Microbiology

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Classification of mycosis based on site

• Black piedra (*Piedraia hortae*),

1. Include black and white piedra 

   • *Piedraia hortae* the causative agent

   • Black piedra
   - is a superficial mycosis due to *Piedraia hortae*
   - is manifested by a small black nodule involving the hair shaft.

   • White piedra
   - Due to *Trichosporon beigeli*
   - Is characterized by a soft, friable, nodule of the distal ends of hair shafts.

• Pityriasis versicolor (*Malassezia furfur*)

• Tinea nigra (*Phaeoannellomyces werneckii*)

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   • Pityriasis versicolor
   - is a common superficial mycosis
   - is characterized by hypopigmentation or hyperpigmentation of skin of the neck, shoulders, chest, and back.

   • Tinea nigra
   - Due to *Phaeoannellomyces werneckii*
Most typically presents as a brown-black silver nitrate-like stain
- Appeared on the palm of the hand or soles of the foot.

B. Cutaneous Mycoses involves deep epidermis and keratinized body areas (skin, hair, nails). Classified as
A. Dermatophytoses (caused by the genera *Epidermophyton*, *Microsporum*, and *Trichophyton*)
B. Dermatomycoses (the most common of which are *Candida* spp.) we care a lot about candida from medical point cuz it causes oral thrush and vaginal thrush

Candida albicans causes nail infection.
- The Dermatophytoses are characterized by an anatomic site-specificity according to genera.

Its classified by the site of infection for example
*Epidermophyton floccosum* infects only skin and nails, but does not infect hair shafts and follicles

*club shape (like tennis club)*
*Microsporum* spp. infect hair and skin, but do not involve nails.*spindle in shape
*Trichophyton* spp. may infect hair, skin, and nails.

*slindrical

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Common genera: *Microsporum*, *Trichophyton*, and *Epidermophyton*
Dermatomycoses

C. Subcutaneous Mycoses

Involves dermis (deeply), subcutaneous tissues and muscle. There are three general types of subcutaneous mycoses:

A. Chromoblastomycosis
B. Mycetoma
C. Sporotrichosis.

All appear to be caused by traumatic inoculation of the etiological fungi into the subcutaneous tissue.

It happens in any trauma or accident or injury.

* Chromoblastomycosis is a subcutaneous mycosis characterized by verrucoid lesions of the skin.

- It is generally limited to the subcutaneous tissue with no involvement of bone, tendon, or muscle, the lower extremities.
- The most common causes of Chromoblastomycosis are *Fonsecaea pedrosoi, Fonsecaea compacta, Cladosporium carionii.*

Mycetoma is a suppurative and granulomatous subcutaneous mycosis, which is destructive of contiguous bone, tendon, and skeletal muscle.

- It is characterized by the presence of draining sinus tracts from which small but grossly visible pigmented grains or granules are extruded.
The causes of Mycetoma are more diverse but can be classified as Eumycotic and Actinomycotic mycetoma.

Eumycotic mycetoma is the mycetoma associated with fungi while actinomycotic mycetoma is associated with actinomyces (associated with bacteria).

**Sporotrichosis**
- This infection is due to *Sporothrix schenckii* and involves the subcutaneous tissue at the point of traumatic inoculation.
- The infection usually spreads along cutaneous lymphatic channels of the extremity involved.

**D. Deep Mycoses**

**Primary versus Opportunistic mycoses**
- The Primary pathogenic fungi are able to establish infection in a normal host; whereas, Opportunistic pathogens require a compromised host in order to establish infection (e.g., any patient with Cancer, Organ transplantation, Surgery, and AIDS (because they are immunosuppressed the virus of aids attack T-lymphocytes T-helper).

Why it attack T-helper?? Because t-helper helps all cells (it's the base of immunity) so that's why the immune system is destroyed.

Types of t-lymphocytes (t-helper, t-killer, t-suppressor, t-delayed hypersensitivity).
- Primary deep pathogens usually gain access to the host via the respiratory tract.
- Opportunistic fungi causing deep mycosis invade via the Respiratory tract, Alimentary tract, or Intravascular devices.

The most important and the easiest way of infection is respiration.

**Primary Systemic fungal pathogens** include:

*Coccidioides immitis* (Coccidioidomycosis),
Histoplasma capsulatum (cave disease)
Blastomyces dermatitidis (Blastomycosis),

. Originate in lungs, phagocytosis by macrophages, spread to many organs.

They've got so many virulence factors so they resist phagocytosis

➢ Most primary infections are inapparent
➢ Progression may produce pulmonary symptoms or ulcerative lesions.
➢ Host responses produce formation of fibrous tissue, granulomas and calcified lesions.

Immune response by production of granulomas and calcified lesions.......when it's intracellular like ""costidiosis emytis""((not sure about the spelling))) forms capsule so it resists phagocytosis…the microorganisms inside the phagocytic cells

Induce immunological reactions like in TB there's formation of fibrous tissue ,granuloma and calcified lesions in lung.

➢ Normally found in soil, these organisms infect via inhalation

➢Histoplasmosis is characterized by intracellular growth (inside the WBC)of the pathogen in macrophages and a granulomatous reaction in tissue.
- These granulomatous foci may reactivate and cause dissemination of fungi to other tissues.
- Usually, acute benign respiratory disease
- Rarely, progressive, chronic or disseminated disease.

This is specially in patients with immune depressed system like AIDS patient

**this is histoplasmosis ...histoplasm capsulatum after dissemination in blood it circulates then appears as skin lasions

*it's palmonary but after it's dissemination it appears on skin
Systemic Mycoses are generally Asymptomatic but may have generalized symptoms including: low grade fever, shaking chills, night sweats, malaise or appetite loss.

Opportunistic Fungal pathogens include: Cryptococcus neoformans (capsulated), Candida spp (the most important one). (Candidiasis), Aspergillus spp. (Aspergillosis), Penicillium marneffei, Zygomycetes (Zygomycosis), Trichosporon beigelii.

- These organisms generally have a low potential for virulence but can produce severe disease involving a variety of body tissues.

Unlike bacteria these organisms have low potential for virulence but can cause serious infections in humans who are immune depressed or compromised... eventually it depend on the state of the patient whether he's compromised or not.

PATHOGENESIS:
Mycotic disease is often a consequence of predisposing factors including
1. Age
Younger and older people have higher risk of infection
2. Stress
It has relativness to all diseases.
3. Other pathologic conditions
(e.g. cancer, diabetes, AIDS)

C. albicans is a member of the indigenous microbial flora of humans. Might exist in vagina or GIT
1. Found in the gastrointestinal tract, upper respiratory tract, buccal cavity, and vaginal tract.
2. Growth is normally suppressed by other microorganisms found in these areas. Why suppressed?? Cuz candida don’t exist alone
.....rather it exist with other populations (bacteria facultative anaerobic, aerobic..)

Any microorganism have limited growth and exist normally in certain numbers this happens by the suppression of other microorganism for it's growth

3. Alterations of gastrointestinal flora by broad spectrum antibiotics or mucosal injury can lead to gastrointestinal tract invasion. Invasion through the skin or increase in number when using broad spectrum antibiotic

4. Skin and mucus membranes are normally an effective barrier but damage by introduction of catheters or intravascular devices can permit candida to enter the bloodstream.

*in vitro* (25°C): mostly yeast; the temperature of lab yeast

*in vivo* (37°C): yeast, hyphae and pseudohyphae

Candida abicans is dimorphic fungi (in yeast (coccus) and hyphae stages)

extension from the cytoplasmic part then it puds outside and form a bud then the bud forms a new full cell
Vaginal Candidiasis (vaginal thrush) is the most common clinical infection. Local factors such as pH and glucose concentration (under hormonal control) are of prime importance in the occurrence of vaginal candidiasis. In mouth: normal saliva reduces adhesion (lactoferrin is also protective).

It causes vaginal and oral thrush

It causes thrush because it secretes white discharge.

The nature of the discharge is thick, white and creamy and it has a smell like yoghurt and it causes: "

It differs from the bacterial infection in the vagina (vaginitis)

In the color of the discharge and: "

*the change in pH and glucose con. is very important in the occurrence of vaginal candidiasis..

The change in glucose con. changes under the influence of hormonal control (before and after period and in the mid time)

So the infection always occurs before and after because of the change in hormones so it affects the amount of glycogen or glucose produced by cells and so it affects its growth.

The pH of vagina is 4.5 or less.

*note: candida or fungi is not acidic but in this pH they don't grow but if the pH raises definitely they'll grow...

Bacteria (lactic acid bacteria) in vagina preserve this pH (4.5)

So once these bacteria eradicate the pH raises and this is a suitable environment for the growth of candida and it's infection (vaginitis)!
Lactoferrin is an iron-binding protein that has antifungal and antibacterial activity. It's present in milk and body fluids (saliva, tears, nasal secretions) and protects us from candida.

**Risk factors for candidiasis**
1. Post-operative status
2. Cytotoxic cancer
3. Chemotherapy
4. Antibiotic therapy
5. Burns
6. Drug abuse
7. Gastrointestinal damage

Fungi generally cause one of three distinct tissue responses:
- Chronic inflammation (Scarring, accumulation of lymphocytes)
- Granulomatous inflammation (Collections of modified epithelial cells, lymphocytes)
- Acute Suppurative inflammation

This is very important in diagnosis of infection (we can define if the causative agent is fungi or bacteria from the type of WBCs.)
Some of the tissue responses may be due to **Mycotoxins**, which are fungal metabolites that are toxic to the host.

Sometimes the infection is not due to the fungi itself but because of the toxin it produces just like bacteria.

- Some agents produce LPS-like endotoxins or Hemolysins or Steroid-like toxins that affect the nervous system.

**Note:** these productions aren't LPS but they have some characteristics in common and their activity like LPS also.

Part of it produces hemolysins and break down RBCs.

- **Aspergillus** produces a toxin called Aflatoxin that has a strong association with liver cancer.

*There are 14 species each one is produced from a specific kind of aspergillus.*

Unlike bacterial toxins these are associated with liver cancer.

*they were found mostly in peanuts ...they cause degeneration of peanuts.

**AFLATOXIN** (the most important group): *When contaminated food is processed, Aflatoxins enter the general food supply where they have been found in human foods as well as in feedstocks for agricultural animals.*

- At least 14 different aflatoxins are produced in nature.
- Aflatoxin b1 is considered the most toxic

Associated with liver cancer

- Animals fed contaminated food can pass Aflatoxin into eggs, milk products, and meat.
- Contaminated poultry feed is suspected in the findings of high percentages of samples of Aflatoxin contaminated chicken meat and eggs.

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Children are particularly affected by Aflatoxin exposure, which leads to stunted growth, delayed development, liver damage, and liver cancer. Adults have a higher tolerance to exposure, but are also at risk. Aflatoxins are among the most carcinogenic substances known.

"The doctor just read them as they are"

HOST DEFENSES:

Host defenses against the fungi include nonspecific and specific factors

We have two types of immunity in our system no matter what the infectious agent was (fungi, bacteria or fungus): specific and non-specific immunity

Nonspecific defenses include the barriers

1. The skin (lipids, fatty acids, normal flora and sweat gland)
2. Internal factors (mucous membranes, ciliated cells, macrophages)

Ciliated cells found in the upper part of the respiratory tract and it help in immunity by using the cilia for trapping the organisms and the movement of cilia kick them away from our body by coughing and sneezing.

Why macrophages are non-specific defense??

Because macrophages don’t determine a specific infectious agent but rather phagocyte different types of organisms (bacteria fungi..) but it’s considered as the line-2 of immunity defense

3. Blood components

Including natural killer cells and many other component that work non-specifically

4. Temperature

5. Genetic
Some genes make the person more predisposing than others for the infection from specific types of MO.


Specific defenses include both
A. Humoral (antibodies may be protective (e.g. antitoxins or opsonins).

humoral

مناعه خلطيه

هي المناعه التي توجد في السوائل النسيجية يعني ان اصلها ليس من خلايا

Examples: are antibodies ..*antibodies : are protein (hemoglobulin!!!)

And complement proteins 9 proteins "in some books they consider it 11 because C1 is (c1q, c1r, c1s) but both are correct.

Note that they're not 20

But maybe they consider the the activated forms of each of the 9 types like c1 when it's activated it gives us c1a and c1b...like this for the other types but mainly they're only 9 types .

also they include cytokines

Noteee: المناعه ضد الطفيليات هي مناعه خلويه وليست نوعية

B. Cell-mediated.

cellular

مناعه خلويه

* T & B lymphocyte

Generally, cell-mediated defenses are probably more important. Acquired resistance is usually T-cell mediated and persons with compromised cellmediated defenses generally show more disseminated disease

t lymphocyte

الشخص الذي عنده مشاكل بالجزء المناعي المتعلق بال

disseminated دائما تكون الاصابه عنده
EPIDEMIOLOGY
Dermatophytes may be communicated from person to person by combs, towels, hair etc.

Patients with diabetes are more predisposed for the infection of candida. Candida is a member of the normal vaginal flora; candidiasis is often associated with diabetes. In some cases of mycosis, occupation seems an important contributor. For example, Sporothrix is normally found in woody plants; hence, agricultural workers acquire disease more often. Similarly, Histoplasma is often found in bird or bat excret; hence caves workers or persons involved in community clean up may acquire more often.

DIAGNOSIS
Clinical: For the dermatophytes, appearance of the lesions is usually diagnostic. For systemic mycoses, the epidemiology and symptomology are useful. Samples include: scrapings of scale, hair which has been pulled out from the roots, brushings from an area of scaly scalp, nail clippings, or skin scraped from under a nail, skin biopsy, moist swab from a mucosal surface (inside the mouth or vagina) in a special transport medium.

Laboratory: Treatment of skin scrapings with 10% potassium hydroxide can reveal hyphae or spores. Most fungi can be grown on Sabouraud's dextrose agar but they are often very difficult to speciate.
In lab we can culture it or make smear (in bacteria we usually use normal saline to make slide or pigmentation) but in fungi

We use 10% of K hydroxide also they can dissolve fatty materials if present to make the vision clearer.

*there's another media used for candida is called romo this media defferentiatre between different kinds of candida each one has a special color

**Skin testing for a delayed hypersensitivity response is useful for epidemiologic purposes but often not for diagnosis**

Some people have sensitivity from some types of spores

They call it skin" " and skin" " I wasn’t sure about what I heard it wasn’t clear enough !!! they make it on the arm or back .and they use the factor that causes the sensitivity

**Germ tube test**

**Is a screening test which is used to differentiate candida albicans from other yeast.**

**When candida is grown in human or sheep serum at 37°c for 3 hours, they forms a germ tubes, which can be detected with a wet films as filamentous outgrowth extending from yeast cells. It is positive for candida albicans .**

How do we make the test???

We take the fungi which we don’t know exactly and make incubation with 1 ml of human serum and the fungi colonies for 4 hours and every 30 min. we take adrop from the mixture and prepare a slide and see it under the microscope if it formed the germ tube ( candida forms an extension outside ).

**CONTROL**

**Sanitary:** Control by sanitary means is difficult, but the incidence of communicable disease can be reduced by good hygiene.

**Immunological:** No vaccines are currently available.

**Chemotherapeutic:** Many antifungals are available but some
are very toxic to the host and must be used with caution.
Topical powders and creams often contain azole derivatives
(miconazole, clotrimazole, econazole) are useful against
superficial dermatophytes.
Sporotrichosis may be treated using potassium iodide
Systemic infections are generally treated by 5- FC, miconazole,
Fluconazole or ketoconazole.
Flagel is the most important and widely used for fungal infections.