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University of Oran 1 Ahmed Benbella

Department : Biology

Teaching handout

Title

Mycology

Course intended for students of

Bachelor's degree (specialty and level) : 'L3 LMD' Parasitology

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Foreword

Microfungi are eukaryotic, heterotrophic organisms, unicellular or multicellular, with a filamentous or yeast-like appearance, belonging to the kingdom Fungi.

In human medicine, these fungi are involved in various pathologies, such as mycetism, mycotoxicosis and mycoses. The latter can be deep, systemic, or superficial, affecting the mucous membranes, skin, and appendages.

These conditions are no longer just an aesthetic issue, but rather a serious health problem, especially for immunocompromised individuals, with repercussions on various aspects of daily life. They can cause functional discomfort, pain, social or professional inconvenience, and spread to other areas of the skin.

The aim of this course is to provide students with an overview of current knowledge in the field of mycoses and their agents (molds and yeasts). They will not only have the opportunity to become familiar with the classic agents responsible for dermatomycoses, but also to address issues related to invasive mycoses, such as candidiasis and aspergillosis, which are increasingly common in our hospitals. Emphasis will be placed on species important in fundamental biology and medical mycology.

Summary

Chapter I : Introduction to Mycology

Medical mycology is the study of diseases caused in humans or animals by microscopic fungi (micromycetes). In human medicine, these fungi are involved in various pathologies :

1. **Mycetisms:** Poisoning due to the ingestion of certain species of higher fungi.
2. **Mycotoxicoses:** Poisoning caused by metabolites introduced into food through the invasion of molds.
3. **Mycoses:** Diseases caused by fungi in a "parasitic" state.

The micromycetes that cause mycoses :

- Most often live as saprophytes in the external environment, deriving nutrients from decomposing organic substrates.
- Live as commensals (e.g., *Candida* spp.) in humans without causing lesions.
- Occasionally live as parasites, which is why the term "mycosis" is used to describe the lesions they cause.

Based on their morphological characteristics, fungi are divided into three groups :

1. **Filamentous Fungi :**
    a. **Dermatohytes :** Keratinophilic fungi adapted to the skin and keratinous structures of humans or animals.
    b. **Molds :** Originating from the soil (terrestrial, e.g., *Aspergillus*), these fungi exhibit opportunistic behavior, and their development in humans is facilitated by a weakened immune system.
2. **Yeast-like Fungi:** The thallus is reduced to a unicellular state.
3. **Dimorphic Fungi:** These fungi appear in the environment in a filamentous form, producing spores. In parasitized human tissues, they exist in a yeast form.

Based on their parasitic capabilities and degree of virulence, medically relevant fungi are classified into :

1. **Fungi Adapted to Parasitism**

   Example : Keratinophilic micromycetes, which have a strong affinity for animal and human keratin. The lesions vary according to the degree of parasitic adaptation.

2. **Fungi that Usually Live as Commensals in Humans**

   These fungi colonize the skin and mucous membranes (digestive or vaginal) without causing apparent lesions. The host-parasite balance can be disrupted if the host's defenses are compromised (e.g., oral or oropharyngeal candidiasis in HIV-infected individuals).

3. **Fungi Apparently Lacking Pathogenicity but Exhibiting Opportunistic Behavior**

   These include molds or yeasts that live as saprophytes in the environment. They sometimes temporarily colonize the skin, orifices, and mucous membranes without causing lesions in a healthy host under normal conditions.

The opportunistic fungus takes advantage of a situation to express its virulence and aggressive nature within the host organism.

Depending on their parasitic capacity and their degree of virulence, mushrooms cause different types of mycoses :

1. **Superficial Mycoses :** Fungi are present only on the external surface of the hair and skin.

   These infections are of moderate severity, cause little to no inflammatory response, and their diagnosis is usually not difficult. The issue is more of an aesthetic concern.

2. **Cutaneous Mycoses ("Dermatomycoses"):** Also known as inflammatory ringworm infections.

   They are cosmopolitan and represent the most common human fungal diseases. These infections occur at sites where the fungi penetrate more deeply.

3. **Subcutaneous Mycoses :** Affect the skin, subcutaneous tissues, and sometimes the bones.

   The fungi must be introduced into the tissues through wounds contaminated with soil containing fungi.

4. **Systemic Mycoses:** Caused by saprophytic fungi from the soil that are inhaled, leading to pulmonary infections that can spread to nearly all tissues in immunocompromised individuals.

5. **Opportunistic Mycoses:** An opportunistic organism is generally harmless in its normal environment but becomes pathogenic in a weakened host with reduced resistance to infection.

Opportunism
The ability to shift from a commensal or saprophytic state to a pathogenic state under the influence of favorable factors (changes in the host's condition).

I.1. Factors Favoring Fungal Infections

The development of fungal infections depends on the host, their environment, underlying diseases, as well as extrinsic factors.

I.1.1. Intrinsic Factors

- Extreme ages in life predispose individuals to cutaneous and mucosal fungal infections (oral thrush in infants and the elderly).
- Pregnancy increases the risk of genital candidiasis by 3 to 4 times during the third trimester (due to the role of steroid hormones).
- The disappearance of ringworm at puberty is related to the composition of adult hair, which is richer in sulfur-containing fatty acids. Additionally, this could be explained by the role of sebum, which has a fungistatic effect against dermatophytic infections.
- Excessive sweating, confined atmospheres in certain places (saunas, showers, etc.), and the maceration of feet in closed shoes are all factors that favor candidiasis and dermatophytosis.
- Certain professions are more exposed to fungal infections (shepherds, athletes, farmers, veterinarians, etc.).
- Travel facilitates the spread of exotic species.
- Various pathological conditions favor the occurrence of fungal infections, such as skin trauma, diabetes, malignant blood disorders, AIDS, etc.

I.1.2. Extrinsic Factors

- Mainly iatrogenic, these factors increase the risk of fungal infections by 3 to 10 times. These include corticosteroids, immunosuppressants, broad-spectrum antibiotics, antimitotic drugs, etc.
- Resuscitation techniques such as catheterization, dialysis equipment, and certain surgical procedures are classic sources of nosocomial fungal infections.

I.2. Modes of Contamination

- **Ingestion :** Rare; through dairy products, fruits (e.g., Geotrichum, Candida).
- **Inhalation :** Aspergillus species, Histoplasma capsulatum, Coccidioides immitis.
- **On the skin surface :** Dermatophytes.
- **Transcutaneous :** Through thorn pricks, injuries, surgical wounds, burns, etc.
- **Urogenital :** Sexual intercourse ; following the insertion of urinary catheters (Candida albicans).
- **Blood and tissues :** Via catheters, surgical interventions, contaminated syringes, etc.

Chapter II. Taxonomy of fungi and generalities

II. 1. Taxonomy

- For a long time, fungi were considered similar to plants due to their morphology, behavior (lack of mobility), and mode of nutrition (absorption).
- Botanists, the first to take an interest in the study of fungi, gave them the following definition: fungi are cellular cryptogamic thallophytes.
- In the 18th century, during the time of Carl von Linné, the living world was divided into two kingdoms: plant and animal. Fungi were classified under the plant kingdom.
- In 1866, the German naturalist Haeckel was the first to break the dichotomy of Plantae/Animalia by creating a third kingdom, that of the protists.
- At the beginning of the 20th century, fungi (which lack photosynthesis) were removed from the plant kingdom and associated with protists.
- In 1969, Whittaker proposed the establishment of a separate kingdom for fungi.

The kingdom of fungi includes :

- Subsets called **divisions** or **phyla**.
- The name of each division ends with "**Mycotina**."
- The phyla are divided into **classes**, with their names ending in "**Mycetes**."
- The suffix "**ales**" is used to designate **orders**.
- The suffix "**aceae**" is used for **families**.

II. 2. General characteristics of fungi

Fungi form an entirely separate kingdom: the kingdom of Fungi or Eumycophyta. They are neither plants nor animals; they are:

1. **Eukaryotes** (Eu = true, karyon = nucleus; with a well-defined nucleus).
2. **Thallophytes**: The basic cellular organization of fungi is the thallus, which constitutes the vegetative apparatus. This can be unicellular, consisting of single, independent cells, or multicellular.

- **Unicellular thallus**, yeast-like, found in yeasts. The mode of reproduction can occur through :

- **Budding** : This is the unequal division of the cytoplasm. It is the most common mode. An outgrowth appears at a point on the mother cell, gradually developing into a new cell, the blastospore or blastoconidium (Figure 1). This budding can be unipolar, bipolar, or multipolar.

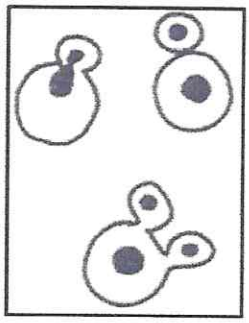

Figure 1: Budding of a Yeast

- **Fission**: which results in the formation of two identical cells.

Some yeasts, however, are capable of forming filamentous structures (pseudomycelium) (Figure 2) under certain conditions.

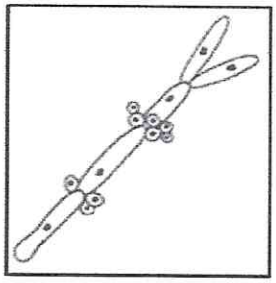

Figure 2: Pseudomycelium

– **Filamentous or multicellular thallus formed of filaments or hyphae**: The fundamental structure of a multicellular fungus is the hypha, a branched tubular tissue. The collection of hyphae forms a mycelium. We distinguish (Figure 3) :

a. Non-septate, siphoned, or coenocytic filaments, in the form of simple elongated cells containing multiple nuclei. These are characteristic of lower fungi.

b. Septate filaments: In the young parts of the mycelium, the septa or partitions have pores that allow the flow of cytoplasmic currents and nuclei from one compartment to another. In the older parts, the septa are closed, isolating the degenerating parts from the active ones.

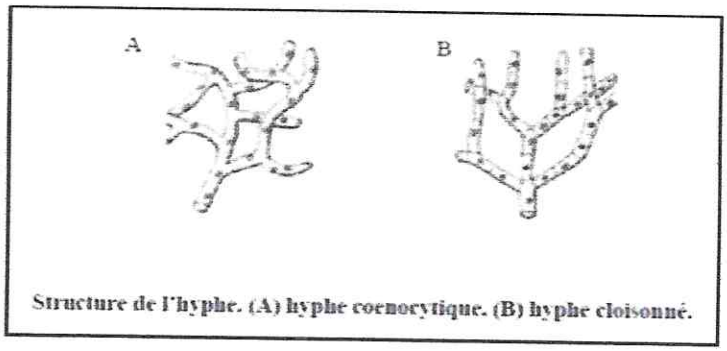

Figure 3: Structure of the Hypha

3. **A chitinous cell wall**
4. **Lacking chlorophyll (nutrition).** The absence of this assimilatory pigment makes them heterotrophic for carbon. Therefore, they must obtain water, nutrients, and mineral elements from the surrounding environment to synthesize their own matter. As a result, they can only live as :

- **Saprophytes**: Growing on dead organic matter, which they decompose into essential minerals.
- **Parasites**: Many are parasitic and obtain their nutrients from other living organisms, which they make ill or kill.
- **Symbionts**: Associated with plant root tissues (mycorrhizae) and algae (lichens).

5. **Cryptogams** (without seeds) : Reproduce by spores.

II.3. Reproduction of fungi

The reproduction of fungi occurs in the form of spores through two mechanisms: asexual and sexual.

A fungus can reproduce in :

- **Asexual form** : it is anamorphic.
- **Sexual form** : it is teleomorphic.
- **Both forms, anamorphic and teleomorphic, simultaneously**: it is termed holomorphic.

II.3.1. Asexual reproduction

The most common and simplest in nature, it involves the division of the nucleus by simple mitoses. The fungal spores produced can be external (thalloid and non-thalloid) or internal.

A. Internal Spores

Formed in Mucorales (*Mucor, Rhizopus*, etc.) within a differentiated vegetative cell, the sporangium, and released by the bursting of this "sac" when it is mature (Figure 4).

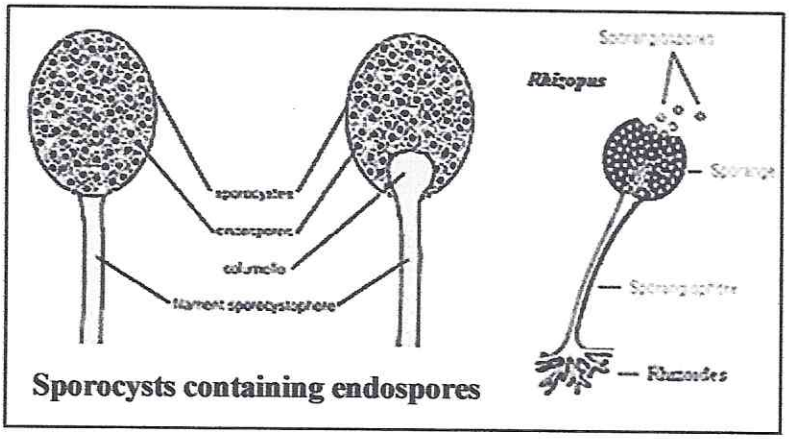

Figure 4 : Internal Spores

B. External Spores

B.1. Thalloid, originating from the thallus

B.1.1. Arthroconidia

In many molds, the fragmentation of hyphae can give rise to new individuals. The isolation of cells through the cleavage of the cell wall allows for the formation of arthrospores or thallosphores, also known as arthroconidia (Figure 5).

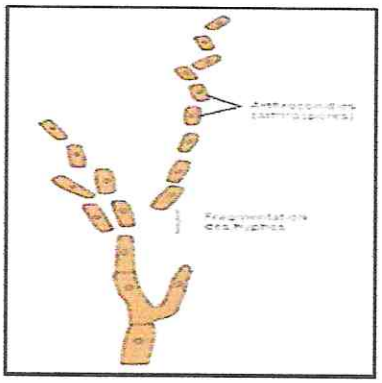

Figure 5 : Formation of Arthroconidia

B.1.2. Microconidia and Macroconidia of Dermatophytes and *Fusarium* (Figure 6)

Microconidia are small-sized spores that can be ovoid or elongated in shape, depending on the fungal species. Their primary role is to participate in asexual reproduction and in the dispersion of the fungus.

Macroconidia are larger than microconidia and are septate, typically appearing in various shapes. They can be fusiform, ovoid, or elongated. They serve the same role as microconidia.

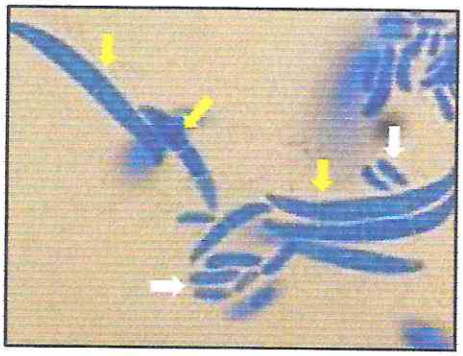

Figure 6 : Microconidia and Macroconidia
Yellow arrows : Macroconidia
White arrow : Microconidia

B.1.3. Chlamydospores : Resistant structures with a thick wall (Figure 7)

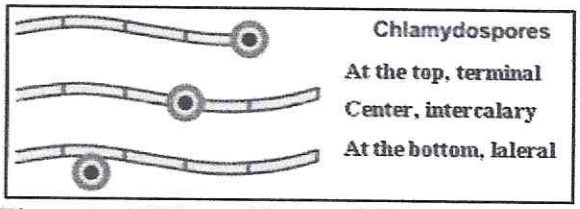

Figure 7 : Different Types of Chlamydospores

B.2. Non-thalloid Spores

B.2.1. Blastoconidia and Pseudomycelium (Figure 8)

Blastoconidia are asexual spores formed by certain fungi, particularly yeasts, through a budding process from the parent cell. Typically unicellular, they can be oval, round, or sometimes elongated in shape.

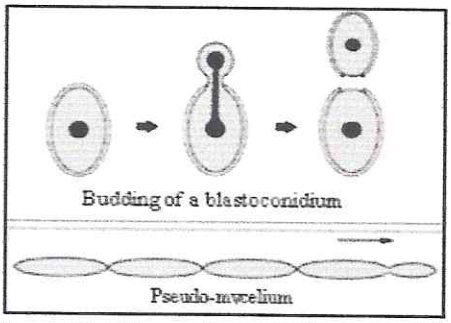

Figure 8 : Formation of Blastoconidia

B.2.2. Phialoconidia

Spore that forms from a specialized cell called a phialide, which remains unchanged after the release of conidia. Phialides are often found on more complex structures, such as conidiophores, which support them (Figure 9).

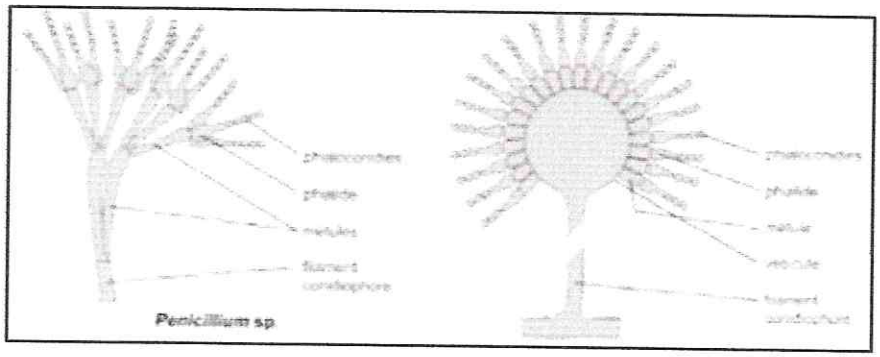

Figure 9 : Phialoconidia

II.3.2. Sexual Reproduction

Less frequent; it is exceptional in fungi. It involves the meeting of specialized filaments, the conjugation of nuclei, and finally a chromosomal reduction. It is summarized in three successive phases (Figure 10) :

1. **Plasmogamy** : Fusion of the protoplasms (cytoplasms) of two compatible hyphal cells from different mycelia.
2. **Karyogamy** : Fusion of the two nuclei.
3. **Chromosomal Reduction or Meiosis**, followed by one or more mitoses.

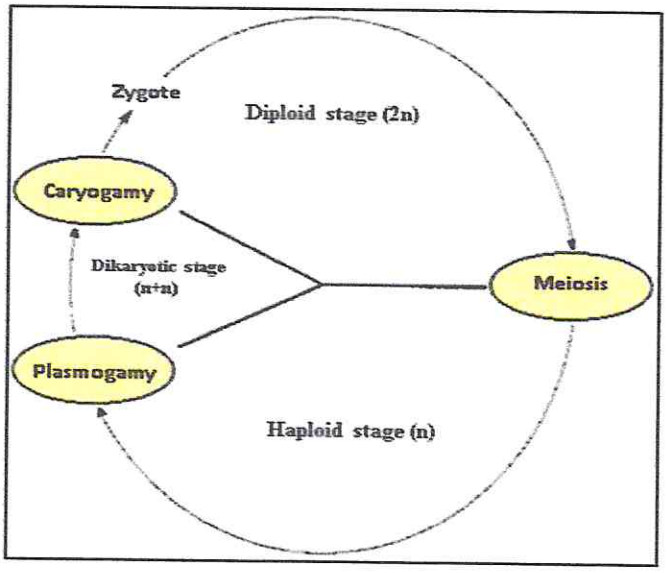

Figure 10 : Reproduction in Fungi

Spores resulting from sexual reproduction are :

- **Ascospores** : Endogenous spores contained in sacs called "asci," characteristic of the Ascomycetes family (e.g. *Aspergillus*). The asci can be either naked or formed within an ascocarp : the perithecium, cleistothecium, and apothecium (Figure 11).

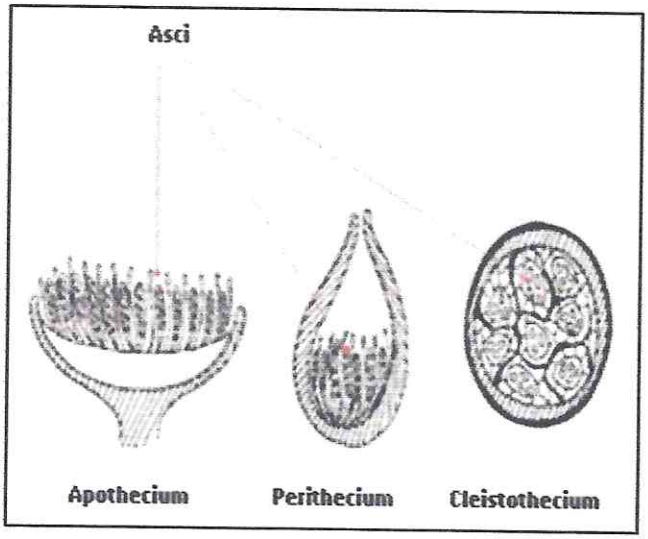

Figure 11. Ascocarps (modified)

- **Basidiospores** (Figure 12) : Formed at the apex of elongated cells called "basidia," characteristic of Basidiomycetes such as *Cryptococcus* sp.

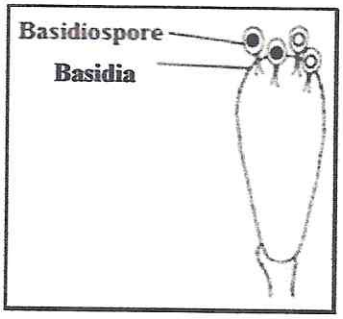

Figure 12 : Basidiospores

- **Zygospore** (Figure 13) : A large, thick-walled spore formed by the fusion of two gametangia, male and female, carried by filaments (e.g., *Mucor*).

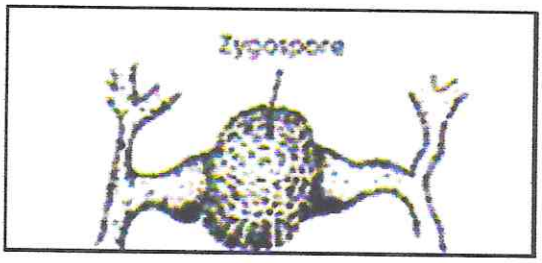

Figure 13 : Zygospore

According to the modes of sexual reproduction, the current classification of fungi distinguishes four divisions (phyla) :

II.3.1. Chytridiomycotina (Chytridiomycetes) :

- The most primitive.
- Aquatic fungi that produce flagellated spores.

II.3.2. Zygomycotina (Zygomycetes) :

- Microscopic with siphonous mycelium.
- Produce spores without flagella.
- Sexual reproduction leads to the formation of zygospores, hence the name Zygomycetes.

❖ **Reproduction cycle** (Figure 14)

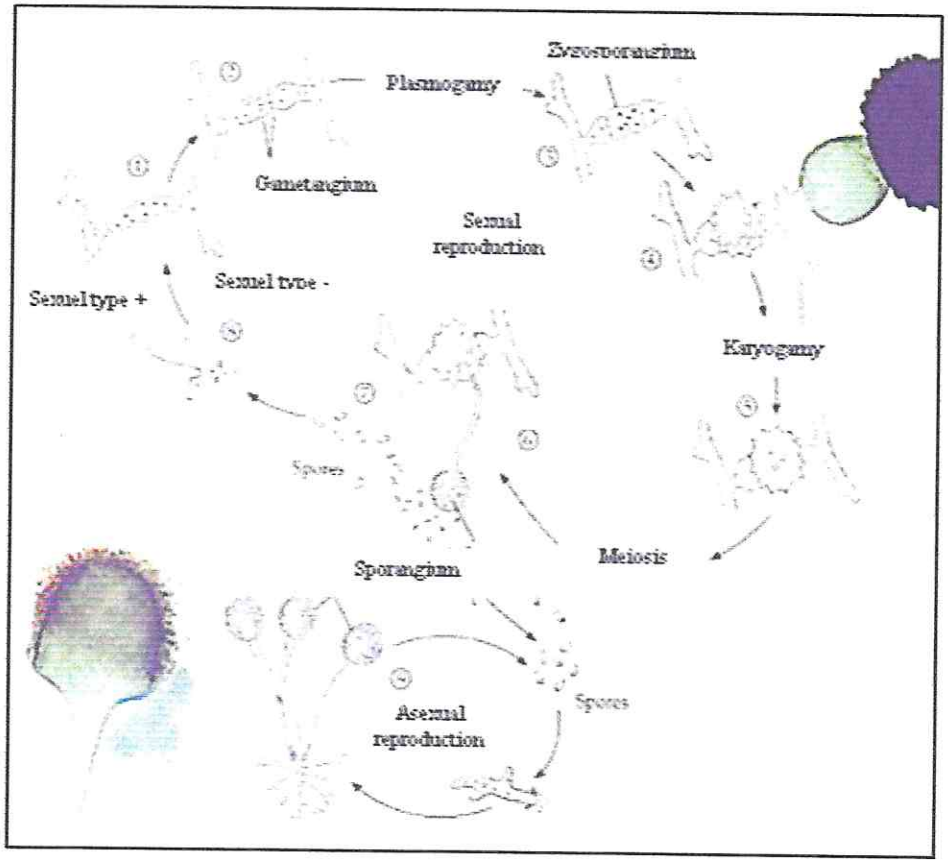

Figure 14: Reproductive Cycle of Zygomycetes (modified)

(1) Mycelia of opposite sexual types form extensions called gametangia with multiple nuclei (2). The haploid gametangia fuse to form a zygosporangium (3). The cell is covered with a thick, rough coating to withstand harsh climatic conditions (4). Following this, karyogamy occurs (diploid zygosporangium) (5). When conditions improve, meiosis occurs, the

zygosporangium germinates, and produces small sporangia. (6) The haploid spores disperse (7), germinate, and become new mycelia (8).

II.3.3. Ascomycotina (Ascomycetes) :

- With septate thallus
- Featuring a characteristic structure "ascus": a sporocyst containing numerous ascospores.

❖ **Reproduction cycle** (Figure 15)

1. Germination of spores (n chromosomes)
2. Release of conidia (nch)
3. Germination of the conidium (asexual reproduction)
4. Mycelium of the fungus (nch)
5. Bringing together two filaments originating from different spores
6. Fusion of the two cells (cell with two nuclei at n chromosomes)
7. Ascogenous hypha (cell with 2N at nch)
8. Fusion of nuclei (karyogamy)
9. 2 nuclei (N) to nch obtained after the first division of meiosis
10. 4 N to nch (second division of meiosis)
11. Mitosis
12. Ascus containing 8 ascospores with nch

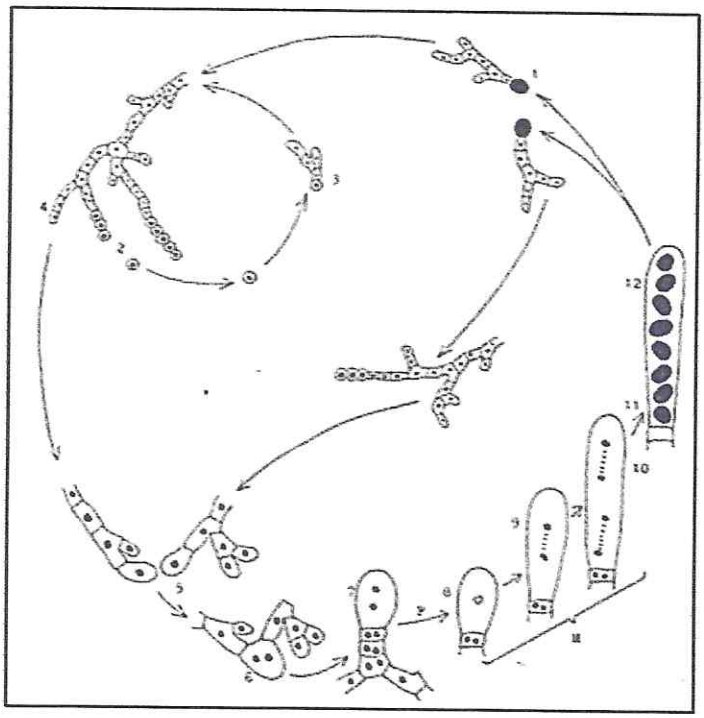

Figure 15 : Reproductive cycle of Ascomycetes

II.3.4. Basidiomycotina (Basidiomycetes) :

- Production of "basidia" spores formed by budding
- With a septate thallus

❖ **Reproduction cycle** (Figure 16)

1. Spores germinate and produce haploid hyphae
2. Hyphae of different sexual types fuse.
3. The result is a dikaryotic mycelium (with two nuclei) which develops more rapidly and outcompetes the parental hyphae.
4. After sufficient development, the dikaryotic mycelium forms compact masses.
5. Basidia develop, which produce spores (basidiospores) (Figure 17).

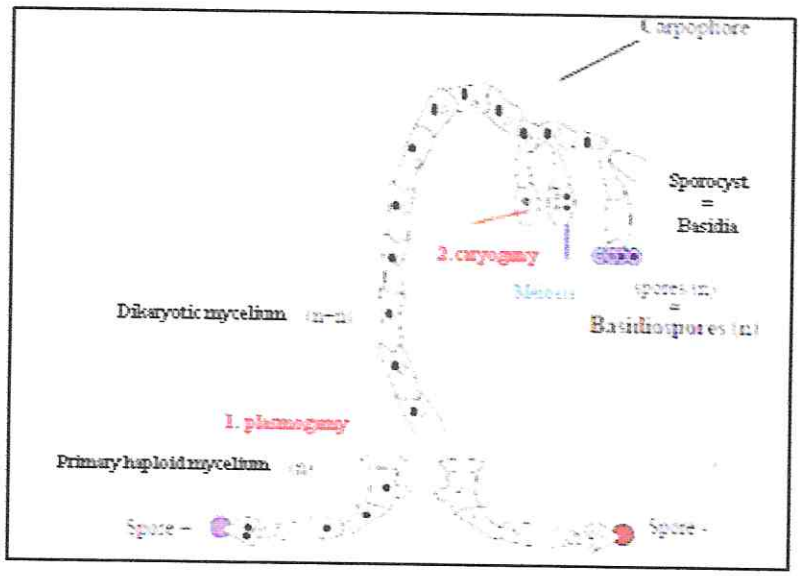

Figure 16: Reproduction cycle of Basidiomycetes (modified)

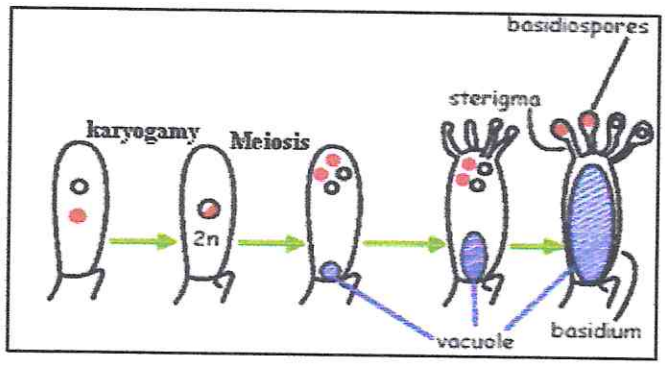

Figure 17 : Formation of Basidiospores

When sexual reproduction is not known, the division is called *Deuteromycotina* = imperfect fungi :

- They don't produce either ascospores or basidiospores. They reproduce using conidia.
- They can be unicellular (yeasts) or have a septate thallus.

Note :

The development of fungi depends on several factors :

- **Temperature :** They grow between 20 and 37°C, most commonly between 15-30°C, with an optimum range of 20-25°C.
- **Humidity :** Depending on water content, fungi can be classified into:
  1. Xerophilic species (water content <80%)
  2. Mesophilic species (80-90%)
  3. Hygrophilic species (>90%)

- **Oxygen :** Fungi are generally aerobic.
- **pH :** They thrive between pH 3 and 8

Chapter III. Toxigenic molds

III.1. Introduction

Molds are ubiquitous and offer significant economic benefits to humans :

- They contribute, alongside other microorganisms, to the biodegradation and recycling of organic matter.
- They are used in the food industry, particularly with *Penicillium roquefortii* and *P. camembertii* for cheese production.
- They are exploited for the production of enzymes and organic acids, such as citric acid and gluconic acid, by species of *Aspergillus* and *Penicillium*.
- They play a crucial role in the production of medications, such as penicillin produced by *P. chrysogenum*. Approximately 22% of known antibiotics are derived from filamentous fungi.

Despite the numerous benefits that fungi provide in daily life, they can also cause significant damage, particularly in the agronomic sector.

Foods generally provide very favorable environments for their proliferation. Several molds, especially those belonging to the genera *Aspergillus*, *Penicillium*, and *Fusarium*, are recognized as contaminants of agricultural products and/or for their ability to produce toxic secondary metabolites known as mycotoxins.

Mycotoxins (from the Greek "mykês" meaning mold and the Latin "toxicum" meaning poison) are **low-molecular-weight secondary metabolites**, ingestion of which at sufficiently high concentrations can lead to poisoning in consumers. They are produced on a wide variety of foodstuffs (cereals, dried fruits, nuts, coffee beans, etc.) before, during, and after harvest. Although more than 300 secondary metabolites have been identified, only about thirty have truly concerning toxic properties. Their decontamination is extremely difficult because they are neither destroyed by prolonged storage nor by thermal or chemical treatments.

Contact with mycotoxins can lead to toxicities affecting :

- The central nervous system,
- The cardiovascular system,
- The respiratory system,
- The digestive system.

They can also have carcinogenic, mutagenic, teratogenic, and immunosuppressive effects. Poisonings caused by these substances can manifest through various syndromes, such as gastroenteritis, hemorrhages, convulsions, paralysis, as well as renal and hepatic lesions.

The production of mycotoxins is associated with fungal development (Figure 18).

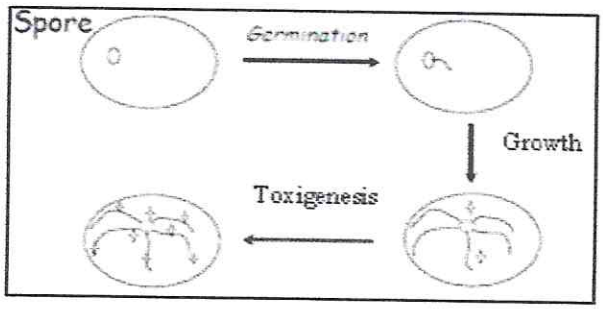

Figure 18 : Toxigenesis (modified)

Toxigenic molds are categorized into :

- Molds that invade their substrate and produce mycotoxins on senescent or stressed plants (field toxins).
- Molds that produce toxins after harvest (storage toxins). Thus, soil fungi or plant debris can spread their spores onto the plant or grains and proliferate during storage if conditions allow.

They can develop :

- In all climates,
- On all solid or liquid substrates as long as there are nutrients, moisture (water activity, Aw, greater than 0.6), which explains the wide variety of contaminated food substrates.

The formation of mycotoxins depends on the following factors :

- Water content (most molds prefer an Aw between 0.85 and 0.99 for their development),
- Temperature (they can develop between 0°C and 35°C ; *A. flavus* or *A. fumigatus* can develop at temperatures up to 60°C),
- Storage time,
- The presence of oxygen and carbon dioxide (most molds are aerobic ; increased CO_2 levels have a significant inhibitory effect on toxigenesis),
- Substrate composition.

The chemical origins of mycotoxins are very diverse :

- Some derive from amino acids,
- Poly-keto acids (aflatoxins),
- Terpene derivatives,
- Fatty acid derivatives (fumonisins).

III.2. Toxigenic Species

III.2.1. *Aspergillus* spp

III.2.1.1. General Information

- Fungi of the genus *Aspergillus* were first described in 1729.
- They are saprophytic fungi that feed on decomposing organic matter.
- They are characterized by hyaline, septate, and haploid filaments.
- They are cosmopolitan and aerobic.
- They play a role in the recycling of carbon and nitrogen in the environment.
- Some of them are thermophilic, capable of surviving temperatures up to 70°C.

III.2.1.2. Classification

Kingdom : Fungi

Phylum : Ascomycotina

Class : Euascomycetes

Order : Eurotiales

Family : Trichocomaceae or Aspergillaceae

Genus : *Aspergillus*

The genus *Aspergillus* includes approximately 185 species, of which around twenty are found in human pathology.

III.2.1.3. Morphology and Characteristics (Figure 19)

- The vegetative thallus is composed of fine, regularly-diametered, septate mycelial filaments.
- On these filaments arise erect, non-septate filaments known as conidiophores.
- The conidiophores end in a vesicle of variable shape, on which conidiogenous cells or phialides are arranged, bearing conidia (dissemination spores).

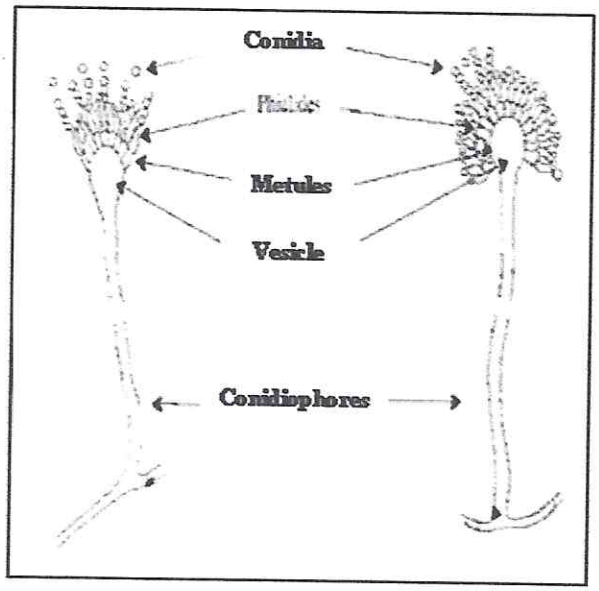

Figure 19 : Morphology of *Aspergillus* (modified)

Aspergillus represent between 1% and 7% of environmental fungi. Due to their small size, conidia are easily suspended in the air and can be found both in dust and in air conditioning systems. An individual inhales between 2000 and 5000 different genotypes per month due to the high biodiversity of *Aspergillus* spores.

The resistance to external agents is significant. Among physical agents, only desiccation and heat at 100°C can kill *Aspergillus* spores. Additionally, cold does not affect them.

III.2.1.4. Biological Cycle

- In the environment, *Aspergillus* exists in the form of mycelium.
- Under stress conditions, conidiophores (fruiting structures) develop.
- Conidia, unicellular and uninucleate asexual spores, are produced at the fruiting structures by the phialides.
- Phialides are fertile conidiogenous cells, bottle-shaped, and originate from the terminal vesicle.
- Conidia, 2 to 3 µm in diameter and highly volatile, are responsible for the dissemination of the fungus in the environment (Figure 20).

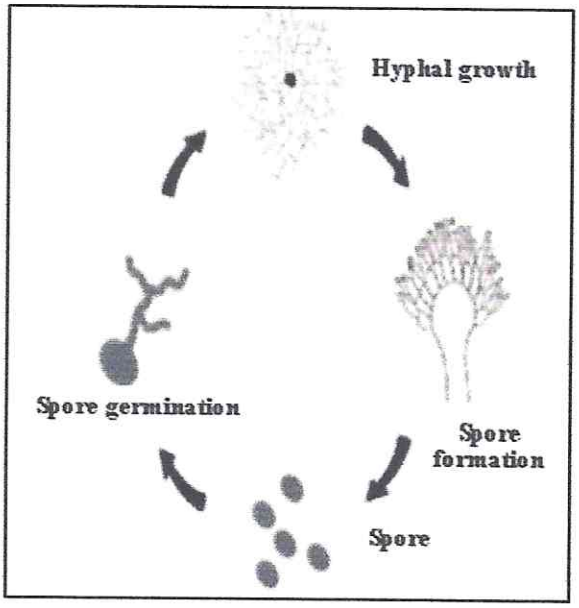

Figure 20 : Growth cycle of *Aspergillus* (modified)

Spore germination occurs in two stages :

1. Conidial swelling phase (lasts 3 to 4 hours at 37°C).
2. Formation of a germ tube that gradually elongates and produces a branched filament, which will form the typical colony of all filamentous fungi.

III.2.1.5. Cultural characteristics

- *Aspergillus* species grow rapidly on Sabouraud medium enriched with antibiotics.
- After 24 to 48 hours of culture, flat colonies consisting of short white aerial filaments appear.
- It is only after the maturation of the conidiogenous structures (between 48 and 96 hours) that the colonies take on their characteristic color : brown, green, yellow, or black, depending on the species (Figure 21). The culture's color allows for rapid species identification.
- *Aspergillus* species grow at temperatures of 22-25°C and at 37°C for thermophilic species.

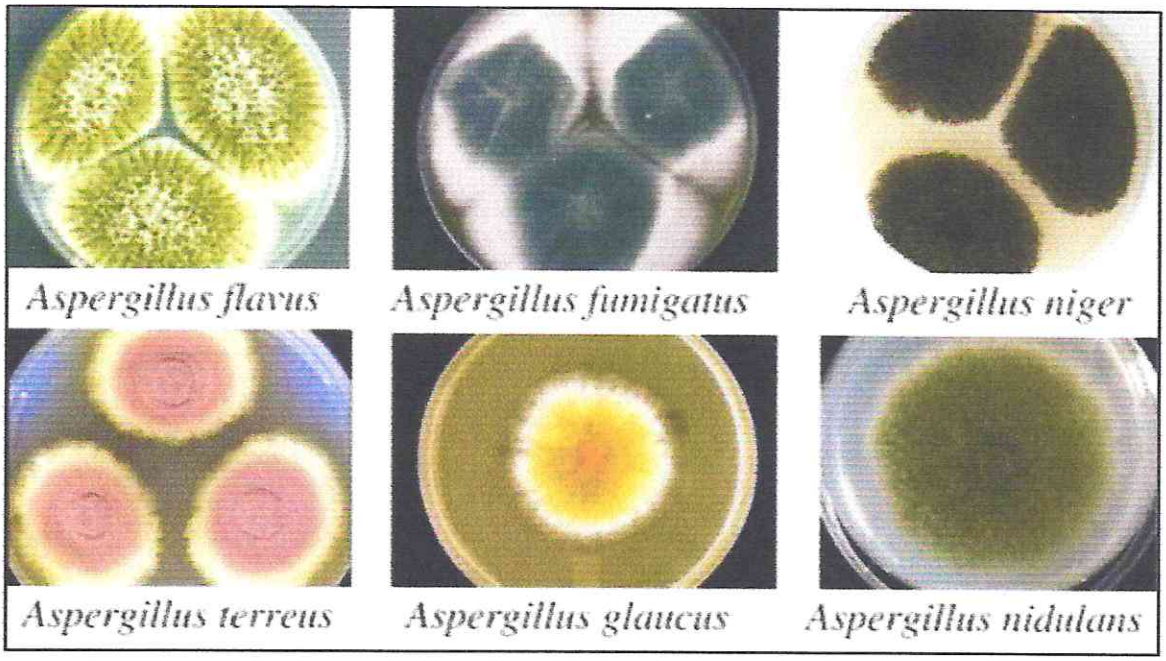

Figure 21 : Distinctive mycelium colors of various *Aspergillus* species

III.2.1.6. Pathogenicity

- Molds are organisms that are not highly virulent but very opportunistic.
- *Aspergillus* infections in non-immunocompromised individuals are primarily characterized by aspergilloma, which is linked to the development of the fungus in a bronchus or in the pulmonary parenchyma, forming a fungal ball called an aspergilloma (Figure 22).
- Toxin production (**Aflatoxins**) also contributes to the pathogenicity.

Figure 22 : Aspergilloma

Aflatoxins

Aflatoxins are secondary metabolites synthesized by strains of *Aspergillus flavus*, *A. parasiticus*, and *A. nomius*. They are widely abundant in oilseeds, cotton crops, and cereals,

particularly wheat and corn. The storage of these foods under humid or warm conditions can increase aflatoxin production.

Aflatoxin B1 (AFB1) is the most studied mycotoxin. However, other aflatoxins produced by toxinogenic molds include B2, G1, and G2, as well as aflatoxins M. Aflatoxins M1 and M2, which are the respective derivatives of aflatoxins B1 and B2, appear in milk and its derivatives.

Toxicity of Aflatoxins

Early studies have shown that, at high concentrations, aflatoxins are powerful poisons and that when administered at low doses to laboratory animals, they induce liver cancer.

According to the International Agency for Research on Cancer, aflatoxin B1 (AFB1) is considered a probable carcinogen. Ingestion of 1.4 µg of AFB1, combined with hepatitis B virus, increases the risk of developing cancer.

In 1971, the carcinogenic activity of aflatoxins in animals was demonstrated, and in 1987, aflatoxins were classified as Group I carcinogens for humans.

II.2.2. *Fusarium* sp

III.2.2.1. General Information

Fungi belonging to the genus *Fusarium* are commonly found in soil, plants, air, and water. Their geographic and climatic distribution is very diverse :

- Temperate regions
- Tropical regions
- Deserts
- Mountains
- Polar regions

The genus *Fusarium* includes several species :

- *Fusarium oxysporum*
- *F. solani*
- *F. equiseti*
- *F. verticillioides*
- *F. proliferatum*

These species are found in atmospheric dust and rainwater.

III.2.2.2. Classification

Kingdom: Fungi

Phylum: Ascomycotina

Class: Ascomycetes

Subclass: Hypocreomycetidae

Order: Hypocreales

Family: Nectriaceae

Genus: *Nectria* (teleomorph)

III.2.2.3. Morphology

Species of the genus *Fusarium* exhibit :

- Septate mycelium

- Three forms of spores :

Macroconidia Microconidia Terminal and intercalary chlamydospores

III.2.2.4. Pathogenicity

- Contact lens keratitis (corneal ulceration)
- Onychomycosis
- Pneumonia
- Eumycetoma (chronic fungal infection characterized by fistulas, grains, and swelling affecting a part of the body, usually the feet). Bone tissue can also be affected.
- Skin infection
- Production of toxins including **fumonisins.**

Fumonisins

Toxins responsible for various pathologies related to the consumption, particularly of corn or corn-based foods, that are contaminated. Fumonisin FB1 is the most important :

- Appears as a solid
- Molecular weight : 722 g/mol
- Melting point between 103°C and 105°C
- Soluble in water
- Even more soluble in methanol

Pathogenicity

FB1 can cause :

- Acute mycotoxicoses in farm animals
- Pulmonary edema in pigs
- Potentially carcinogenic effects in humans (a correlation between fumonisin exposure in South Africa and esophageal cancer has been suggested).

Chapter IV. Pathogenic molds and yeasts

IV.1. Dermatophytes and Dermatophytoses

IV.1.1. Dermatophytes

IV.1.1.1. General characteristics

Fungi that are :

- Filamentous with septate mycelium.
- Sexually reproducing, producing ascospores.
- Adapted to animal and human keratin.
- True parasites (always pathogenic).
- Cosmopolitan or specific to certain countries.
- Capable of surviving for long periods in the external environment.
- Mechanically penetrating in the form of spores that produce mycelium.
- Characterized by the presence of two types of spores (macroconidia and microconidia).

Based on the relative abundance of these two types of spores and their morphology, three genera are distinguished among these fungi :

1. The genus ***Epidermophyton*** **(Sabouraud, 1907)** includes only one species : *Epidermophyton floccosum*. This species is characterized by the absence of microconidia and the presence of thin-walled, club-shaped macroconidia (Figure 23). It never infects hair, fur, or nails.

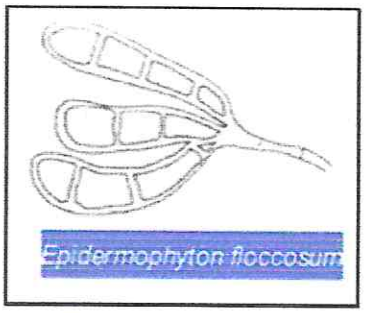

Figure 23 : Macroconidia of *Epidermophyton*

2. The genus ***Microsporum*** **(Gruby, 1843)** includes about ten species. These species parasitize the skin and hair but rarely attack the nails. This genus is characterized by the presence of fusiform macroconidia (Figure 24) and microconidia that are usually pear-shaped but sometimes round.

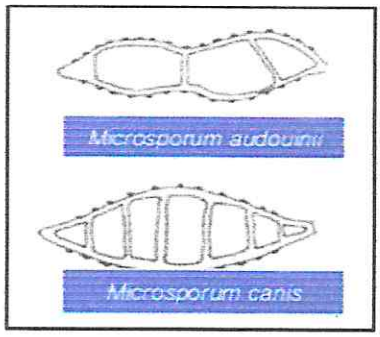

Figure 24 : Macroconidia of *Microsporum*

3. The genus ***Trichophyton*** **(Manson, 1845)** includes the majority of dermatophytes, with more than twenty species capable of parasitizing the skin and appendages in humans. This genus is characterized by the presence of smooth-walled macroconidia and microconidia that are either round or pear-shaped, depending on the species (Figure 25).

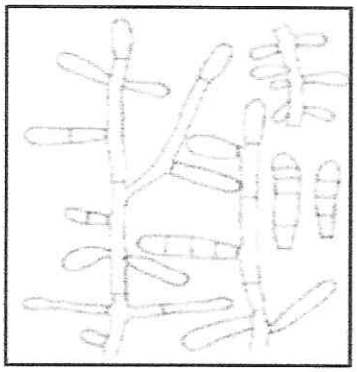

Figure 25 : Macroconidia of and micronidia of *Microsporum*

IV.1.1.2. Epidemiology

The sources of contamination by a dermatophyte are threefold : soil, animals, and humans. Based on their natural habitat, three groups are distinguished (Figure 26) :

- **Anthropophilic species** : These originate exclusively from humans, and their isolation implies human-to-human transmission.
- **Zoophilic species** : These originate from animals, and transmission to humans requires direct or indirect contact with an infected animal (or a healthy carrier).
- **Geophilic or soil-borne species** : These accidentally parasitize humans following an injury. They are species that contaminate the soil.

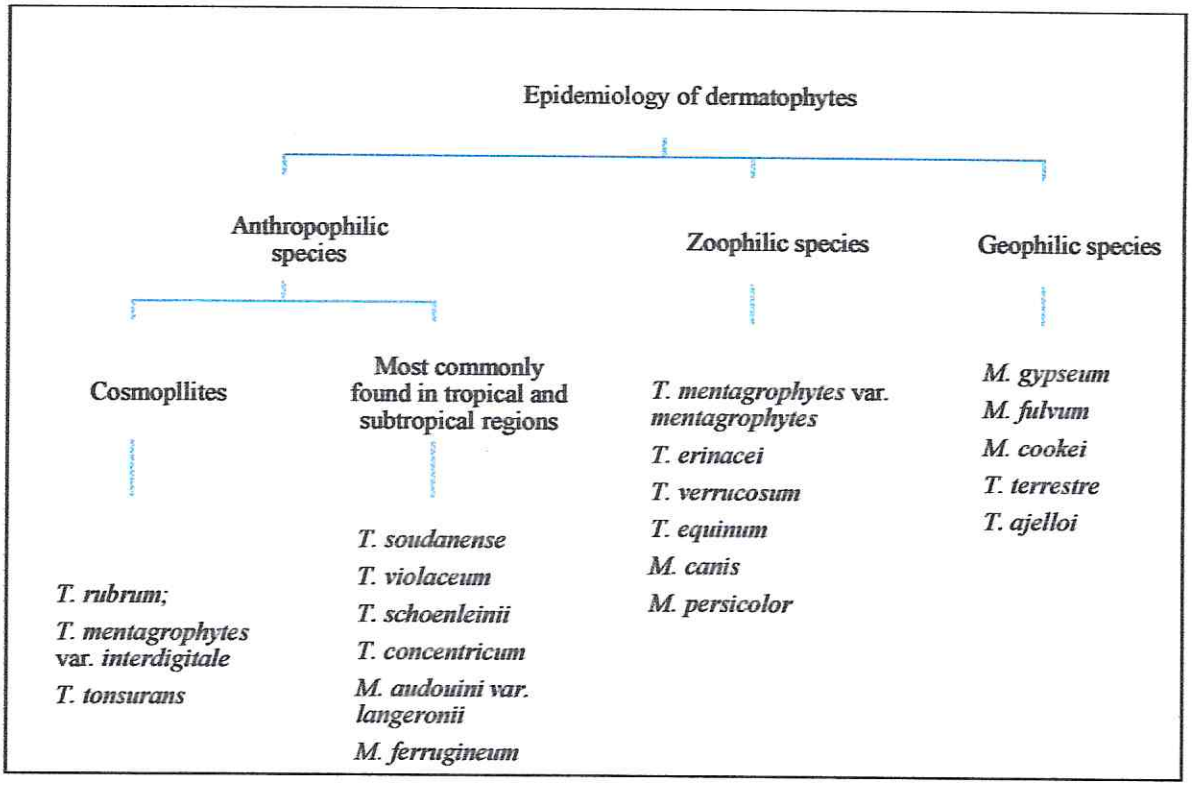

Figure 26 : Origin of dermatophytes (modified)

IV.1.2. Dermatophytoses

Dermatophytoses (referred to as dermatomycoses or Tinea by English speakers) are superficial fungal infections caused by dermatophytes. Given their affinity for human and animal keratin, these fungi attack the skin, particularly the epidermis and keratinized tissues.

IV.1.2.1. Pathogenicity

A.Tinea (Ringworm)

These lesions correspond to infections of the scalp. The outcome of parasitized hair will differ depending on the species involved :

- They will break in the case of **trichophytic shearing ringworm**.
- The parasitized hair becomes completely fragile, with secondary invasion of the hair bulb in **favus ringworm**.
- They will be expelled due to the inflammatory reaction in **kerion**.

It is important to note that tinea is rare in adults. It is typically observed only in children. Depending on the type of hair parasitism, four clinical forms are classically distinguished :

a. Microsporic Shearing Ringworm

This type exclusively affects children before puberty and is characterized by the presence of a small number of large, well-defined alopecic patches, covered with scales and broken hairs (Figuren27). Examination under a Wood's lamp shows a characteristic green fluorescence. Three species are implicated : two anthropophilic (*Microsporum audouinii*, *M. ferrugineum*) and one zoophilic (*M. canis*).

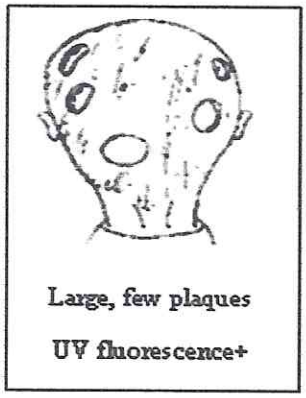

Figure 27 : Microsporic Shearing Ringworm

b. Trichophytic Shearing Ringworm

Also known as **endothrix**, it affects children as well as women. It is characterized by the presence of often numerous, small, poorly defined alopecic patches (Figure 28). Examination under a Wood's lamp shows no fluorescence. The responsible dermatophytes are exclusively anthropophilic species.

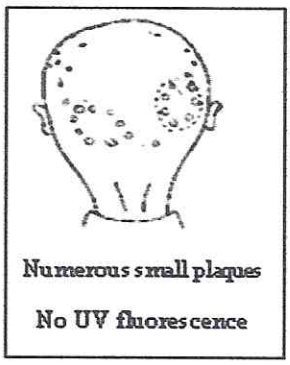

Figure 28 : Trichophytic Shearing Ringworm

c. Inflammatory Ringworm (Kerions)

This usually affects the scalp of children, and more rarely, the scalp of women. In this form, the alopecic patch quickly becomes erythematous, rises, and takes on the appearance of a more or less prominent dome where pus seeps from the hair follicles. The lesions are painful. These ringworms are more commonly caused by zoophilic or geophilic species.

d. Favic Ringworm

Starting in childhood, they can progress into adulthood. They are characterized by the formation of thick, cup-shaped crusts on the scalp. When these crusts fall off, they leave behind a smooth scalp where hair never regrows. Parasitized hairs exhibit fluorescence along their entire length under a Wood's lamp.

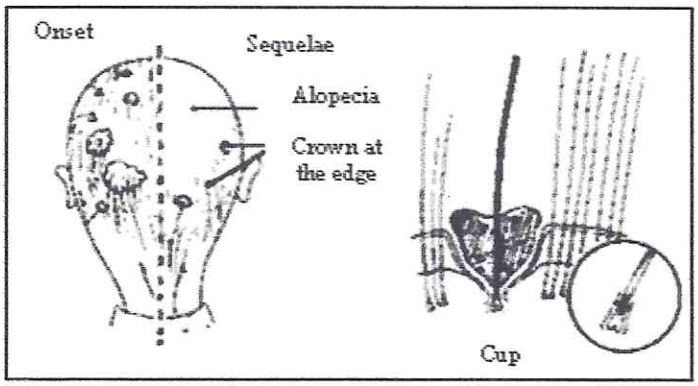

Figure 29 : Favic Ringworm

These ringworms are exclusively caused by the anthropophilic species *T. schoenleinii*. Photos of the different types of ringworm mentioned above are presented in Annex 1.

The different hair lesions are presented in the following figure.

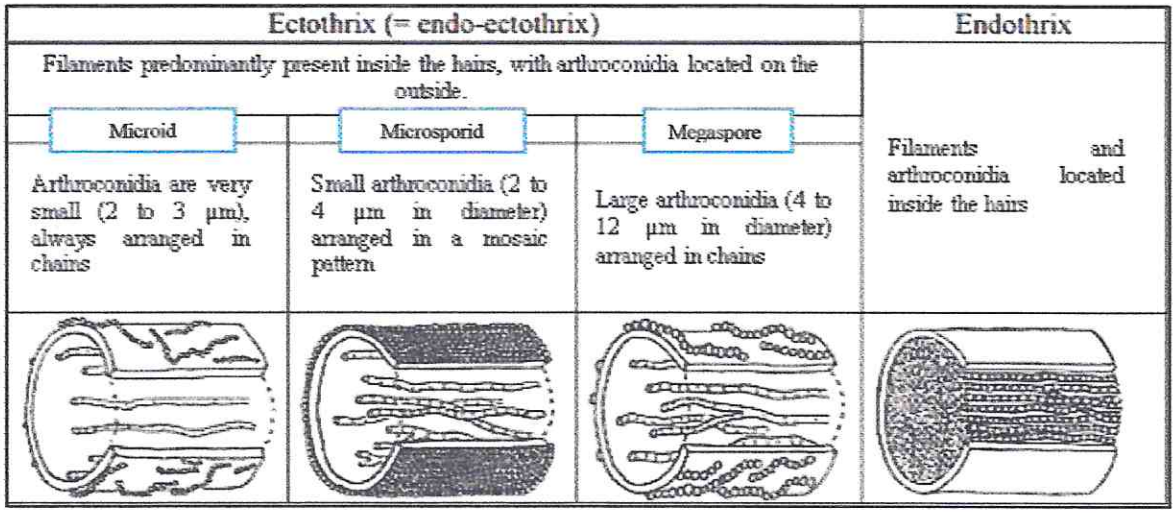

Figure 30 : Different types of hair invasions

Ringworm can be transmitted in the following ways :

- Directly from person to person
- Through objects such as hats, hairdressing tools (combs, hairbrushes, clippers, etc.),

Contamination due to spore inoculation can occur long after contact between the object and the hair of the infected individual due to the long lifespan of spores in the external environment.

B. Tinea Pedis (Athlete's Foot)

- This is the most common dermatophyte infection, representing 30% of dermatophytoses.
- Found in 1/3 of athletes (marathon runners, etc.).
- Often caused by anthropophilic fungi.

The infection usually begins in the interdigital spaces with lesions such as desquamation, fissures, erythema, and itching (Annex 2).

The lesions progress to the sole of the foot and eventually involve the nail (onychomycosis) (Annex 2).

Contamination by the fungus occurs :

- From soil (pool edges, etc.).
- From human keratin debris (parasitized scales or nail fragments).
- By frequenting showers and locker rooms in sport facilities.
- By sharing bath mats and towels among athletes or within a family.
- 2% to 20% of the population is affected by this mycosis (increases with age, 48% at 70 years old).
- Mainly affects toenails.

1. Appearance of Lesions (Annex 2) :
   - Annular "herpes circiné."
   - Geographic patches with well-defined borders.
   - Sometimes, very inflammatory lesions.
2. Common Features of Lesions :
   - Itching.
   - Presence of an erythematous-vesicular-squamous border with a centrifugal pattern of evolution.
3. Mode of Transmission :

- From tinea pedis (extension by scratching of the feet) : anthropophilic dermatophytes.
- From a pet or farm animal through direct contact (petting, etc.) or indirect contact (hair on a chair, etc.) : zoophilic dermatophytes.

IV.1.2.2. Diagnosis of dermatophytoses

A mycological examination is essential before treatment, confirming the mycosis through direct examination and identifying the dermatophyte through culture.

Step 1 : Skin sampling away from any antifungal treatment :

- Epidermophyte infection : scraping scales at the lesion edges.
- Onychomycosis : cutting the nail and scraping scales at the junction of the diseased and healthy areas.
- Ringworm : scraping + removal of broken hairs.

Step 2 : Direct microscopic examination confirms the diagnosis : mycelial filaments or hair parasitism.

Step 3 : Culture in 2-3 weeks : identification of the dermatophyte.

IV.1.2.3. Main factors favoring dermatophytoses

- Heat and humidity, particularly at the feet (synthetic fabrics or plastic shoes preventing evaporation).
- Maceration (inguinal folds, interdigital spaces).
- Lifestyle (sports activities), profession (farmers, cattle breeders, lifeguards).
- Microtrauma : onychia of the feet in athletes, palm pachyderma in manual workers.
- Hormonal factors : most scalp ringworms resolve at puberty.
- Immunosuppression.

IV. 2. Cryptococcosis

A cosmopolitan mycosis caused by an encapsulated yeast : *Cryptococcus neoformans*. Its usual location is meningeal and encephalic. It affects both healthy individuals, especially in the tropics, and at-risk patients such as immunocompromised individuals. A resurgence linked to the AIDS pandemic was noted in 1980.

IV.2.1. Classification

Kingdom : Fungi

Division : Basidiomycota

Class : Tremellomycetes

Order : Tremellales

Family: Tremellaceae

Genus: *Cryptococcus*

IV.2.2. Morphology

- Round yeast 3 to 8 µm in diameter, surrounded by a characteristic mucopolysaccharide capsule (Figure 31).
- Culture on Sabouraud medium is slightly ochre.
- The capsule is well highlighted by mounting in diluted India ink and observation under a microscope.

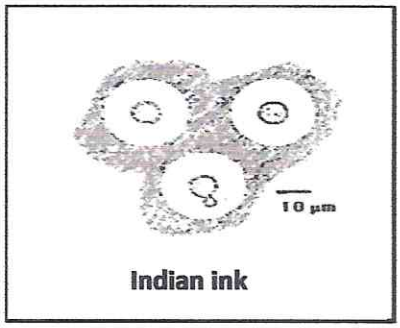

Figure 31 : Capsule of *C. neoformans* stained with India ink

There are two varieties : *C. neoformans* var. *neoformans* and *C. neoformans* var. *gattii* (widespread in Sub-Saharan Africa).

IV.2.3. Epidemiology

Cryptococcus neoformans is a saprophytic fungus in the external environment and an opportunist : cryptococcosis most often occurs in immunocompromised individuals (especially those with AIDS) or those with severe hematological disorders. *Cryptococcus neoformans* is often found in bird droppings, especially pigeon droppings. Contamination is airborne, through pulmonary routes.

IV.2.4. Clinical Presentation

- **Pulmonary Cryptococcosis**

  Corresponds to primary infection, almost always asymptomatic. If symptomatic, it mimics flu-like symptoms.

- **Meningoencephalic Cryptococcosis**

  Cryptococcus neoformans has a tropism for the central nervous system. Symptoms include headaches, nausea, mild fever, neck stiffness (variable), personality changes, memory and sleep disturbances, and intracranial hypertension.

- **Cutaneous Cryptococcosis**

  Results from hematogenous dissemination. It is characterized by the presence of acneiform papules and ulcers on the face (Annex 3).

- **Generalized Cryptococcosis** (Annex 3)

  Common in AIDS. The yeast is found in blood cultures, urine, bronchoalveolar lavage fluids, and cerebrospinal fluid.

IV.2.5. Mycological Diagnosis

- Samples : CerebroSpinal Fluid (CSF), urine, bronchoalveolar lavage, pus, biopsies
- Direct Examination : Presence of encapsulated yeasts (highlighted by mounting in diluted India ink)
- Culture : At 37°C on Sabouraud medium without actidione : beige, mucoid colonies in 3 to 5 days.
- Identification : Presence of a capsule.

IV.3. Candidiasis

Candidoses are cosmopolitan infections caused by yeasts of the genus Candida. Their pathogenicity depends on their various locations. Favoring factors include :

- General Factors :
  - Age : premature infants, elderly
  - Therapies : antibiotics, corticosteroids, immunosuppressants, psychotropics
  - Pathological states : diabetes, Hodgkin's lymphoma, AIDS
  - Special physiological states : pregnancy
- Local Factors : Moisture, maceration, acidity, radiotherapy

IV.3.1. Morphology

Candida are white, non-encapsulated yeasts. The yeast form is unicellular and multiplies by budding, with the possibility of growth in the form of pseudomycelium (Figure 32).

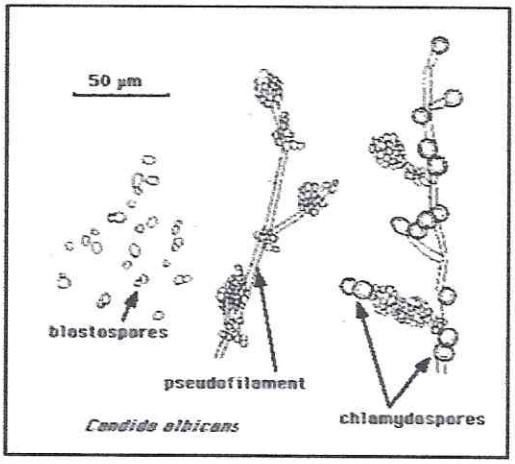

Figure 32 : Morphological appearance of *Candida albicans*

C. albicans is the most frequently encountered species in pathology. This species is also a commensal (saprophyte) of the digestive tract. Other species encountered in pathology include *Candida glabrata*.

IV.3.2. Epidemiology

Contamination often comes from the host's own saprophytic strain.

IV.3.3. Clinical Presentation

- **Cutaneous Candidiasis :** Characterized by skin lesions in folds (intertrigo : buttocks, inguinal, under breasts) with erythema, pain, burning, and itching ; and on nails, especially hand fingernails, with perionychia and onycholysis (Annex 4). The causative species is *C. albicans*. This species is absent on healthy skin, so it is always pathogenic when isolated from the skin.
- **Mucosal Candidiasis**
    1. **Oral Thrush (Oropharyngeal) :**
        - **Clinical Aspect :** Pseudomembranous lesions on an erythematous mucosa (Annex 4), pain, and dysphagia.
    2. **Angular Cheilitis :** Cracking and inflammation of the labial commissures.
- **Vaginal Candidiasis**
    - *C. albicans* (+++), but also *C. glabrata*
    - Very common

- Triggered by pregnancy or antibiotic therapy
- Clinical Aspect : White leucorrhea, erythematous and inflammatory mucosa, vulvar itching, burning, and dysuria.

- **Balantitis :** Itching, inflammation, and pain of the penis.
- **Deep Candidiasis :** Systemic candidoses (Annex 4), including hepatic, splenic, renal, and ocular.

IV.3.4. Diagnosis

- Mycological Diagnosis
  - Samples : Scraping of dry lesions, swabbing of moist lesions, nail debris, stool, etc.
  - Direct Examination : Yeasts + pseudohyphae
  - Culture : Colonies in 48 hours on Sabouraud medium
  - Identification : Antifungal susceptibility testing
- Immunological Diagnosis : In visceral infections, by detecting antibodies and circulating antigens (especially in immunocompromised individuals).

IV.4. Aspergillosis

Aspergilloses are cosmopolitan mycoses, most often pulmonary, caused by a filamentous fungus (mold) of the genus Aspergillus. These are opportunistic infections.

IV.4.1. Morphology (see course on toxin-producing molds)

IV.4.2. Epidemiology

- *Aspergillus fumigatus* is responsible for 80% of human aspergilloses.
- Aspergilli produce numerous airborne spores.
- They are opportunistic : they grow if they encounter favorable conditions such as a residual pulmonary cavity (e.g., tuberculosis sequela) or immunodeficiency.

IV.4.3. Clinical Presentation

- Pulmonary Aspergilloma

  In healthy individuals, inhaled spores are removed by the mucociliary apparatus or destroyed by alveolar macrophages. If these mechanisms are deficient, spores can germinate in a residual cavity, forming an "aspergilloma." *A. fumigatus* is favored by its thermophilic nature (grows up to 55°C). Clinical signs include hemoptysis, cough, expectoration, fever, asthenia, and weight loss.

- Invasive Aspergillosis
  - Involves the development of the fungus in the lung parenchyma in immunocompromised individuals (e.g., transplant patients).
  - Often fatal.
  - Possible dissemination with renal, cerebral, hepatic, and cardiac involvement.
- Allergic aspergillosis
  - Extrinsic allergic alveolitis (farmer's lung)
  - Aspergillus asthma
  - Allergic bronchopulmonary aspergillosis (ABPA): asthma with pulmonary eosinophilia.
- **Localized Extra-Pulmonary Aspergillosis**

  Aspergillus can also develop in the ear canal (otomycosis), sinuses (sinus aspergillosis), or on the skin of burn patients.

Conclusion

Medicinally relevant fungi are microscopic heterotrophic eukaryotes, some of which cause poisoning through the secretion of mycotoxins that contaminate food products, while others trigger allergic reactions in humans following the inhalation of spores. However, the most significant are the mycotic agents that invade skin tissues, whether superficial, subcutaneous, or deep.

With the increasing number of immunodeficiency cases, environmental micromycetes, once considered mere contaminants in cultures, have become pathogenic and are responsible for invasive fungal infections.

This clear, well-documented, and illustrated booklet helps Biology students familiarize themselves with the world of fungi and contribute to the diagnosis of mycoses.

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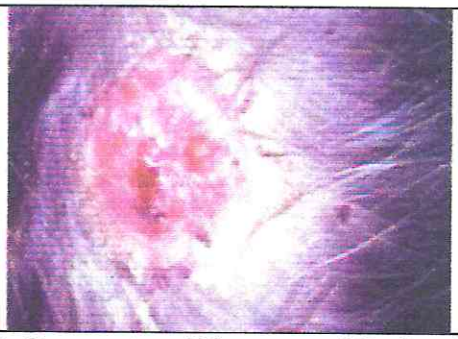
Annex 1

Different types of ringworm

	
Microsporic Shearing Ringworm	**Trichophytic Shearing Ringworm**
	
Inflammatory Ringworm (Kerions)	**Favic Ringworm**

Annex 2

Tinea Pedis, nails and smooth Skin

Dermatophyte infection of the interdigital spaces

dermatophyte infection of the sole of the foot

Ungal infection of the nails

Smooth skin

Annex 3

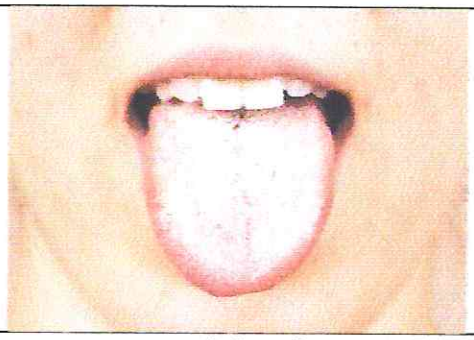
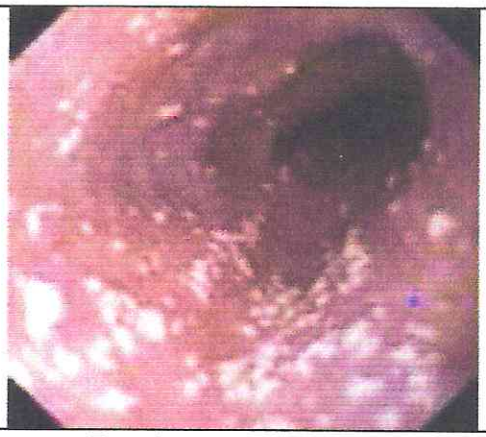
Cryptococcosis

Cutaneous Cryptococcosis

Generalized Cryptococcosis

Annex 4

Candidiasis

	
oral thrush	**Angular Cheilitis**
	
Esophageal candidiasis	**Intertrigo**
	
Nail candidiasis	**Systemic candidiasis**

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Chapter IV. Pathogenic molds and yeasts