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Microbiology

Doctor 2017 | Medicine | JU

Sheet Slides

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Fungal infections

Outline of lecture:

1- Skin infections (superficial/cutaneous/subcutaneous)
2- Opportunistic infections
3- Endemic or systemic infections (briefly) because the species responsible of them are geographically restricted; found only in ……..

As we said, there are **three entities of fungal diseases**, the first one is fungal allergies especially with aspergillums species, the second; mycotoxitocis aphlatoxin b1 and the third is fungal infections collectively known as mycosis. Fungal infections are classified based on type tissue infected, we'll start with skin infections which are common.

1. Superficial infections: infection of the outermost layers of skin, hair, and nail.

there is no tissue damage or living tissue injury, it's just as simple as colonization, no inflammatory response elicited, and no pathologic changes taking place. Therefore, it is not destructive and if left untreated it wouldn't be harmful for the patient.

- It's only of cosmetic importance.

Example 1: pityriasis versicolor (the most common)

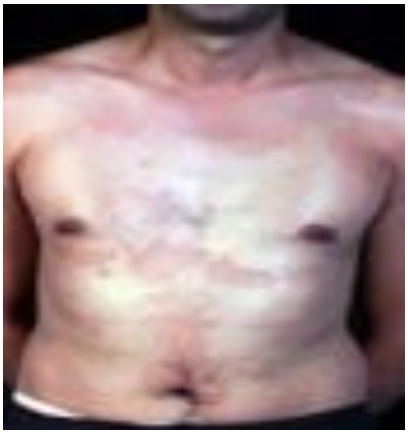
Causative species: malessezia furfur complex (lipophilic yeast)

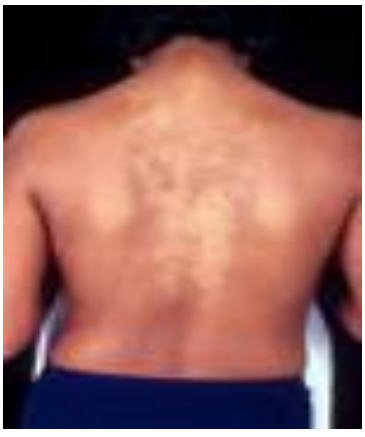
- Normal commensals (normal flora) of skin in animals and humans
- this complex has many species, the most common are M. furfur and M. globosa, and M. symbodiaris. They cause **depigmentation** of skin represented by hyper/hypo-pigmented macules on skin.
- Can cause skin infections and catheter associated infections

- Occurs in healthy individuals, common in tropical, and usually precipitated by excessive exposure to sunlight.
- Skin (stratum corneum) infection

Caucasian people(light-skinned) → hyperpigmentation (one of the most common forms of disease)

Dark-skinned →hypopigmentation (depigmentation)





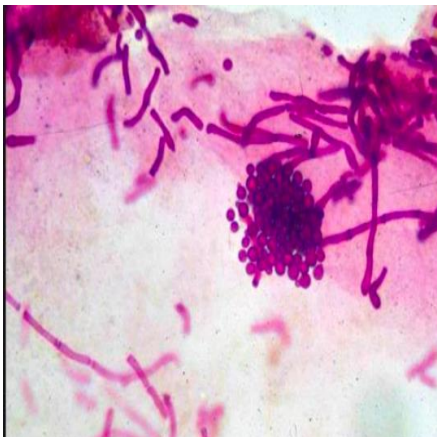
Note: The color varies according to: 1- normal pigmentation 2- exposure to sun 3- severity of disease

Pathogenesis: It's believed that the carboxylic acid produced by them is responsible for the depigmentation or hyper-, by changing melanin concentrations.

Characteristics: Chronic infection, with well-demarcated white, pink or brownish lesions, often qualisapes and covered with furfusious skin scales

Clinically: Asymptomatic, non-itchy macules hypo or hyper pigmented, can coalesce to form scaly plaques

Location: Upper chest, trunk, proximal limbs, and rarely on neck and face



Diagnosis: as mentioned in introductory lecture we rely in the laboratory on microscopic examination after treating the sample with KOH.
We can examine it either by direct visualization or by adding carboflore stain which requires immune-fluorescent microscopy.

- Or under UV light: pale greenish color under Wood's ultra-violet light
- Skin scraping then Ink and KOH staining

The picture is showing thick septate hyphae, and clusters of round oval budding yeast cells, collectively they appear like "spaghetti and meatballs"

- Culture preparation is not necessary with superficial mycotic infections.

Treatment: if needed for cosmetic reasons

- ❖ Some resolve **spontaneously**
- ❖ **selenium sulfide** ointment/cream
- ❖ Topical **azoles** cream/ shampoo for 2 weeks or in severe cases use oral azoles
- Recurrence is common

Example 3: seborrheic dermatitis (a small entity)

- Skin hyper-proliferation
- Seborrheic dermatitis is a collective term, and the simplest/mildest manifestation is hair dandruff which is an inflammation of the head scalp in which it becomes dry, itchy, and red lesions are formed covered with greasy scales.
- There's a **hypothesis** that states that **M. furfur** is the causative agent or at least a major attributer in the **seborrheic dermatitis**. It also suggests that malessezial infections speed up the skin renewal cycle, and this causes the white scales (dead skin).

- ❖ **The hypothesis is proved by**: antifungals; as it helped a lot with seborrheic dermatitis treatment as well as dandruff
- ❖ **Treatment**: azoles

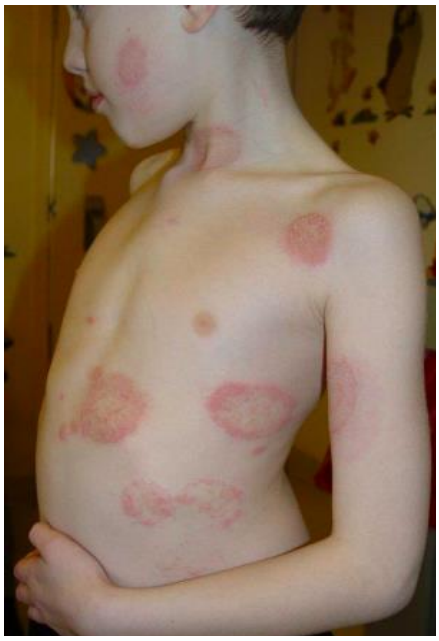
Other Examples:

Tinya nigra**, White** nigra **& Black** nigra

2. Cutaneous infections

Are infections in the outermost layer of the skin, hair, and nail, **but** they elicit an immune response and produce minimal pathologic changes which are caused by fungi itself or its metabolites.

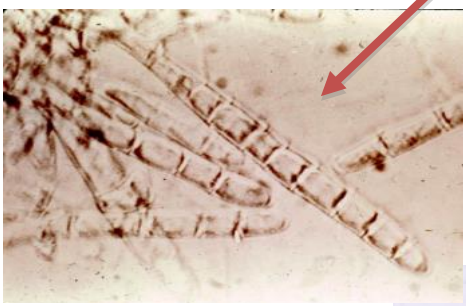
Example 1: Dermatophytosis

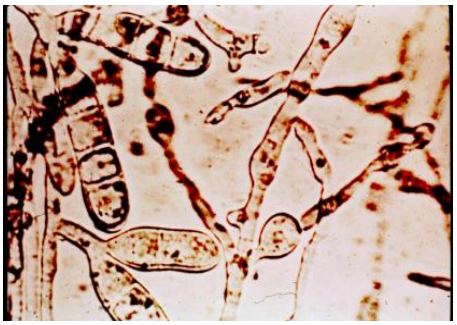


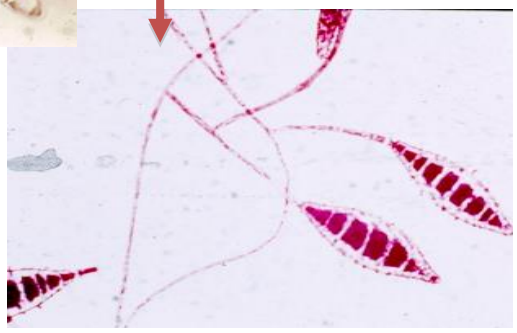
- Another name is "ring worm disease" because of the typical pattern of macules formed on the body as they appear as red, itchy scaly rash, ring like with raised inflamed border on the body **or** groin, with diminishing of inflammation toward the center which appears as clear circle.

➢Also, scaling and hair loss leaving black dots.

Causative species: Dermatophytes (filamentous fungi / molds), include 3 genres: epidermophyton+ trichophyton + microsporum.







Pathogenesis: this infection affects keratinized tissues as skin, hair, and nails. the three organisms have keratinase which gives them the ability to utilize keratin in the skin as a nutrient source due to their enzymatic activity. (symbiotic relationship) - They don't invade subcutaneous or deep tissues.

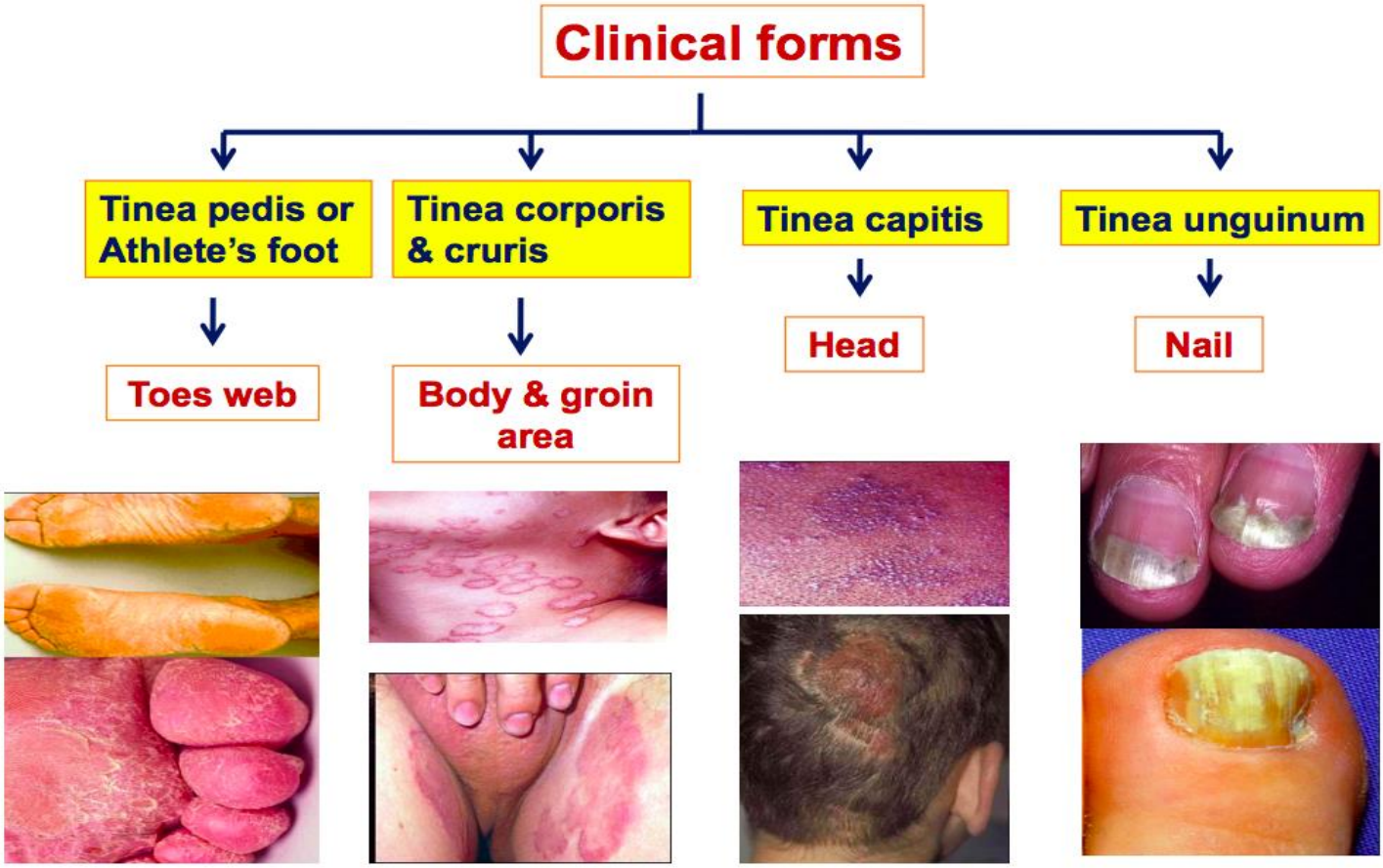
➢The intact skin is an important barrier against infection.

➢Heat and humidity enhance the infection.

Transmission (sources of infection):

1- **[Anthrophilic transm.] directly by human contact:** the scales contain viable fungi so they are infectious elements, and may remain infectious for months or years.
2- **[Zooephilic transm.] From infected animal**
3- **[Geoophilic transm.] indirectly from intimate objects:** when skin scales reach clothes /carpet/wardrobes/swimming pools/ dusting …..

- zooephilic + geophilic → acute diseases
- anthrophilic → chronic diseases, that's why human to human transmission they might take ……for long periods (years)



Localization: the localization of 1ry infection corresponds to the contact site with dermatophytes. Clinically divided into;

- **Tinya pedis**, known as "athlete's foot": lower limb and foot: laceration in back of the foot. Cause by trychophyton
- **Tinya corporis**: infection of glaburous skin (smooth, hairless)
- **Cruris**: perineum, buttocks, and proximal aspect of medial thigh.

- Usually in males
- it's believed that it originates from tinya pidis (it may develop after tinya pidis)

- **Tinya capitis**: skin and scalp hair

- **Tinya pardi:** in bearded area in men
- **Tinya anguium**: when the nail is infected "oncomycosis". White and opaque / yellow, thickened &broken nails.

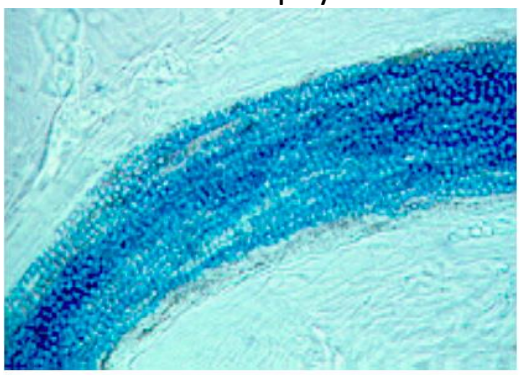
➢ So as we said, the classical pattern of dermatophytosis is the ring worm**:** inflammatory

> Note*: oncomycosis is also caused by candida infection. The main difference between the two is that candida infection causes painful oncomycosis.*

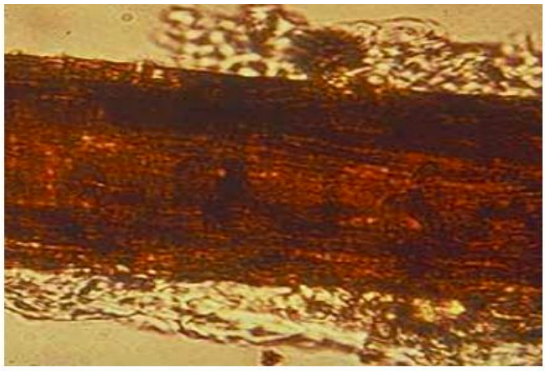
scaling with diminishing of inflammation towards the center.

- **Endthrix and Ectothrix:**

Endothrix: dermatophyte infection of hair that hair shaft and internalize into the cell.
Exothrix: dermatophyte infection remains confined in the hair surface only.



Endothrix



Ectothrix

Diagnosis:

- Microscopy: Skin scales, nail & hair are examined microscopically based on morphology after digestion using 10% KOH. Branching hyphyae are detected among epithelial cells of skin & nails.
- Culture: 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.
- Hyphae or spores are detected in the hair. Spores either detected inside the hair (endothrix) or outside the hair (ectothrix).

Treatment: usually you start with

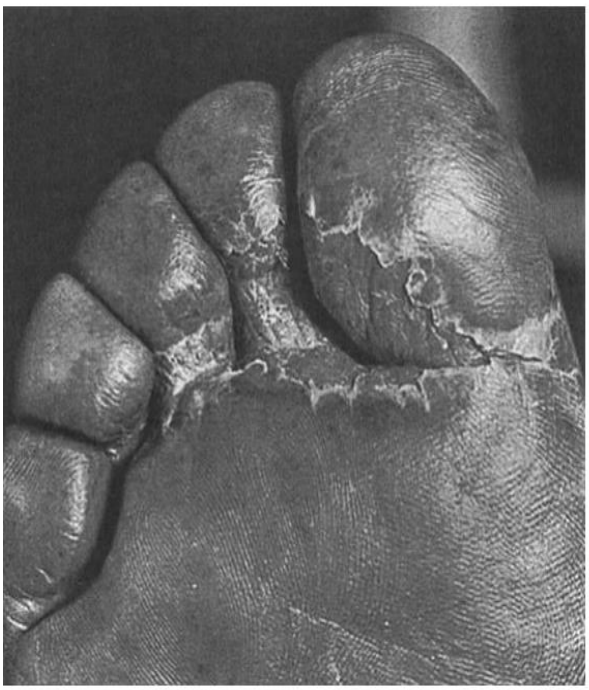
❖ Local **antimycotic** cream as miconazole (Topical)
❖ In cases of massive infection of hair and all nails: oral **allilamine agents like** terbinafine, weeks to months
❖ oral **azole compounds**

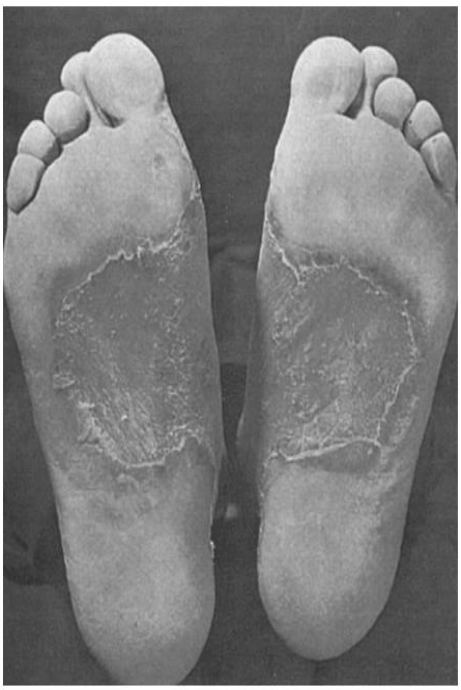
(Refer to pictures in the next page)

Example 2: Candidiasis

(discussed later in opportunistic infections since it's a wide spectrum of diseases .)

- **Candidiasis** can be cutaneous (superficial) and opportunistic (systemic).



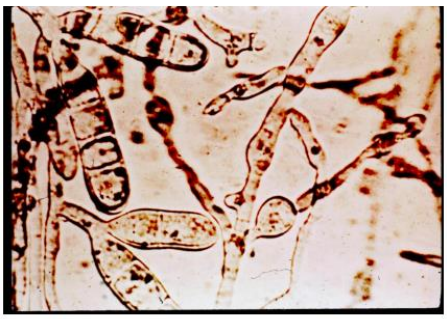


- Tinea pedis showing interdigital scalping
- *T. mentagrophytes*

Dermatophytos of the soles

- on the left, mild maceration under the big toe. More severe infection with extensive maceration of soles is shown in the right picture.

Common Dermatophytes



Epidermophyton floccosum:

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

Microsporum:

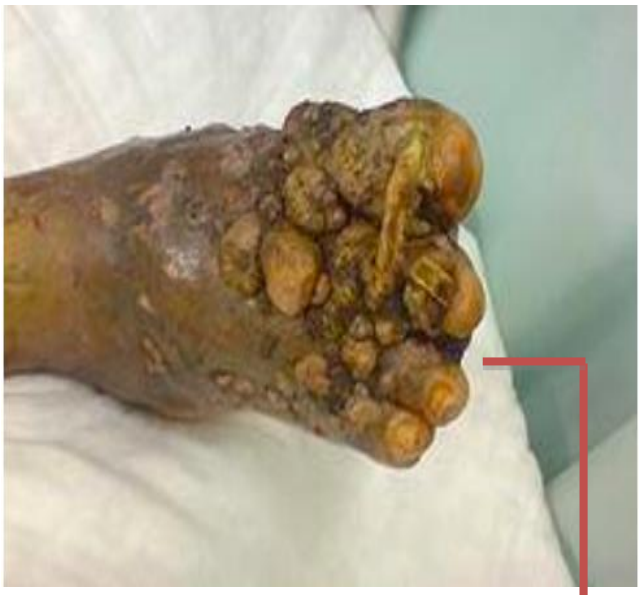
Thick wall spindle shape multicellular

Trichophyton:

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

Madura foot / "farmer foot disease"

The most common infection is Madura foot. Further, this infection usually affects barefooted farmers. Usually occur through traumatic inoculation of **saprophytic bacteria** (lives in soil or on decaying vegetations).



➢**Mycetoma** is a chronic granulomatous infection usually affects the lower limbs and hands.

- Types of subcutaneous **mycetoma** :-

1- **Eumycetoma:** caused by fungi; Madurella mycetomatis which have true septate hyphae.

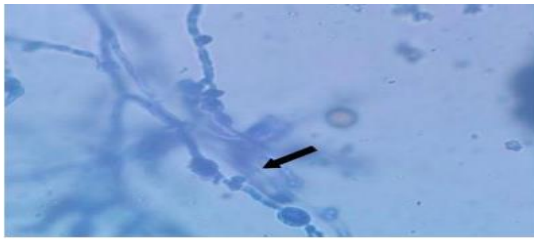
2- **Antinomycetoma**: caused by actinomyces Israeli (filamentous aerobic bacteria).It is more invasive and severe & might invade the muscles.
[treatment of each is totally different from the other]

Clinical features: Regardless of the causative agent;

1- painless nodules which overtime begin to soften skin surface resulting in ulceration.
2- Formation of puss and granulomas (too much abscesses are seen)
3- Sinuses and fistulas; Hyperplasia of sinus openings

Diagnosis:

- **Macroscopically**: it depends on color of granule. One of diagnostic features of Eumycetoma is the black nodules or granules.



***Madurella mycetomatis* with intercalary chlamydospores**

-**Microscopically**: we look for **septate hyphae** with **spores** after mounting the specimen.
- culturing on SDA

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

Treatment: usually difficult as it involves:

- **Surgical** debridement and excision
- **Chemotherapy** with Antifungal agents: ketoconazole / Itraconazole .
- More severe cases: **ampotrecine B**

4. Opportunistic mycosis

Almost exclusively happens with immunocompromised patients (very young, very old, cancer, hematologic dyscrasias (e.g. leukemia & neutropenia), Diabetes Mellitus, debilitated patients, patients with indwelling urinary catheters, patients taking broad-spectrum antibiotics, post-transplantation therapy, immunosuppressant therapy (e.g., corticosteroid or cytotoxic drugs).

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.
The fungi that cause opportunistic mycosis, except for Cryptococcus, have low inherent virulent ability. So, healthy individuals are resistant to them, whereas systemic infections affect both healthy and those with impaired immune system. However, it would be more severe and fatal in immunocompromised patients.

- Some are part of our normal flora, like Candida albicans.
- Opportunistic infections are either endogenous (i.e. Candida, because it's part of normal flora) or exogenous (from outside of the body).

Example 1 : candidiasis

Primary or secondary mycotic infection; each caused by different members of the genus candida.

Causative species: (most common): Candida albicans

- Candida albicans is oval gram positive budding yeast which produce pseudohyphae.
- Dimorphic fungi, some textbooks call it polymorphic since it assumes pseudohyphae morphology.
- Part of normal flora: skin, mucous membranes of the upper respiratory, female genital tracts & GI tract.
  They colonize mucosal surfaces immediately after birth and become part of our microbiota.
- Candida infections are endogenous, except for one exogenous infection that's RARELY transmitted through sexual intercourse.

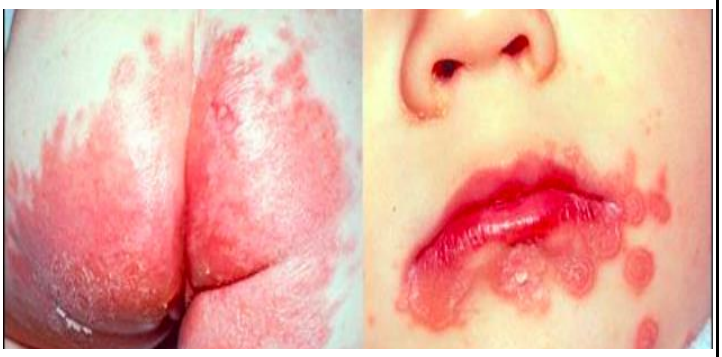
Superficial	occurs most commonly in immunocompromised patients so it is one of the opportunistic fungi
cutaneous candidiasis	Infection of skin or mucous membranes usually due to genito-impaired epithelial barrier function. Can be localized to mouth, called oral thrush or vagina, called vulvovaginitis.

Systemic candidiasis

Can take place anywhere in the body. seen in patients with cell-mediated immune deficiency especially cancer, patients using catheters, diabetic patients, and drug abusers who use IV needles [immunocompromised]. Associated with transient candidemia (candida in the blood). Candida can lead to UTIs.

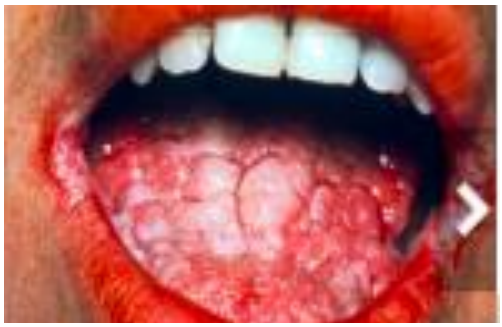
NOTE: once candidiasis is suspected; **1-** blood culture must be done because there might be candidemia. **2-** urine sample must be taken beacause there might be an UTI.

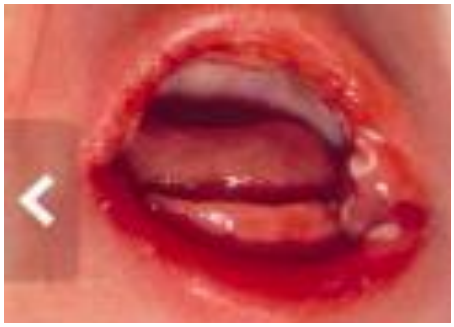
Clinical forms:



1- **Skin invasion**: They are red & weeping lesions. post-trauma or in burned patients who have lacerations. Candidiasis invades moist warm parts like the axilla, groin, intraglutial fold and inframammary folds.
   - Pseudo diaper rash
   - common in obese diabetic patients

2- **Orapharengeal candidiasis (**mouth infection**)**: C. albicans produces white patches in the mouth (oral thrush or moniliasis). Sometimes oral leukoplakia, esophagitis, gastritis. Oral thrush (infection of tongue) is the simplest form, common in AIDS patients, 70-80% of them.

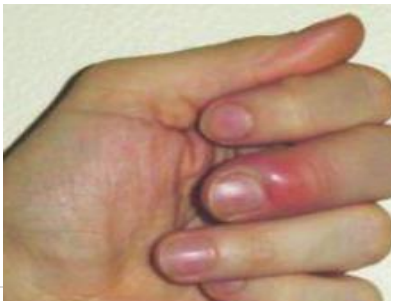


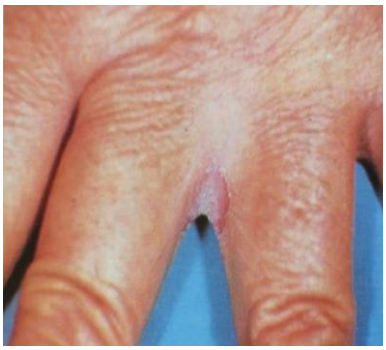


Oral candidiasis of a new born granules.

3- **Vulvovaginitis**: candidiasis in vaginal mucous membranes (vulvovaginal space), characterized by irritation, proctitis, itchiness, and white creamy thick discharge. Common with diabetic woman & prolonged use of antibiotics, IUCD, Pregnancy (it lowers immunity).

4- **Oncomycosis (paronychia)**: infection of nail plate. It is painful (*in contrast to oncomycosis caused by tinya*). Red, tender, inflamed, swollen nail folds and thickening & loss of nails. Occurs with repeatedly immersing in water (dish washing).

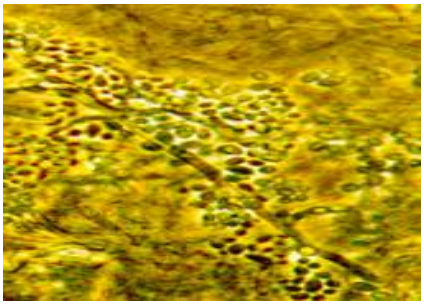




5- **Candida fingerweb erosion** (Interdigital candidiasis): related to fatness, and occupation. Seen especially in individuals who work a lot with water (i.e; cooks, fish and vegetables handlers)

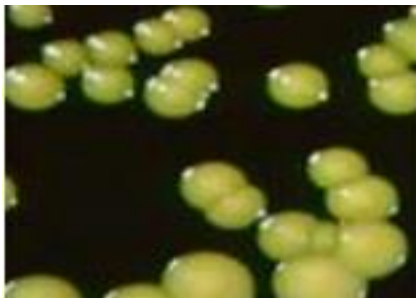
Diagnosis:

- **Microscopically:** specimens should be broad; involving vaginal discharge or exudates from mucous surfaces. Also, blood, urine, materials removed from IV or urinary catheters or cerebrospinal fluid(CSF). We look for an oval budding yeast as well as branching pseudohyphae. **C.albicans** is gram positive yeast.



- Culturing on SDA, nutrient agar, and corn meal: white to creamy colonies, with smooth waxy surface. **Identification is done by :-**

- **Morphology:** oval budding gram + budding.
- **Differentiation tests:** spore formation test / germ-tube test / biochemical reactions.

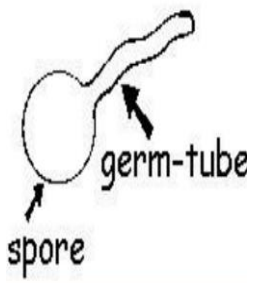


Chlamydospore (Spore formation test) :

- Subcultures are grown on "corn meal agar". When colonies start to grow, the plate is inverted and examined microscopically → classical picture of clamydospore formation is seen.

Germ-tube test :

- after culturing, colonies are incubated in human serum for 30 minutes at 37°C. then a sample is taken to be examined under the microscope → usually Candida produce the germ tube.



Biochemical tests :

- C.albicans ferments glucose and maltose to produce acid and gas.

Treatment:

❖ Oral thrush and cutaneous forms→ topical **Nystatin** or **Fluconazole**

❖ Systemic → the fungicidal **amphotrecine B**

❖ Skin lesions → **Nystatin ointment**

Notes:
- *Candidiasis is one of the differential diagnosis of diper rash in infants.*
- *Candidiasis is one of the common causes of UTIs.-*

Example 2: Cryptococcosis

- A severe disease and common infection of AIDS, cancer or diabetes patients [immunocompromised].

Causative species: cryptococcus neoformans / creptocpccus agatie

- the only opportunistic fungi that is NOT with low inherent virulence since it's an **encapsulated** yeast.
- **SAPROPHITE:** widespread fungus that exist in nature and inhabits soil around pigeon roosts. Also, it enters the body through lungs. Infection of lungs leads to cough, fever, and lung nodules.

Unique feature: large Polysaccharide capsule; anti-phagocytic and it's the prime factor of its pathogenesis

Neurotropic (can travel to the brain): Leads to meningitis and encephalitis which cause severe neurological disturbance and death.

- Meningitis is the most commonly recognized form of the disease.

Since there is CNS involvement, sample must be taken from CSF.

Diagnosis:

- Microscopically: smaple from the CSF.
  A special stain called "india ink" is added for the capsule stain (50-80% + CSF) to aid visualization of the capsule

- Culture: there's a *more selective (than SDA) and a differential* agar for it, called "bird-seed agar". But it still can grow on SDA.
  Routine blood culture
  PCR

Example 3: Aspirogillosis

- Diseases of the genus **ASPERIGILLUS**.
- Serious opportunistic threat to AIDS, leukemia and transplant patients.
- Occur worldwide + high incidence and prevalence.

Causative species: Aspiragillus fumigatus / aspiragillus flabous

- SAPROPHIC microorganisms found in nature. (Very common airborne soil fungus)
- 600 species, 8 involved in human disease
- can colonize sinuses, ear canals, eyelids, and conjunctiva
  - infection follows inhalation of the conidia (the asexual elements of the fungi) which contain potent allergins. → Infection usually occurs in lungs
  - Atopic or Susceptible individuals develops hypersensitivity rxn. Based on the localization of the hypersensitivity rxn the clinical pictures pop up.

Allergic aspirogilosis (bronchopulmonary allergy)

IgE formation and secretion left mild laceration

Invasive aspirogillosis

More severe

- Bronchopulmonary allergy or Invasive aspergillosis in preformed cavitirscan produce necrotic pneumonia, and infection of brain, heart, and other organs.

Aspergilloma

In between invasive and allergic. Spores germinate in lungs and form fungal balls, requires *surgical* treatment.

Treatment:

- The fungicidal Amphotricine B
- Nyastin
- Surgery

Example 4: zygomycosis

Genera involved: Mucorales; Rhizopus/ Absidia/ and Mucor.

- Collectively these diseases are called Zygomycosis •
- Zygomycota are extremely abundant saprophytic fungi found in soil, water, organic debris, and food.
- 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.

- The disease can spread rapidly to the sinuses, or to the eyes. So, it's a serious disease.
- main host defense is phagocytosis

Clinical form: the major clinical form is "Rhinocerebral mucormycosis"

Diagnosis:

- Microscopically: Specimens should include CSF. Direct smear and by isolation of molds from respiratory secretions or biopsy specimens. Look for hyphae or yeast.
- Culture: SDA

Treatment:

- ❖ Nyastin Control Diabetes
- ❖ surgery
- ❖ the systemic fungicidal antifungal, amphotericin B

Prognosis: very poor

Example 5: pneumocystosis

- lethal pneumonia in immunocompromised persons, AIDS patients are at very high risk.

Causative species: Pneumocystis jirovecii / Pneumocystis carinii

Unique feature:

1- previously, they were classified as protozoa.
2- Not cultivable, so we rely on microscopic examination only.

Diagnosis:

- depends on finding organisms of typical morphology in appropriate specimens (Sputum, BAL)
- The organism has not been grown in culture

Treatment: Combination of TMP(trimetoprin) - SMX(sulfamethoxazole) is a treatment of choice for all types of pneumocystosis.

5. Endemic mycosis

- The difference between systemic and endemic is that Endemic mycosis take place in both healthy individuals and immunocompromised. **However**, in immunocompromised patients it's more severe and might be fatal.
  - Patients with impaired cell-mediated immunity are at higher risk.
- the infections are initiated in the **lungs** following inhalation of the respective conidia.
- Most infections are **asymptomatic** or mild and resolve without treatment. However, a small but significant number of patients develop pulmonary disease.

Examples:

Coccidioidomycosis - histoplasmosis - blastomycosis – paracoccidioidomycosis.

- Each of the four primarily systemic is **geographically restricted** to specific areas of endemicity.

Causative species: caused by a thermally dimorphic fungus (i.e. *filamentous fungi in the environment and parasytic yeast form inside the body*).

GOOD LUCK! ☺