections is the presence of red, itchy, scaly, ring-like rashes, with a raised and more inflamed border, on the body or groin.

-These rashes/lesions result in scaling and hair loss, leaving black dots.

-This infection also may result in white and opaque/yellow, thickened & broken nails.

Ring like lesions with central diminutions

-Differential Diagnosis (DDx) of Ringworm infections:

Eczema, psoriasis, impetigo, alopecia, and drug reactions.
(all of which are conditions with symptoms similar to that of Ringworm infections, and thus need to be differentiated from them)

Diagnosis:

Diagnosis can be done either by microscopic examination or by culture:

1- Microscopic examination:

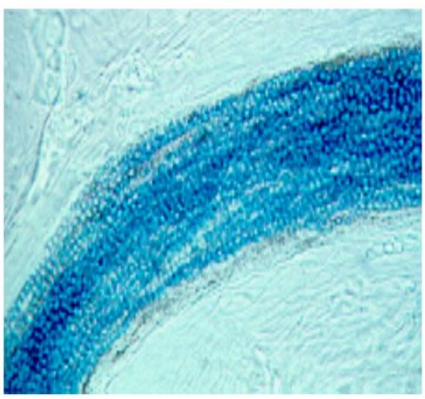
- Skin scales, nails, & hairs are examined microscopically after digestion using 10% potassium hydroxide (KOH) similar to the microscopic process of Pityriasis versicolor diagnosis (nail and hair samples are not used for Pityriasis versicolor diagnosis however).
  - Branching hyphae are detected among epithelial cells of skin & nails (with no presence of single yeast cells, unlike Malassezia infections).
  - Hyphae or spores can be detected in the hair. Spores can be either detected inside the hair (endothrix) or detected outside the hair (ectothrix).

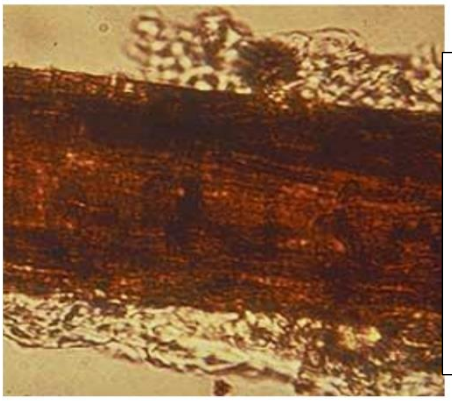
Dermatophyte infections in which spores are formed on the outside of the hair shaft, leaving the hair shaft intact, are known as ectothrix infections, while those in which the spores develop within the hair itself are known as endothrix infections.

Hair Examination

Endothrix:

Arthrospores formed within the hair shaft. As in Tinea Capitis.

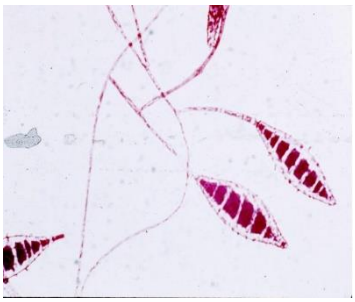


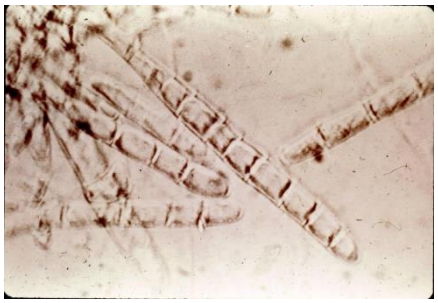


Ectothrix:

Arthrospores formed outside the hair shaft, keeping it intact.

Common Dermatophytes under the microscope:





Epidermophyton floccosum	Microsporum	Trichophyton:
Bifurcated hyphae with multiple, smooth, club shaped macroconidia/spores (2-4 cells).	Thick wall spindle shape and are multicellular.	Large, smooth, thin wall, septate, and pencil-shaped.

2- Culture:

- **Dermatophytes could also be isolated and grown in culture on Sabouraud's Dextrose Agar (SDA):**
- **The agar is incubated at room temperature for 4 ws.**
  The arising colonies are examined microscopically after staining with lactophenol cotton blue stain. This is done to specify the exact species of Dermatophytes responsible for the infection.

Treatment:

Local antifungal cream such as miconazole or oral terbinafine (an allylamine that inhibits squalene epoxidase enzyme) used for weeks to months.

Subcutaneous Mycoses

Subcutaneous fungal infections are ones that may cause inflammation in the hypodermis, fascia, muscles, or even in the cornea of the eye. These fungal infections occur due to traumatic implantation or by infiltration through wounds.

A famous example is Sporotrichosis, also known as Rose gardener's disease, caused by Sporothrix schenkii (has two forms, it either creates skin nodules or causes Pulmonary Sporotrichosis). Other examples include Chromoblastomycosis and Eumycetoma / Madura foot.

Mycetoma (Madura foot):

-Mycetoma is a chronic granulomatous infection that usually affects the lower limbs and hands.

This disease is characterized by the formation of hard nodules at the sites of infection which can transform into abscesses that are filled with purulent fluid, sinuses (nodules that open and release discharges), or fistulas (when two nodules open up on each other with no discharge).
The discharge from these nodules contains granules of a certain color depending on the causative organism of the Mycetoma.

-These infections can be caused by fungi that grow in soil & on decaying vegetation.

-The causative organism is introduced into subcutaneous tissues through trauma.

-It occurs after trauma and usually affects farmers (especially ones that work barefooted in soil fields).

Causative organisms of Mycetoma:

Mycetoma may result from fungal infections (known as Eumycetoma) or from bacterial infections (known as Actinomycetoma). In both cases, they share the same presentation and pathogenesis (chronic granulomatous infections at the affected sites).

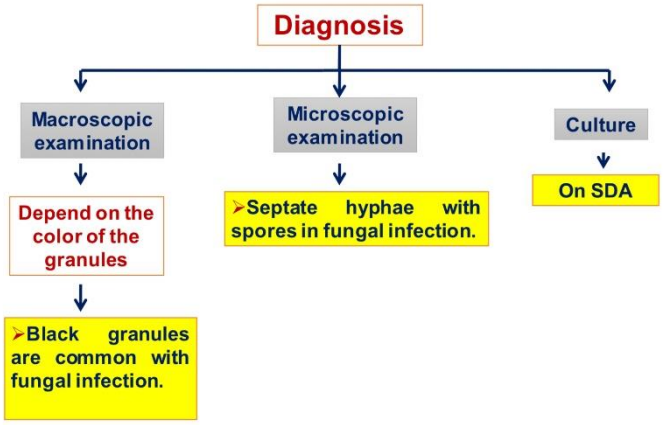
1- **Eumycetoma: caused by the fungi *Madurella mycetomatis* which has true septate hyphae.**
   The granules released from the nodules of Eumycetoma are black in color, while the nodules themselves don't cause pain (therefore the patients don't show symptoms in the form of pain).
2- **Actinomycetoma: caused by species of actinomycetes such as Nocardia (filamentous aerobic bacteria that is viewed using acid fast stain).**
   The granules released from the nodules of Actinomycetoma are not black (they are usually silver, but can also be other colors such as yellow, white, or red), while the nodules themselves are painful.

Clinical pictures:

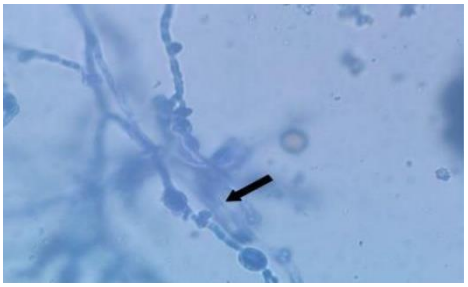
Swelling following trauma, purplish discolouration & multiple sinuses that drain pus containing yellow, white, red, or black granules.

Results in the distortion of the foot which can possibly lead to loss of function (pain in Actinomycetoma also plays a role in loss of function).

Diagnosis:



Upon taking a sample of <u>cultured Eumycetoma</u> on <u>Sabouraud's dextrose agar (SDA)</u> and viewing it under the microscope, <u>intercalary chlamydospore formation</u> can be observed (intercalary means that the spores are forming in the middle of the shafts of the hyphae rather than at their distal ends).



Treatment:

1- Medical:

- ketoconazole

- Itraconazole

- Amphotericin B (IV administration in extremely severe cases)

2- Surgical:

Sometimes medical treatment using only Antifungals is not enough in advanced cases and surgical debridement of the hard nodules is required.

Now let's see the difference between <u>OPPORTUNISTIC FUNGAL INFECTIONS</u> and <u>ENDEMIC SYSTEMIC FUNGAL INFECTIONS</u>.

Immunocompetent individuals are usually resistant to opportunistic mycosis, but in the case of immunocompromised patients or if the fungi gained new virulence features, it'll become pathogenic. On the other hand, in endemic systemic fungal diseases, even immunocompetent individuals are susceptible to be affected with them (but they have certain geographical distributions).

We must remember that immunocompromised patients' numbers have increased due to increased numbers of AIDS patients, congenital immunodeficiency patients, cancer patients, organ transplantation patients, and even patients who take broad-spectrum antibiotic. Therefore, fungal infections are in the top differential diagnosis in the ICU since these patients are given broad-spectrum antibiotic (it protects all patients from bacterial infections but not fungal infections).

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

Opportunistic Mycosis

- **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 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.**

Candidiasis:

Might be cutaneous, mucocutaneous, or systemic candidiasis in the form of fungemia (candidemia).

- **Candida albicans is the most important species of candida (other species…).**
- **Candida albicans is an oval gram-positive budding yeast which produces pseudohyphae.**
- **It colonizes (meaning that it's part of the normal flora) the mucous membranes of the upper respiratory, Upper GIT (on the mucous membranes) & female genital tracts.**

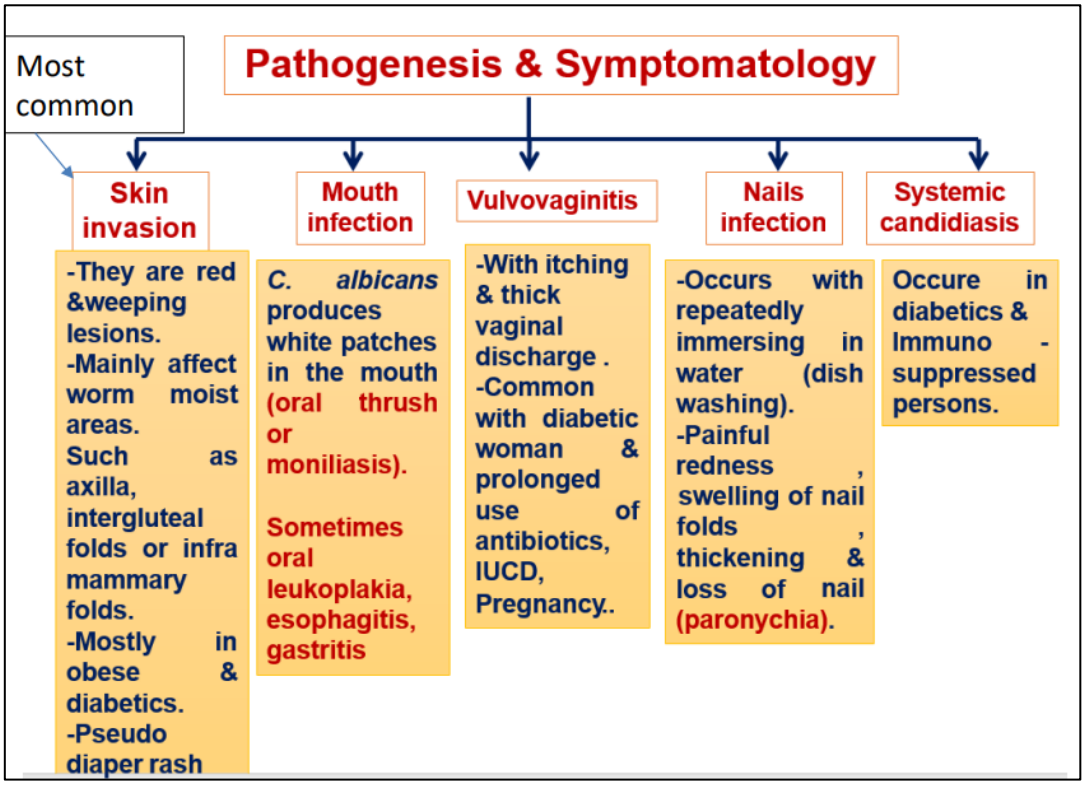
Who is affected by candidiasis?

- **It's your own flora so if you become immunocompromised, you'll be affected.**

- A special case is when there is a direct contact with vesicular lesions, an example is when a baby is born by normal vaginal delivery there is a direct contact when the baby passes through the birth canal.

Predisposing factors to Candida infections:

1. Diseases as AIDS & diabetes melllitus.
2. Drugs: prolonged treatment with broad spectrum antibiotics & corticosteroids.
3. General debility (general weakness, e.g: patients in the ICU).
4. Indwelling urinary catheter (foley's catheter), venous catheter and arterial catheter which is an invasive procedure.



-Skin invasion: Cutaneous candidiasis (in humid areas).

-Pseudo diaper rash is named so because other skin invasions are in body folds, but the diaper rash is because of contact dermatitis (the diaper is not in direct contact with infra gluteal folds, but it compresses it).

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

- Every AIDS patient suffers or has suffered from oral thrush in his/her life.

-IUCD: Intrauterine contraceptive device (مثل اللولب).

-Vulvovaginitis is characterized by the vaginal discharge (also called cotton cheese discharge).

-Candida's discharge is white and creamy, but in psychromonas vaginalis the discharge is green, yellow and frothy (with smell).

-Pregnancy is considered to be an immunosuppressive condition.

-Systemic candidiasis in AIDS patients and impaired cell mediated immunity patients is in the form of candidemia which mainly affects the respiratory tract, joints and causes meningitis.

The picture on the left shows a newborn with a whitish color on his lower lip which is a cutaneous candidiasis, the picture on the right shows an adult with oral thrush.

This picture shows a paronychia: Inflamed nail fold, red and painful (to be more specific it's tender).

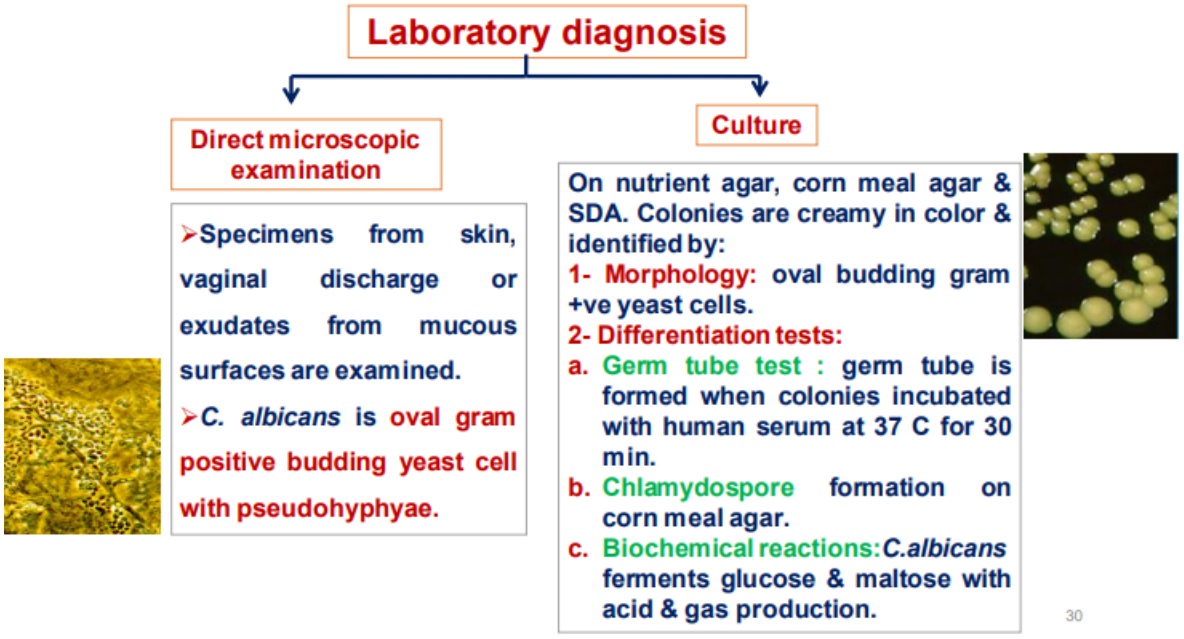
The difference between tender and pain; the patient tells you when it's painful, but tender is when you press the area then it becomes painful.

"Pain is patient's perception, while tenderness is a sign that a clinician elicits."

The picture on the left shows a pseudo diaper rash (there are lesions inside the infra gluteal fold).

The second picture shows what happens if there is not enough hygiene, for example after the mother changes the diaper, she would touch the baby's mouth which will infect the mouth too.

Another case in cutaneous candidiasis is called fingerweb erosion in people who always wash dishes, chefs and cooks who deal with vegetables.

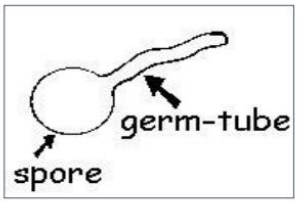


Diagnosis depends on the area: skin, vagina and GIT (the infection might be in the oral cavity only or it might affect the esophagus causing esophagitis or affect the stomach causing gastritis or even affect the lower GIT).

In the direct microscopic examination, we treat the swap with potassium hydroxide then we use the microscope which will show us a single oval budding yeast if there was an infection.

In culturing, we cultivate it in Sabouraud Dextrose Agar (SDA), and we'll see white, creamy globous smooth waxy colonies (*the description of Candida albicans*). To know the species, we cultivate it in a chromogenic agar.

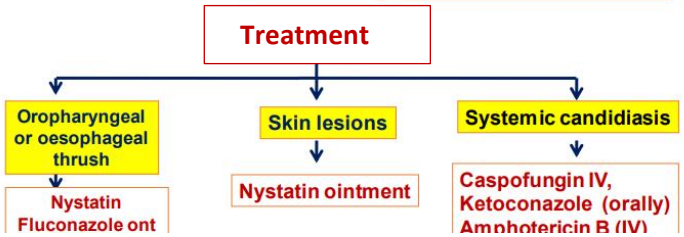
Germ-tube formation is a differential sign for *candida albicans*. We see terminal chlamydospore & pseudohyphae when we use corn meal agar.



Germ tube


Terminal Chlamydospore & pseudohyphyae

Treatment depends on the infected part and the severity of candidiasis.



Cryptococcus neoformans:

Another opportunistic yeast infection is cryptococcosis, it is an exogenous infection, yeast, single cell caused by *Cryptococcus neoformans*. It's related to the occupation or the lifestyle especially in the soil where there is bird dropping so it's common in people who keep birds (breeders) and if they were immunocompromised, they might develop severe cryptococcosis.

When inhaling the spores of *Cryptococcus neoformans,* especially the neurotropic spores, they tend to travel to the central nervous system causing meningitis, that's why in diagnosis we take CSF (cerebrospinal fluid) samples.

- **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

1-Microscopic diagnosis

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

This technique shows a halo around the fungi. Note that in this lecture *Cryptococcus neoformans* is the only capsulated fungi (even *Histoplasma capsulatum* fungi is not capsulated). This test's sensitivity is only 50-80% so if you didn't find *Cryptococcus neoformans* in it this doesn't mean that the patient does not have it so we use another test with higher sensitivity called Latex Particle Agglutination.

2-Culture

- **Bird seed agar**
- **Routine blood culture**

3-PCR (PCR searches for genes but the presence of genes does not always mean there is an expression for these genes).

(If it was by inhaling spores into the respiratory tract, it's called acute, if it infects the brain/meninges then it's called systemic).

Aspergillosis:

Another opportunistic fungal infection is 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 cavities can produce necrotic pneumonia, and infection of brain, heart, and other organs.**
- **Surgery, Amphotericin B and nystatin**

There are three species for medical importance: *Flavus* and *parasiticus* in aflatoxins, *fumigatus* in allergies.

So, the simplest form in aspergillosis is allergic rhinitis, if it goes deeper however, it's visualized as an asthma so it's IgE mediated (bronchopulmonary aspergillosis). If it reaches the alveoli then it causes extrinsic allergic alveolitis and if the patient has already preexisting lung lesions, there'll be a formation of cavitary lesions instead of the previous lesions and they'll be filled with fungal balls aspergilloma (fungoma).

Patients with predisposing factors like AIDS, leukemia, and transplant patients, might develop invasive aspergillosis, if it was in the lungs, it'll cause interstitial fibrosis and might reach the brain and meninges. If it was caused by burns, it'll result in cellulitis, in these cases antifungal drugs are not enough and they need a surgery.

Zygomycoses:

- Zygomycota –also called zygomycetes or Mucoromycetes- are extremely abundant saprophytic fungi found in soil, water, organic debris, and food.
- The genera most often involved are Rhizopus, Absidia, and Mucor.
- Usually, harmless air contaminants invade the membranes of the nose, eyes, heart, and brain (cerebrum) of people (Rhinocerebral mucormycosis) with diabetes (diabetic ketoacidosis) and malnutrition, with severe consequences (usually causes death after a few days or a week).
- The 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 (or the underlying risk/predisposing factor), surgery & amphotericin B

Prognosis: very poor.

Pneumocystis:

- Pneumocystis jirovecii -also called pneumocystis carinii- (in the old days it was considered a parasite but now it's considered a fungi) is the cause of lethal pneumonia (atypical pneumonia), interstitial lung fibrosis or even the typical pneumonia (not the pneumonia caused by streptococcus pneumonia) in immunocompromised persons, particularly those with AIDS.
- Can't be cultured ex vivo or isolated in the laboratory, we can see it in a histopathology section under eosin methylene blue staining as honeycomb appearance or we can use silver staining.
- 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 (trimethoprim/ sulfamethoxazole and in health centers they call it cotrimoxazole) is a treatment of choice.

Endemic Mycosis

- Endemic mycosis is caused by a thermally dimorphic fungus (if we are talking about dimorphic fungus, we have the four that are mentioned below and an extra one which causes rose-gardener's disease), and the infections are initiated in the lungs following inhalation of the respective conidia (spores).
- Each of the four primary systemic mycoses—Coccidioidomycosis, Histoplasmosis, Blastomycosis, and Paracoccidioidomycosis—is geographically restricted to specific areas of endemicity in north and south America (so they can infect immunocompetent people).
- Most infections are asymptomatic or mild and resolve without treatment. However, a small but significant number of patients develop pulmonary disease.
- They also affect immunocompromised patients with more severe disease, and all these diseases begin with the inhalation of spores in the respiratory tract.

The End~

اللهم ارزق إخواننا في فلسطين الصمود والقوة في وجه الطغيان وانصرهم.

اللَّهُمَّ أَنْجِ المُسْتَضْعَفِينَ مِنَ المُؤْمِنِينَ.

اللهم انصر ضعفهم ورد إلينا المسجد الأقصى ردًا جميلًا.

اللهم إنّا نبرأ من حولنا وقوّتنا وتدبيرنا إلى حولك وقوّتك وتدبيرك لا إله إلا أنت لا يعجزك شيء وأنت على كل شيء قدير.

اللهمّ إنّي اسألك فهم النبيّين، وحفظ المرسلين والملائكة المقربين، اللهمّ اجعل ألسنتنا عامرة بذكرك، وقلوبنا بخشيتك، وأسرارنا بطاعتك، إنك على كل شيء قدير.

V2

White and creamy instead of white and green (pages 15 &16)