1

University - Chahid Chikh Larbi Tébessi- Tebessa
Faculty: Exact Sciences And Natural and Life Sciences

Field: Natural and Life Sciences
Fields of study: Biological Sciences
Department: Applied Biology

Speciality Master 01 Applied Microbiology

course :

# APPLIED MYCOLOGY

*Dr. Smaali Saoussene*

***2024-2025***

**Semestre: 2**
**Intitulé de l'UE : UEM2 : Unité Méthodologique 02**
**Intitulé de la matière 1: Mycologie appliquée**
**Crédits : 04**
**Coefficients: 02**

**Objectifs de l'enseignement :**

Cette matière visera à familiariser le candidat avec le monde de la mycologie. Seront abordés, après quelques rappels sur les caractéristiques générales des champignons, les champignons toxiques et comestibles, les différents syndromes d'intoxication fongique, l'intérêt de l'utilisation dans les industries (fermentations, médicaments, industrie papetière, biocarburants), implications quotidiennes positives ou négatives (fromage, mycotoxines, mérule).

**Thèmes abordés :**
**CARACTERISTIQUES GENERALES DES CHAMPIGNONS**

- Composition chimique et structure des cellules
- Croissance et reproduction
- Culture au laboratoire et à grande échelle

**II. CLASSIFICATION DES CHAMPIGNONS**

- Levures
- Zygomycètes
- Ascomycètes
- Basidomycètes
- Deuteromycetes

**III. INTERET DE L'UTILISATION DES CHAMPIGNONS**

**A. Agro-Alimentaire**

1. Utilisation des moisissures :
2. Utilisation des levures :

**B. Industrie Pharmaceutique**

Champignons producteurs de métabolites : vitamines, antibiotiques et enzymes

**IV. ASPECTS PATHOLOGIQUES**

A. Chez le végétal
- Champignons de stockage
- Mycotoxines

B. Chez l'Homme et l'Animal

- Candidoses
- Dermatophytes

## 2- Semestre 2 :

| Unité d'Enseignement | VHS | V.H hebdomadaire | | | | Coeff | Crédits | Mode d'évaluation | |
|---|---|---|---|---|---|---|---|---|---|
| | 14-16 sem | C | TD | TP | Autres | | | Continu | Examen |
| | | | | | | | | | |
| **UEF2** | **202.30H** | **6H** | **4H30** | **3H** | **247.30H** | **09** | **18** | | |
| **Matière 1 : Microbiologie clinique II** | 67.30H | 1,30H | 1,30H | 1,30H | 82.30H | 3 | 6 | + | + |
| **Matière 2 : Microbiologie de l'environnement II** | 67.30H | 1,30H | 1,30H | 1,30H | 82.30H | 3 | 6 | + | + |
| **Matière 3 : virologie** | 67.30H | 3.00H | 1,30H | | 82.30H | 3 | 6 | + | + |
| | | | | | | | | | |
| **UEM2** | **105H** | **3H** | **2.30H** | **1.30H** | **120H** | **5** | **9** | | |
| **Matière 1 : mycologie Appliquée** | 45H | 1,30 | 1,30 | | 55H | 2 | 4 | + | + |
| **Matière 2 : contrôle microbiologique des aliments** | 60H | 1,30 | 1.00 | 1,30H | 65H | 3 | 5 | + | + |
| | | | | | | | | | |
| **UED2** | **45H** | **1,30 H** | **1.30H** | | **5 H** | **1** | **2** | | |
| **Matière 1 : Parasitologie** | 45H | 1.30H | 1.30H | | 5 H | 1 | 2 | + | + |
| | | | | | | | | | |
| **UET2** | **22.30** | **1,30** | | | **2.30H** | **1** | **1** | | |
| **Matière 1 : Législation** | 22.30 | 1,30 | | | 2.30H | 1 | 1 | | + |
| **Total Semestre 2** | **375H** | **12.H** | **8.30H** | **4.30H** | **375H** | **16** | **30** | | |

## Table des matières

## Introduction

Mycology, the scientific study of fungi, is important to many domains, from biotechnology to ecology. In-depth knowledge of the biological characteristics of fungus, their practical uses in a range of sectors, and the pathological risks they offer to people, plants, and animals are the main goals of this applied mycology course.

We will examine **the general properties of fungi** in the first section of the course, including information on their shape, life cycle, and ecological function. Despite being disregarded a lot, fungi have a special place in the living world. Their unique cellular structure, variety of reproductive strategies, and environmental adaptability—from forest soils to aquatic habitats—set them apart. Their long-debated taxonomy emphasizes their basic distinction from plants and animals by placing them in a separate kingdom.

The seminar will next go into **the advantages of using fungus in various industries.** In addition to serving as a direct source of nutrition, fungi are essential to the food industry because they act as fermentation agents during the creation of alcoholic drinks and other food products. Moreover, they have a wide range of pharmacological and medical uses, such as the synthesis of immunosuppressants, anticancer drugs, and antibiotics. Fungal biotechnology is making significant strides that could lead to the generation of biofuels and bioremediation, making fungi extremely valuable creatures for sustainable development.

Lastly, we shall look at **the pathogenic features related to fungus**. Although these organisms are helpful in a variety of situations, they may also seriously harm people, plants, and animals. Whether superficial or systemic, human mycoses pose a serious threat to public health, especially in light of the rise in antifungal resistance. Conversely, phytopathogenic fungi cause large-scale agricultural losses that have an immediate impact on the world's food security. The seminar will emphasize the difficulties in controlling these infections while highlighting contemporary preventative and treatment approaches.

In addition to enhancing students' theoretical understanding, this course seeks to provide them with the skills necessary to use that knowledge in real-world contexts, such as laboratories, businesses, or research projects. Students will be more prepared to contribute to innovation in their future professional domains if they have a greater awareness of fungi, including its traits, applications, and risks.

## I. 1. Definition of Mycology

The Greek word "mykes," which means mushroom, is where the name "mycology" originates. Thus, the study of fungi is known as mycology.

Even though it was known that fungi could penetrate plant and animal tissue as early as the 19th century, the first documented case of a fungal infection in animals was Bassi's 1835 investigation of the silkworm muscardine sickness and the subsequent evidence that the fungus Beauveria bassiana was the source of the infection [(1)]

## I. 2. General characteristics of fungi

Fungi, or mycetes, constitute an extremely vast group, composed of more than 100,000 species. They are eukaryotic organisms, whose cells have a wall and lack chloroplasts (hence they are chemoheterotrophs), whose vegetative apparatus consists of a thallus, and which bear spores, capable of both sexual and asexual reproduction.[(2)]

**The thallus:** This is the name given to the vegetative apparatus of fungi. Fungi, like algae, belong to the thallophytes = which do not possess true differentiated tissue. The thallus can consist of a single cell. Unicellular fungi are called yeasts. Multicellular thalli consist of a mycelium and fruiting bodies. They are called filamentous fungi or molds.

**The mycelium** is formed of tubes (hyphae), which may be interrupted by septa. Fruiting bodies (spores) may appear on certain hyphae.

Tiny strands of chitin, a complex carbohydrate, significantly reinforce the hyphae's cell walls. Septa, or partial cross-walls, partition the hyphae in certain fungal species into compartments that resemble cells (single septum). The term "septate hyphae" refers to these split hyphae. Septa do not seal up hyphal chambers entirely. Organelles and occasionally even nuclei can migrate across compartments in a regulated manner thanks to pores in the septa's cores (Fig. 1). Other fungal species have hyphae that may have hundreds of nuclei but lack septa. We call these undivided, multinucleate hyphae coenocytic. Coenocytic conditions are caused by multiple nuclear divisions that do not involve cytokinesis. [(3)]

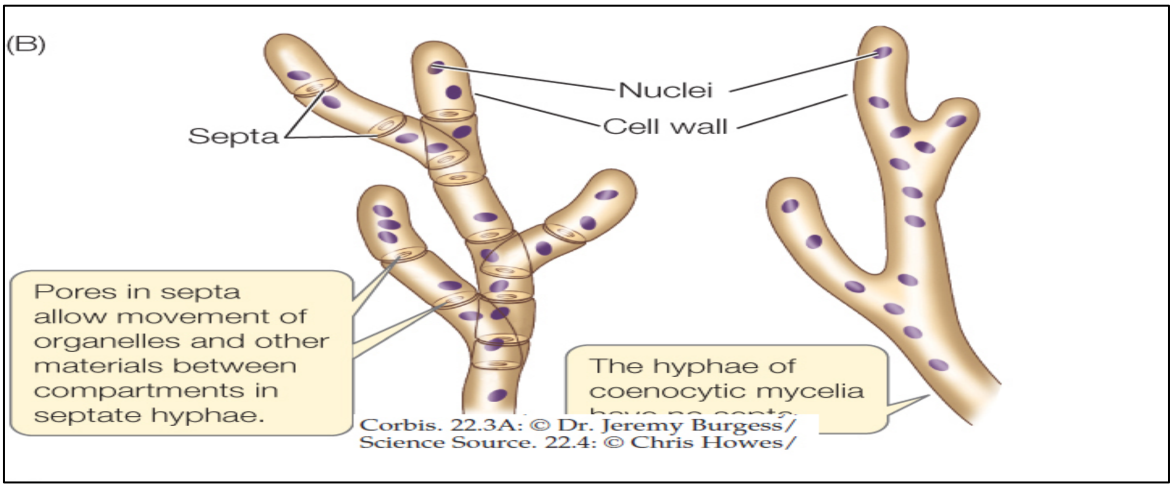


**Fig. 1.** Mycelia are made up of hyphae [(3)]

## I. 3. Chemical Composition and Cellular Structure

The fungal cell is composed of cytoplasm, with a pH of 5, and contains numerous enzymes, reserves (glycogen), and organelles (Fig. 2): endoplasmic reticulum, Golgi apparatus, mitochondria, reserve vacuoles (containing glycogen), cytoskeleton (actin and tubulin filaments), and ribosomes. The nucleus (some structures have one, others two or more). The plasma membrane, rich in ergosterol, is protected by a rigid and thick wall (Fig. 3) composed mainly of polysaccharides (including chitin, a polymer of N-acetyl glucosamine).[(4)]

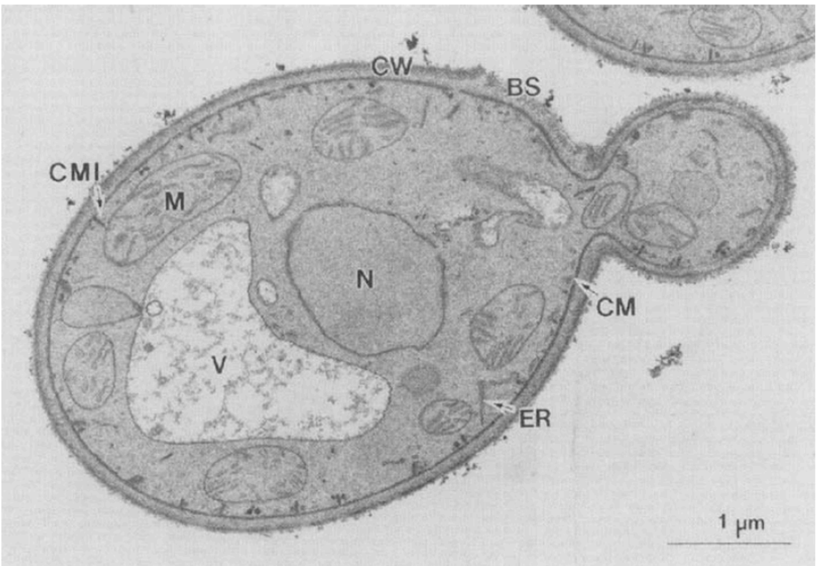


**Fig 2.** Electron micrograph of a yeast cell.[(4)]
V, vacuole; CW, cell wall; ER, endoplasmic reticulum CM, BS, bud scar; cell membrane; CMI, cell membrane invagination; M, mitochondrion; N, nucleus;

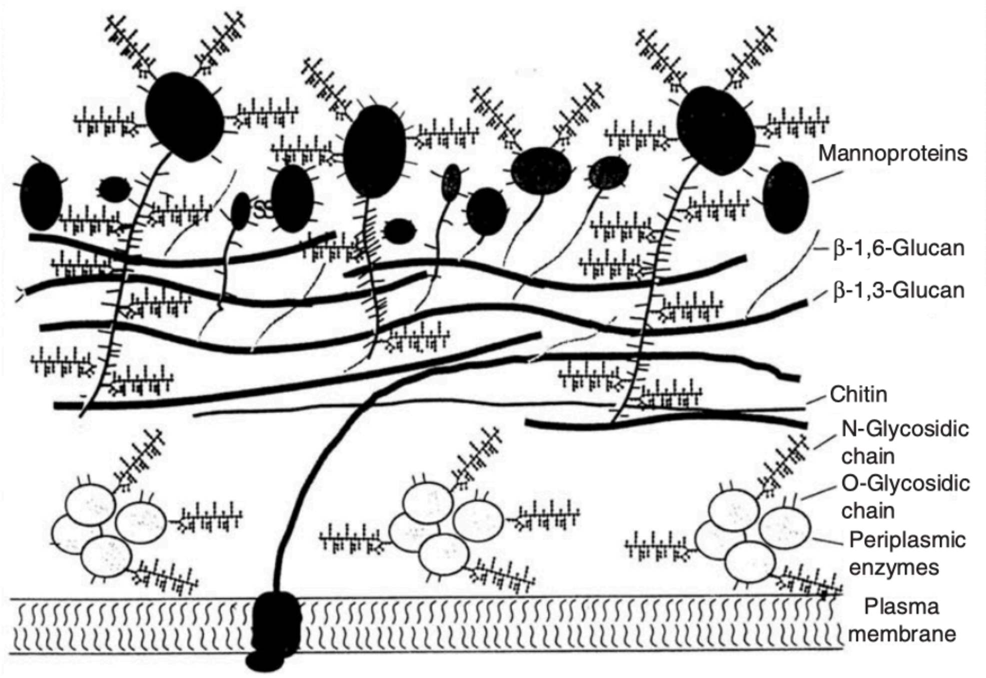


**Fig. 3.** Cell envelope structure of the yeast *S. cerevisiae* (5)

## I. 4. Nutrition

As heterotrophic organisms, fungi are unable to produce their organic matter. They must therefore obtain the nutrients necessary for their growth by absorbing pre-existing organic compounds. There are three main modes of fungal nutrition(6)

- **Saprophytism:** Saprophytic fungi feed on dead organic matter, such as wood, dead leaves, or excrement.
- **Parasitism:** Parasitic fungi live at the expense of other living organisms, often causing diseases.
- **Symbiosis:** Symbiotic fungi, such as those found in lichens, live in a close and beneficial association with other organisms, notably algae.

## I. 5. Classification of fungus

Botany has an impact on the categorization of fungi since they were originally categorized alongside plants and were of interest to botanists. All living things were divided into five kingdoms by R.H. Whittaker in 1969: Monera, Protista, Fungi, Plantae, and Animalia. The categorization process often works like this:Kingdom Subkingdom, Phylum/Phyla, Subphyla, Class, Order, Family, Genus, and Species (1)

Originally, the main fungal groupings were identified by their sexual reproductive structures and processes, as well as, to a lesser extent, by other morphological variations(1).

***Depending on sexual reproduction:***

- **Zygomycetes:** these organisms generate zygospores by manufacturing.
- **Ascomycetes:** these organisms generate ascospores naturally in asci, which are cells.
- **Basidiomycetes**: these organisms create basidiospores, which are exogenous spores, in cells known as basidia.
- **Deuteromycetes**, also known as Fungi imperfecti, are fungi that are not known to generate ascospores or basidiospores, which are sexual spores. There has never been any evidence of sexual reproduction in this diverse species of mushrooms.

***According to Morphology:***

- **Moulds**: Fungi that are filamentous For example: *Trichophyton rubrum, Aspergillus sp*.
- ***Yeasts:*** *Single-cell, bud-forming cells Saccharomyces cerviciae and Cryptococcus neoformans are two examples.*
- **Similar to yeast**: Like yeasts, but they also create pseudohyphae such as *Candida albicans*
- **Dimorphic:** Fungal species that exhibit two distinct morphological forms under two distinct environmental circumstances.

The six main groups of fungi are microsporidia, chytrids, zygospore fungi (Zygomycota), arbuscular mycorrhizal fungi (Glomeromycota), sac fungi (Ascomycota), and club fungi (Basidiomycota), though the diversity of fungal life cycles is even greater than previously thought. (Table 01)

They exist as molds in the wild and as yeasts in tissue and in vitro at 37°C. They also thrive at room temperature in vitro. As an example, *Blastomyces dermatidis, Coccidioides immitis, Paracoccidiodes brasiliensis, and Histoplasma capsulatum.* A little over 200 "human pathogens" have been identified out of an estimated 1.5 million fungal species(1).

**Table 01.** Classification of the Fungi (3)

| Group | Common name | Features |
|---|---|---|
| Microsporidia | Microsporidia | Intracellular parasites of animals; greatly reduced, among smallest eukaryotes known; polar tube used to infect hosts |
| Chytrids (paraphyletic)[a]<br>Chytridiomycota<br>Neocallimastigomycota<br>Blastocladiomycota | Chytrids | Mostly aquatic and microscopic; flagellated gametes and zoospores |
| Zygomycota (paraphyletic)[a]<br>Entomophthoromycotina<br>Kickxellomycotina<br>Mucoromycotina<br>Zoopagomycotina | Zygospore fungi | Reproductive structure is a unicellular zygospore with many diploid nuclei in a zygosporangium; hyphae coenocytic; usually no fleshy fruiting body |
| Glomeromycota | Arbuscular mycorrhizal fungi | Form arbuscular mycorrhizae on plant roots; only asexual reproduction is known |
| Ascomycota | Sac fungi | Sexual reproductive saclike structure known as an ascus, which contains haploid ascospores; hyphae septate; dikaryon |
| Basidiomycota | Club fungi | Sexual reproductive structure is a basidium, a swollen cell at the tip of a specialized hypha that supports haploid basidiospores; hyphae septate; dikaryon |

[a]The formally named groups within the chytrids and Zygomycota are each thought to be monophyletic, but their relationships to one another (and to microsporidia) are not yet well resolved.

## I. 6. Growth and Reproduction

### I.6.1. Thallus Growth

"Apical growth" refers to the unique growth that happens at the tips of the filaments in fungus.

This apical growth requires the breakdown of the existing cell wall and the synthesis of new wall material. The filament's apex, or tip, is generally rich in vesicles containing precursors for the new wall. The elongation of the apex results from a cytoplasmic flow oriented towards this area, guided by these vesicles. The newly synthesized wall is initially fluid and then becomes more rigid. Lateral branches generally appear a few tens or hundreds of micrometers from the apex (Fig. 4). The frequency of these branches is directly linked to the availability of nutrients. However, apical growth exerts dominance over these lateral branches. Nutrients are transported from the oldest parts of the mycelium to the newly formed parts [7;8]

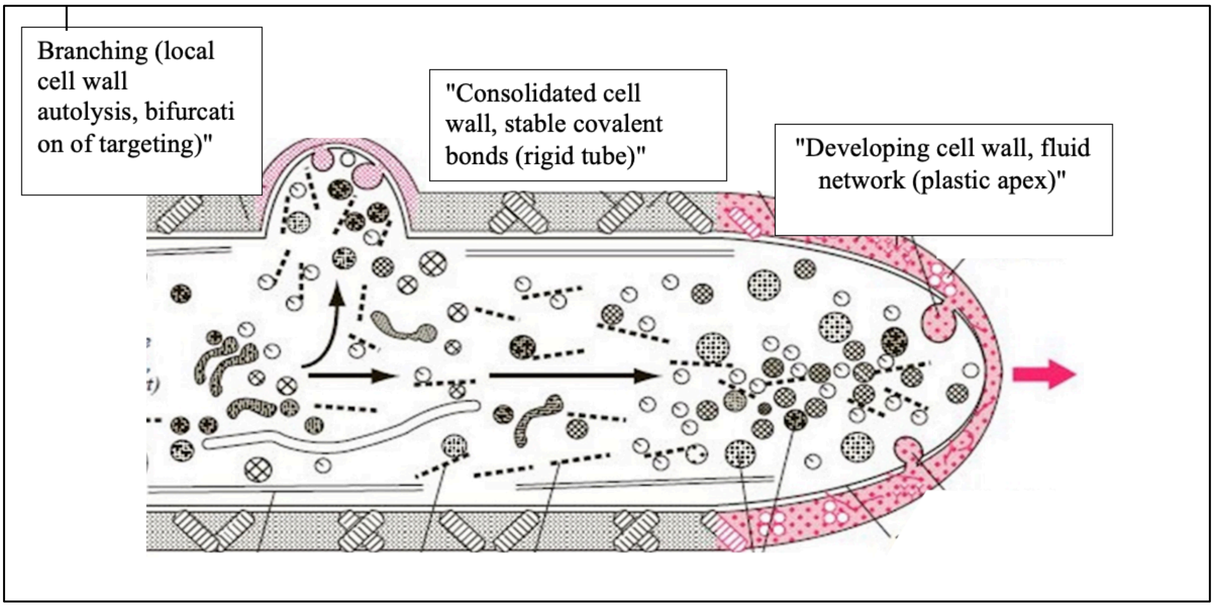


**Fig 4.** Apical cytoplasmic flow [8]24

### I.6.2. Life cycle

Depending on the species, fungi can have a wide variety of life cycles. Different mushrooms reproduce in different ways. There are asexual and sexual ways for fungus to reproduce. As a result, we will examine the asexual and sexual phases of the fungal life cycle (Fig. 5).

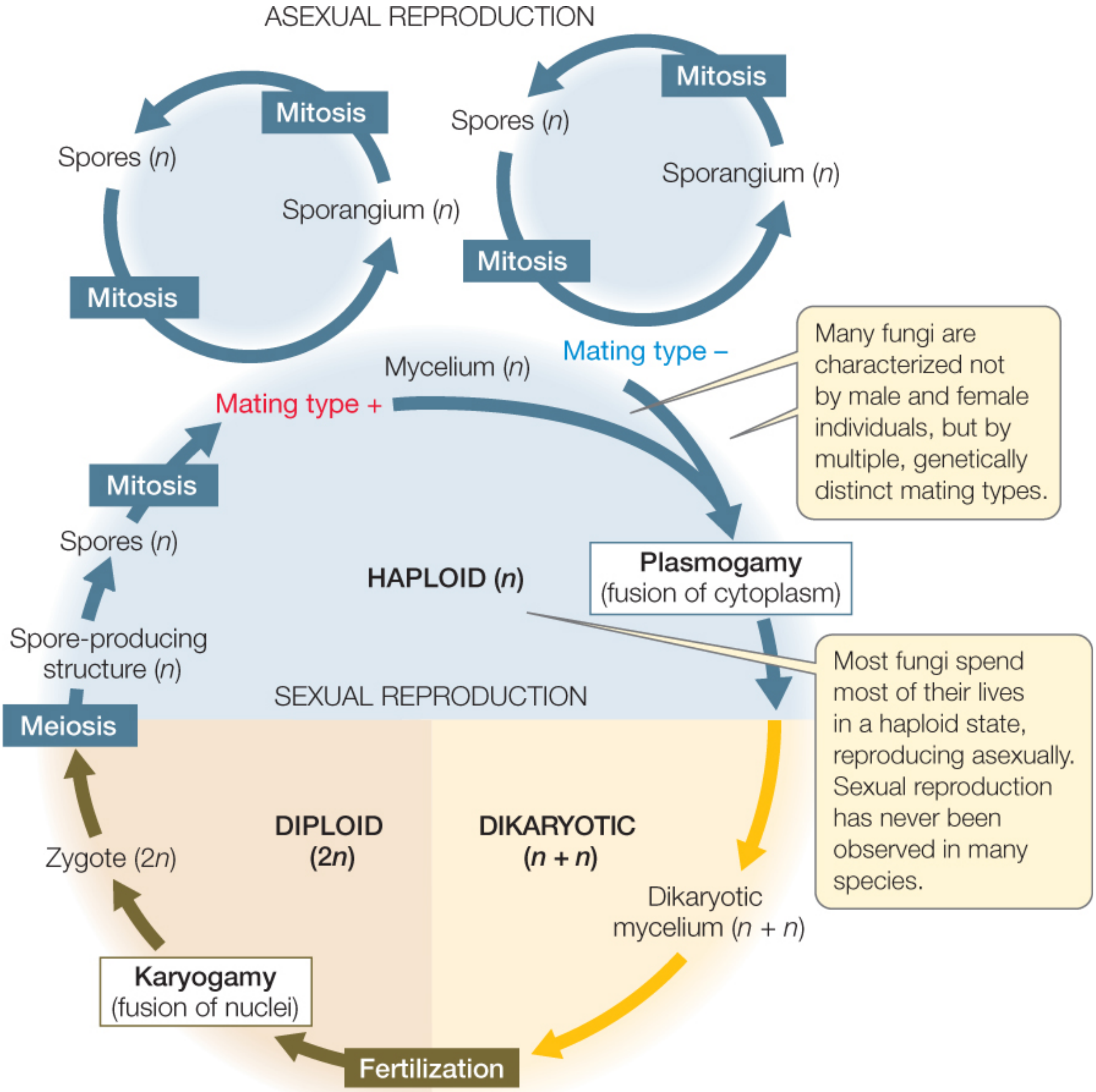


**Fig. 5.** A Generalized Fungal Life Cycle [3]

## A. Fungi's Sexual Reproduction

***Spore :***The earliest stage of the fungal life cycle is called a spore (Haploid). At start, all spores are haploid, which means that only one copy of their whole genetic code exists. These spores travel great distances either by flying or by attaching themselves to other living things. Once they have found a suitable place to live, they produce a large number of structures known as mycelium that resemble roots.

Nutrients are transferred through the mycelium to create spores. Conidia and sporangiospores are the two main asexual spore forms produced by fungi. The feature of sporangiospores [9]:

- Endogenous: developed and housed inside a sporangium

- In certain instances, the creation of a wall surrounding each nucleate piece of protoplasm occurs after the cleavage of protoplasm around nuclei, which is how they developed.
- Fungal characteristics include belonging to the oomycota, hyphochytridiomycota, and chytridiomycota groups, which comprise two primary kinds.
- They are non-motile aplanospores and motile zoospores.

**Mycelium (Diploid):** As the mycelium expands and matures, it may come into contact with more fungi. A haploid cell from each fungal mycelium combines with another to generate a new diploid cell if the two fungi are compatible. Since their genetic material is duplicated, these newly united cells are diploid. [9]

**Meiosis**: The fungus proceeds to the following stage, called meiosis, once it has transformed into a mycelium. During meiosis, a single cell splits into two, combining the genetic material of both parents. The two daughter cells that were produced don't look like their parents at all. The two daughter cells that were created do not resemble each other or have traits that are exactly like those of their parents. [9]

**B. Fungi's Asexual Reproduction:**

The fungus has the option of sexual or asexual reproduction when in the mycelium stage. The asexual life cycle results in mitospores that are exact replicas of their parents. Afterward, these mitospores develop into fresh mycelium, and the whole life cycle is repeated.
A diploid zygote is created during the process of sexual reproduction when two haploid gametes fuse. Certain species may develop sexually compatible gametes on the same mycelium and are self-fertile. In other species, it is required to cross individuals[9].
In fungi, the fusing of nuclei (karyogamy) and cytoplasms (plasmogamy) frequently occurs after a certain amount of time. As a result, cells go through a dikaryotic stage during which they have two distinct haploid nuclei, one from each parent (Fig. 5).

In The kingdom fungi or mycota only four divisions are involved in medical mycology

## I.6.1. Ascomycetes:

Ascomycetes are the most widespread fungi. Their sexual reproduction occurs in closed structures (sac-like) called "asci", hence the name Ascomycetes given to these species. Their asexual stage (anamorph) is most involved in human and animal pathology [10]Fig.6.

it is characterized by[1]:

- Sexual spore produced within a sac-like structure called ascus.
- Sexual spore are called ascospore
- Asexual reproduction occurs by single celled or multi celled conidia
- Ascomycetes are also known as sac mycetes.
- Hyphae are generally septated
- Examples: *Saccharomyces, Arthroderma, Gibberella*

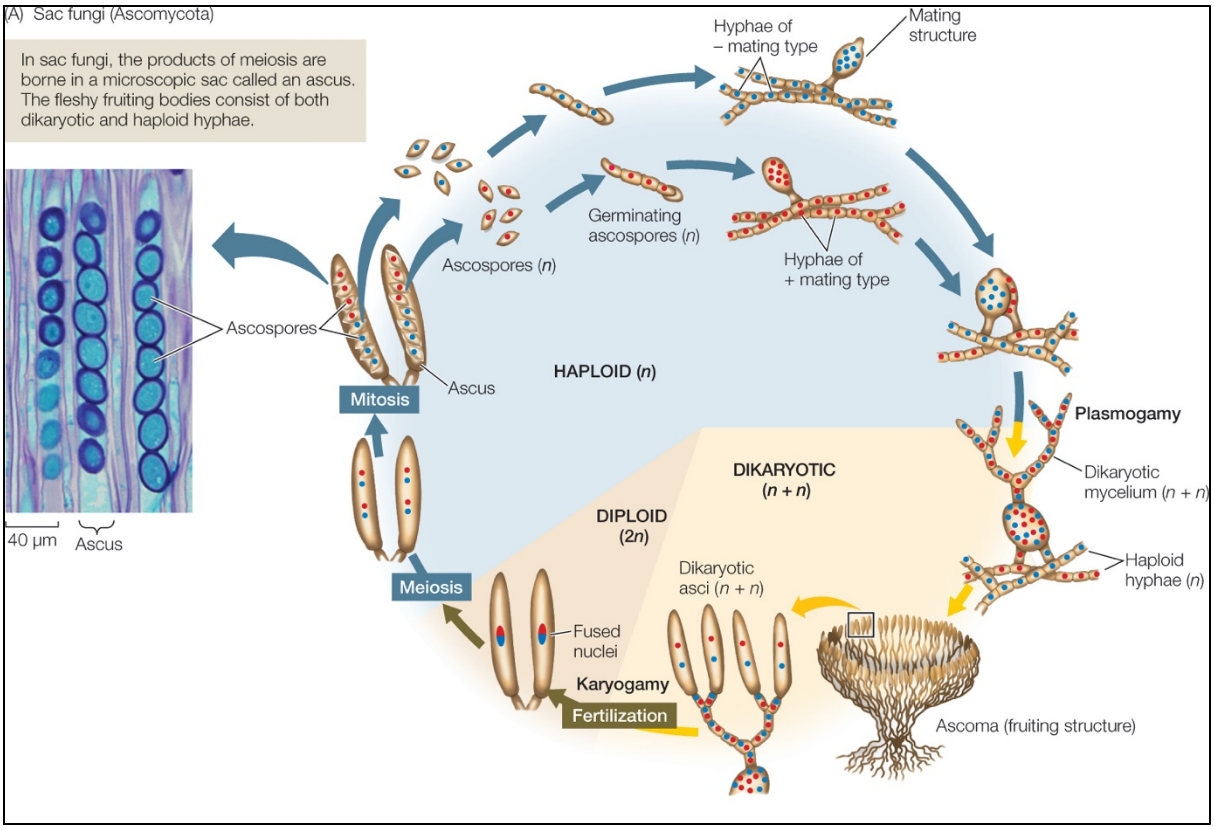


Fig. 6. **Sexual Life Cycles among the Dikarya** ; The fruiting structure of sexually reproducing sac fungi is the ascoma, often a cup-shaped structure. [3]

## I.6. 2. Basidiomycetes:

They encompass all species that share the common feature of producing sexual reproductive structures called "basidia" giving rise to exogenous spores, the basidiospores. Many of them are Macromycetes (large, capped fungi), some are plant parasites, and others are formidable opportunists in humans (Cryptococcus, etc.) [10] (Fig. 7).

it is characterised by[1]:

- Sexual spore are produced externally on a basidium
- Sexual spore are known as basidiospore
- Asexual reproduction occurs by budding, fragmentation or conidia formation
- They are commonly called as mushroom group
- Hyphae are generally septated
- Examples: *Amanita, Agaricus, Filobasidiella*

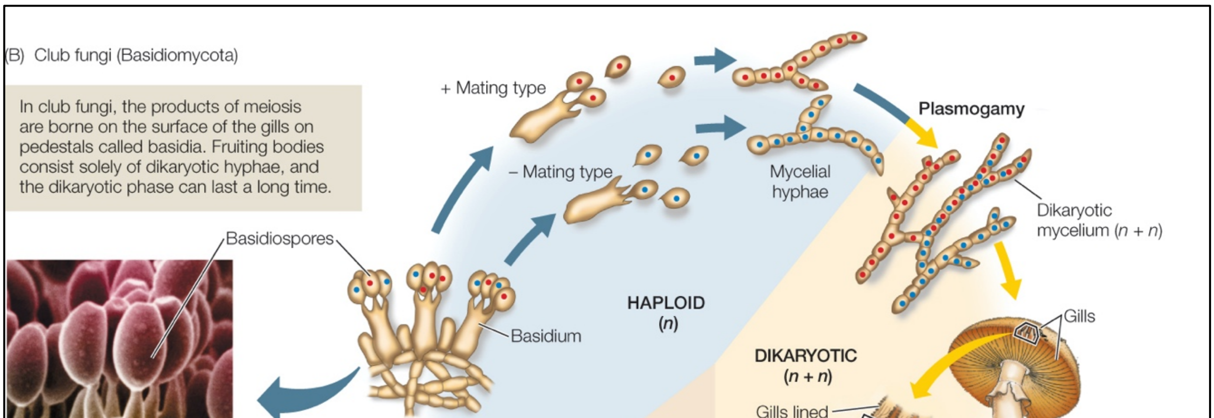

Fig 7. Sexual Life Cycles among the Dikarya. basidiomata, [3]

## I.6.3. Zygomycetes:

They have a coenocytic mycelium. Sexual reproduction results in the formation of zygospores, hence the name Zygomycetes. They are widespread saprophytes; some species prove to be formidable parasites in humans, especially in immunocompromised individuals (Mucorales) [10] (Fig. 8).

it is characterised by[1]:

- Sexual spore are known as Zygospore
- Zygospore is formed by fusion of two similar cell.
- Asexual reproduction occurs by sporangiospore
- Hypahe are generally aseptated.
- Examples: Rhizopus, Mucor, Basidiobolus, Conidiobolus

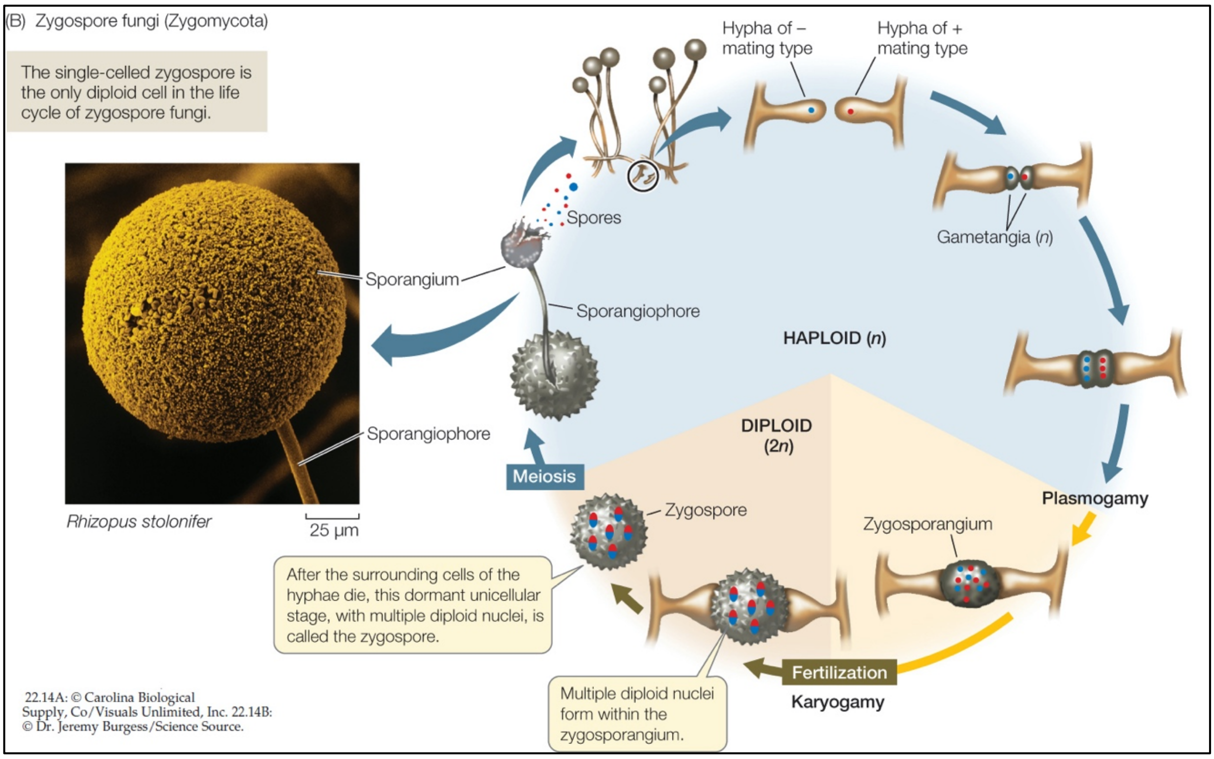


Fig. 8. **Sexual Life Cycles of Zygospore Fungi**[3]

## I.6.4. Deuteromycetes:

Deuteromycetes include all species that are isolated and identified based on their asexual (anamorphic) stage. Taxonomically, they represent an artificial group awaiting final classification among the Ascomycetes and Basidiomycetes. In practice, yeasts and filamentous fungi with regular, septate thalli are distinguished[10].

it is characterised by[1]:

- No sexual stage is present
- Deuteromycetes are also known as fungi imperfecti.
- Asexual reproduction occurs using conidia.
- Most of the human and animal pathogens are present in this class.
- Examples: *Candida, Cryptococcus, Trichophyton, Epidermophyton, Histoplasma*

### 1.7.1. Laboratory Culture

The physicochemical culture conditions are:

- **Culture media:** Numerous media are used in mycology, including Sabouraud, Malt Extract, Potato Dextrose Agar (PDA), Czapek Yeast Agar, etc. These media allow the growth of fungi and inhibit other microorganisms, particularly bacteria. These media are referred to as "routine media" or "standard media". To allow the growth of a particular group, family, or genus of fungi, "specific media" are used. They consist of a routine medium to which a growth inhibitor is added. Examples include Sabouraud with chloramphenicol and gentamicin, Eggins and Pugh Medium, Malt Yeast 20, etc. These media target specific fungi and enhance the inhibition of bacteria[7;11]

- **Temperature:** The growth temperature of fungi varies between 25 and 35°C. Generally, 25°C is an ideal temperature for the development of molds, and 30 to 37°C is the suitable range for the growth of yeasts (pathogenic yeasts for humans are preferably cultivated at 37°C).
- **pH:** Fungi grow in pH ranging from 4.5 to 8.0, but most species prefer a slightly acidic pH, between 5.5 and 6.5.
- **Oxygen:** Fungi are facultative aerobes, even though many of them ferment carbohydrates. Nevertheless, some species are anaerobic and colonize particular habitats such as the rumen of animals [7;11]
- **Light**: It is not essential for the vegetative growth of fungi. However, light can play a role in sporulation: it favors sporogenesis in some species [7]

### 1.7.2. Large-scale Culture

This is carried out in bioreactors or fermenters, the types of which vary according to:

- The producing strain (yeast or mold, fast or slow growing, demanding or not, etc.)
- The medium used (liquid or solid, renewed or not, etc.)
- The desired product (constituent of cells or excreted into the medium, primary or secondary, etc.)
- The economic cost. Depending on the setups, two types of cultures can be performed:
- "Batch culture" or "discontinuous culture": It requires bioreactors equipped with systems for measuring and adjusting culture parameters. Once the medium and physicochemical conditions become unfavorable (e.g.,depletion of substrates, acidity), the growth of microorganisms stops.
- " Renewed media culture, also known as "continuous culture," requires that the bioreactor be able to replace the strain and culture medium as needed in addition to monitoring and modifying culture parameters. This type of setup allows for extending the culture time. It is often used for industrial productions [13] The strain used must be perfectly pure (purified with successive subcultures or using reference strains). Culture in bioreactors is carried out using solid media, stationary liquid media, agitated liquid media, or culture gels (immobilized culture). To avoid contaminations, the bioreactor must be cleaned and sterilized before use. For large formats, the assembly is carried out in situ under aseptic conditions [7]

## II. Interest in using fungi

The enzymatic equipment of fungi makes them very important to humans. They have an active and highly diversified metabolism that allows their use in several fields, notably in the food and pharmaceutical industries. Indeed, yeasts, molds, and even wild mushrooms are increasingly used by humans for the many benefits they offer. In the food industry, they can be used as food or to prepare numerous products (e.g., cheeses, bread, alcoholic beverages). Also, in the pharmaceutical industry, they are used to produce numerous bioactive molecules (e.g., vitamins, enzymes, antibiotics)[(13).]

### II.1. growth cycle

The main phases of mold growth have a growth cycle similar to that of all microorganisms (Fig. 9 A ). However, when cultivating molds for industrial purposes, only two growth phases are important[(13).]:

- **"Trophophase"** or **"trophic phase"**: This stage which the microbe eats and grows significantly to the point of maximal growth. When the medium conditions are favorable, it is obtained. The acceleration phase and the exponential phase are included in the trophophase. (Fig. 9/B). It is ideal for the production of primary metabolites (e.g., organic acids, and vitamins) and biomass production.

- **"Idiophase"**: It is obtained when the medium conditions become unfavorable. It encompasses the deceleration phase and the stationary phase (Fig. B. 9). The idiophase is suitable for the production of secondary metabolites (e.g., antibiotics, flavors).

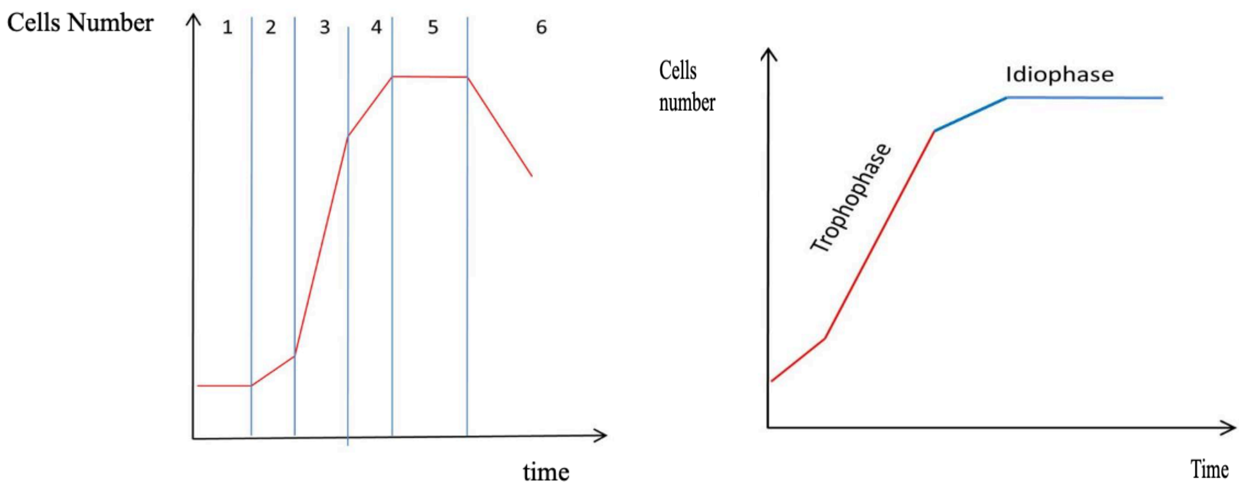


Fig. 10. Growth curve for fungi
(1: Latent phase, 2: Acceleration phase, 3: Exponential phase, 4: Slowdown phase, 5: Stationary phase, 6: Decline phase) [(13).].

;

## II. 2. Primary and Secondary Metabolite Production

The mold's development phase determines which main metabolites and secondary are produced. [13].

- **The carbon source** should be easily biodegradable, such as glucose. However, the concentration of glucose must be closely monitored to protect the mycelium from osmosis and diffusion phenomena. For the production of secondary metabolites, a more difficult-to-biodegrade carbon source is better to induce the idiophase. The most commonly used sources are lactose, cellulose, and starch.

- **The nitrogen source** also plays a very important role in production as it influences the growth rate and formation of secondary metabolism enzymes. Ammonium can initiate the trophophase, and natural sources such as soy, amino acids, and flour are suitable for inducing the mold to enter the idiophase.

- **pH,** slightly acidic values (between 5.5 and 6.5) are used to induce primary metabolism as they represent optimal values for growth. On the other hand, a pH between 7 and 8 favors secondary metabolism. pH is a very delicate parameter as small variations can influence the production rate.

- **The temperature** depends on the mold used. Generally, the optimal growth temperature is also used for the production of primary metabolites. For secondary metabolites, molds require a temperature lower than the optimum.

- **oxygen concentration** :The majority of molds are aerobic. Therefore, aeration must be provided for almost all productions. Nevertheless**, the oxygen concentration** must be adjusted for each metabolite. For example, the production of penicillins requires low aeration, while the production of cephalosporins requires a high oxygen level.

- **Phosphate** is a key element in choosing the growth phase. Its presence directly induces trophophase and inhibits secondary metabolism. It is therefore only added to the medium for the production of primary metabolites.

Apart from these parameters, the medium must contain the trace elements and minerals necessary for mycelial growth.

# II.3. Use of fungi in industrial

## II.3. 1. Food and Agriculture

### A. Dairy Products

Molds are widely used in the production of dairy products, especially cheeses, where they contribute to the ripening process by providing highly appreciated flavors, textures, and appearances.

Among the species used, we can mention[9]:

- *Penicillium camemberti*: This mold forms a white coating on soft-ripened cheeses with a bloomy rind, such as Camembert. This species is white and grows slowly.
- *Penicillium roqueforti*: Unlike Penicillium camemberti, this species has a green color and grows rapidly. It grows in the cavities of blue-veined cheeses, giving rise to Roquefort.

### B. Edible Mushrooms

Several wild mushrooms can be consumed by humans. However, it is very important to know how to differentiate edible species from toxic and poisonous ones.

Tuber: (Truffles) Truffles are underground Ascomycetes. They are globular and have a warty crust. The color varies depending on the species. Truffles are used to flavor culinary preparations. [9]

- Tuber melanosporum:
- Tuber aestivum:

Agaricus: (Psalliota) Species of this genus are morphologically very similar. They are all edible and flavorful, except for *Agaricus xanthodermus* which is toxic. The genus *Agaricus* belongs to the Basidiomycetes.

- Agaricus bisporus (the common button mushroom):

*c antharellus:* (Chanterelles) Chanterelles are Basidiomycetes with a convex, funnel-shaped fruiting body, making the gills perfectly visible. All species in the genus are edible and delicious. [9]

- Cantharellus cibarius:

Yeast Utilization The main genera used are *Saccharomyces* (alcoholic yeasts) and *Kluyveromyces* (protein-enriching yeasts). The use of these species is based on their ability to produce ethanol and CO2 from glucose.

- Ethanol is used to produce alcoholic beverages.
- CO2 is used to leaven dough.

## II.3. 2. Pharmaceutic industrial

Origin Fungi can be isolated from various natural habitats (soil, air, plants, etc.). Other sources can also be exploited for the search of molds and yeasts, such as biodeteriorated food, damaged textiles, cereals, patients with mycoses, etc. Fungi are also commercialized as pure strains. They then require a simple revival before use. The same species can be used for several productions, depending on the composition of the medium and the culture conditions[10]..

Therapeutic Applications and Uses Industrial fungal production offers many advantages in the therapeutic field (**Antibiotics, Antifungals, Hormones** , **Enzymes, Immunostimulants, etc** )( table 2). It provides substances with high activity, while using more practical techniques than classical chemical processes. Fungi require fewer requirements for the implementation of production processes, are low-cost, and provide a very good yield. [10]

**Table2.** fungal products of economic importance [4]

| Class of product | Typical example | Industrial/commercial application | Common production organism |
|---|---|---|---|
| Enzymes | Amylase | Starch processing | *Aspergillus niger* |
| | | Fermentation application | *Rhizopus oryzae* |
| | Cellulase | Animal feed industry | *Trichoderma longibrachiatum* |
| | | Brewing | |
| | Protease | Meat/leather industry | *Aspergillus oryzae* |
| | | Cheese manufacture | *Rhizopus oligosporus* |
| Organic acid | Citric acid | Soft drinks industry | *Aspergillus niger* |
| | Itaconic acid | Chemical industry | *Candida/Rhodoturula* |
| | Malic acid | Beverage/food industry | *Candida* |
| | Fumaric acid | Food industry | *Candida* |
| Vitamins | Riboflavin | Health industry | *Candida* |
| | Pyridoxine | Health industry | *Pichia* |
| | D-erythro-ascorbic acid | Health industry | *Candida* |
| Antibiotics | Penicillin | Human/animal health | *Penicillium chrysogenum* |
| | Cephalosporin | Human/animal health | *Cephalosporium acremonium* |
| Fatty acids | Stearic | Food industry | *Cryptococcus* |
| | Dicarboxylic | Chemical industry | *Candida* |
| Alcohol | Industrial alcohol | Fuel industry | *Saccharomyces* |
| | Beverage alcohol | Beverage industry | *Saccharomyces* |
| Pharmaceuticals | Lovastatin | Human health | *Monascus ruber* |
| | Cyclosporin | Human health | *Tolypocladium inflatum* |
| Amino acids | Lysine | Health industry | *Saccharomyces* |
| | Tryptophan | Health industry | *Hansenula* |
| | Phenylalanine | Health industry | *Rhodoturula* |
| Recombinant proteins | Insulin | Treatment of diabetes | *Saccharomyces cerevisiae* |
| | Phytase | Phosphate liberation | *Aspergillus niger* |
| | Hepatitis B | Vaccine preparation | *Saccharomyces* |

## II.3. 3. Ecologic industrial

## A. Biological Control

The use of fungi like biological resources to protect plants from pathogenic microorganisms[13].

- *Biopesticides*: Active molecules targeting plant and animal parasites. Objective: To reduce chemical inputs (pesticides) and increase the sustainability of agricultural systems.
    - Predatory Fungi with trapping mechanisms: These fungi create traps in the form of nets, rings, sticky knobs, or coils. Example: *Arthrobotrys irregularis*.
    - Ovicidal Fungi: These fungi can kill nematode eggs. Examples: *Paecilomyces lilacinus*, *Verticillium chlamydosporium*.
    - Nematophagous Fungi with adhesive spores: These fungi attach to the cuticle (outer layer) of nematodes. Examples: *Catenaria anguillulae*, *Myzocytium lenticulare*.
- *Beauveria bassiana* - a fungus that attacks respiratory tissues and whose mycelial growth obstructs respiratory channels.
- Many fungal species are saprophytes and thus allow the degradation of litter, the removal of diseased trees, stumps, droppings, or carcasses. => *They fertilize the soil and play a role in ecosystems.*

## II.3. 4. Storage Fungi

The storage of plant-based products is often problematic due to biodeterioration caused by fungi. This phenomenon involves all undesirable processes that induce organoleptic and chemical alterations of the product. It thus represents a risk of contamination for the consumer (human or animal) and often causes significant economic losses. The majority of fungi involved belong to the Mucorales, Ascomycetes, and Hyphomycetes. [13]

The biodeteriorative activity is primarily due to the cellulolytic, lipolytic, and proteolytic enzymes produced by fungi. Storage conditions also play a significant role in product deterioration. They can inhibit the growth of many microorganisms and thus favor the proliferation of harmful fungi. The most important factors are temperature, oxygen,and humidity. These parameters are generally low during storage. Indeed, although fungi are aerobic, mesophilic, and grow at a humidity above 30%, they can withstand unfavorable storage conditions, resulting in a linear growth rate that is halved. When storage occurs in humid places (eggs, meat, dairy products, etc.), fungal growth can become more significant [13].

- **Cereals and their derivatives**: Common fungi include *Aspergillus candidum, Aspergillus ochraceus, Aspergillus versicolor, Eurotium amstelodami*, etc.
- **Meat and charcuterie**: During meat refrigeration, *Aureobasidium pullulans, Cladosporium herbarum, Cladosporium cladosporioides*, and *Penicillium hirsutum* are often encountered. However, on salted products, the main contaminants are halophiles, such as *Penicillium expansum, Penicillium chrysogenum, Eurotium halophile*, and *Wallemia sebi*.
- **Eggs:** Humidity in storage rooms promotes fungal growth on the shell and inside the egg. *Penicillium* species are the most common in this type of spoilage.

## II.3. 5. Mycotoxin

Food poisoning and other unpleasant symptoms are caused by mycotoxins, which are produced by a variety of fungus (Table 3). They are [13]:

- **Food toxins:** While any plant products can produce toxins, the majority of contaminated foods are grains and oil seed crops. Four major categories of toxins are mostly linked to illnesses in humans.
- **Flavonoids:** Aspergillus flavus, A. fumigatus, A. parasiticus, and Penicillium islandicum are the producers of aflatoxins.
- **Ochratoxin:** mostly produced by Aspergillus ochraceus and Penicillium viridicatum during the infesting of mixed animal diets, stored maize, peanuts, and beans.
- **Zearalenone**: When Fusarium species thrive on maize, they create a phenolic resorcyclic acid lactone.
- **Trichothecenes:** generated by several species of Fusarium, Myrothcium, Trichoderma, and Cephalosporium.
- **Ergot Toxins:** Toxic alkaloids such as ergotamine, ergometrimine, ergonorin., and ergocristine are found in the sclerotia of Claviveps purpurea.
- **Mushroom toxins:** : Several mushrooms create mycotoxins, which, in mild situations, induce vomiting and diarrhea; in severe ones, however, they can cause liver damage, renal failure, and even death. About ten poisons are produced by Amanita phalloides. The species of Helmella produces a poison called gyromitrin, which is extremely deadly. Inocype and Clitocybe create the muscarine toxin. The coprine toxin, which is produced by some Coprinus species, impacts the autonomic nervous system.

Table 3. list of some mycotoxins and mycotoxin-production fungi [9]

| *Mycotoxin* | *Mycotoxin-producing fungi* |
|---|---|
| Aflatoxin | *A. flavus, A. parsiticus, etc* |
| Ascladiol | *A. clavatus* |
| Butenolide | *F. tricinctum, F. nivale, F. equiseti* |
| Ergot alkaloid | *Claviceps* sp. |
| Fumigatin | *A. fumigatus* |
| Chlorine-containing peptide | *P. islandicum* |
| Muscarine, etc. | *Amanita muscaria, etc* |
| Ochratoxin A | *A. ochraceus* |
| Patulin | *P. urticae, A. clavatus, P. claviforme, P. expansum, A. giganteus, etc.* |
| Penicillic acid | *P. puberculum, P. cyclopium, P. thomii, etc* |
| Phalloidine | *Amanita phalloides* |
| Psilocybine | *Psilocybe* sp. |
| Psoralens | *Sclerotinia sclerotiorum* |
| Rubratoxin B | *P. rubrum, P. purpurogenum* |
| Scirpenols (nivalenol, fusarenon) | *F. nivale, F. tricinctum* |

## III. Fungal Infections

Medical mycology studies microscopic fungi that can cause a pathological state in humans related to:

- A superficial location: affecting the skin and its appendages as well as all mucous membranes, particularly the digestive and genital tracts.
- A deep location: affecting organs, multiple organs, and viscera, and causing sepsis. Others define medical mycology as a branch of medical biology that consists of isolating and characterizing yeasts, filamentous fungi, or dimorphic fungi in various human fluids or tissues to characterize the mycologic origin or otherwise of a pathology.

These infections are often chronic (long-lasting) because fungi grow slowly. Mycoses are categorized into five groups based on the depth of tissue penetration and the host's resistance to the fungus(table 4)[(14).] they are;

### A. Systemic mycoses

These are deep fungal infections that can affect multiple tissues and organs. They are typically caused by fungi found in the soil and are acquired through inhalation. The infection often starts in the lungs and then spreads to other parts of the body. Two examples are histoplasmosis (caused by *Histoplasma capsulatum*) and coccidioidomycosis (caused by *Coccidioides immitis*).

### B. Subcutaneous mycoses

These fungal infections occur beneath the skin, caused by saprophytic fungi that live in soil and on vegetation. Infection occurs when spores or fragments of the fungus are directly implanted into the skin through a puncture wound. An example is sporotrichosis, which commonly affects farmers and gardeners.

### C. Cutaneous mycoses

Caused by dermatophytes, these fungi infect only the epidermis, hair, and nails. The resulting diseases are called dermatomycoses or cutaneous mycoses. Dermatophytes produce keratinase, an enzyme that breaks down keratin, a protein found in hair, skin, and nails. These infections can be spread from person to person or from animals to humans through direct contact or contact with infected skin cells or hair (e.g., on barber's tools or shower floors).

### D. Superficial mycoses

These infections are caused by fungi that colonize the hair shafts and superficial epidermal cells. They are common in tropical climates. The human body's natural defense mechanisms provide relatively good protection against this type of mycosis.

### E. Opportunistic mycoses

These infections are caused by opportunistic pathogens that are usually harmless in their normal habitat but can cause disease in severely immunocompromised hosts, those who have experienced significant trauma, or those taking broad-spectrum antibiotics or immunosuppressants. *For example, Stachybotrys* is an opportunistic pathogen. This fungus typically feeds on the cellulose of decaying plants but can also grow on water-damaged walls. Once inhaled, the spores germinate and the fungus produces toxins that can cause fatal pulmonary hemorrhages in infants. *Rhizopus* and *Mucor* cause mucormycosis, an opportunistic infection primarily seen in patients with diabetes, leukemia, or those taking immunosuppressants.

Table 4. The major mycoses and causative fungi [15]

| *Type of mycosis* | *Mycosis* | *Causative Fungal Agents* |
|---|---|---|
| **A. Superficial** | Pityriasis versicolor | *Malassezia* species |
| | Tinea nigra | *Hortaea werneckii* |
| | White piedra | *Trichosporon* species |
| | Black piedra | *Piedraia hortae* |
| **B. Cutaneous** | Dermatophytosis | *Microsporum* species, *Trichophyton* species, and *Epidermophyton floccosum* |
| | Candidiasis of skin, mucosa, or nails | *Candida albicans* and other candida species |
| **C. Subcutaneous** | Sporotrichosis | *Sporothrix schencki* |
| | Chromoblastomycosis | *Phialophora verrucosa, Fonsecaea pedrosoi*, others |
| | Mycetoma | *Pseudallescheria boydii, Madurella mycetomatis*, others |
| | Phaeohyphomycosis | *Exophiala*, bipolaris, *exserohilum*, and others |
| **D. Systemic (prlmary, endemic)** | Coccidioidomycosis | *Coccidioides immitis, C. posadasii* |
| | Histoplasmosis | *Histoplasma capsulatum* |
| | Blastomycosis | *Blastomyces dermatitidis* |
| | Paracoccidioidomycosis | *Paracoccidioides brasiliensis* |
| **E. Opportunistic** | Systemic candidiasis | *Candida albicans* and other candida species |
| | Cryptococcosis | Cryptococcus neoformans |
| | Aspergillosis | *Aspergillus fumigatus* and other aspergillus species |
| | Mucormycosis (zygomycosis) | Species of *Rhizopus, Absidia, Mucor*, and other zygomycetes |
| | Penicilliosis | *Penicillium marneffei* |

# III.1. CANDIDIASIS

## III.1.1. Pathogens

The genus *Candida* belongs to the yeast group. These microorganisms are either endogenous or exogenous, and their pathogenic potential is only expressed in the presence of local or general predisposing factors. They are found as normal saprophytes in the digestive tract, on the skin, and mucous membranes. *Candida* is primarily responsible for localized lesions (cutaneous and/or mucosal) and, more frequently in hospitalized patients, for invasive forms[(17).] The genus *Candida* includes 35 species:

- ***Candida albicans*,** accounts for nearly 60% of all yeasts isolated in humans.
- ***Candida glabrata***, a commensal in the genitourinary tract and intestine (representing 10 to 20% of isolates).
- ***Candida tropicalis*** can be found on both healthy skin and mucous membranes and is responsible for septicemia.
- ***Candida parapsilosis*** is a commensal yeast of the skin, responsible for lesions of the skin and nails. There are also *Candida* species of food origin, such as *Candida kefyr* found in fermented dairy products, *Candida krusei* found in grape juice and with primary resistance to fluconazole, *Candida famata*, etc.

## III.1. 2. Contamination and Predisposing factors

- Endogenous (digestive tract focus)
- Exogenous (therapeutic act) Modification of the intestinal microbiota following antibiotic therapy Rapid growth of Candida Colonization

These factors may be intrinsic or extrinsic [(16)];

- **Intrinsic factors:**
    - **Physiological:** extreme ages of life, pregnancy
    - **Local**: perspiration, maceration, humidity, trauma, dental prostheses
    - **Host factors**: diabetes, immunosuppression, pneumonia, neutropenia, cancer
- **Extrinsic factors:**
    - **Medication**s: antibiotics, corticosteroids, immunosuppressants, contraceptive hormones, antiseptics
    - Radiotherapy, digestive and cardiac surgery, organtransplantation, intravenous **catheters, prostheses**

The Figure 10. Representative scheme of interactions between the main variables related to candidiasis[(18).]

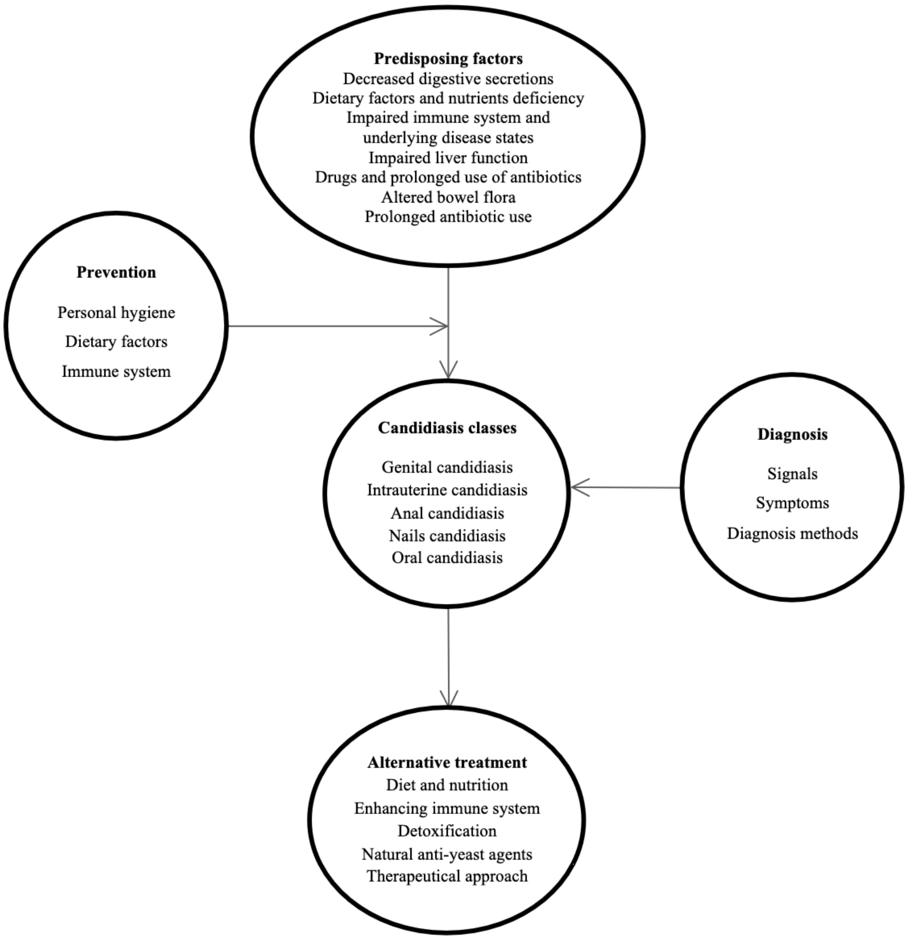


Fig. 10. Representative scheme of interactions between the main variables related to candidiasis[17].

## III.1. 3.Diagnosis

## A. Clinical Aspects

Candidiasis causes superficial infections:

- On the skin (skin and appendages)
- On mucous membranes (digestive and urogenital)
- As well as deep lesions affecting numerous organs such as the liver, kidneys, and eyes.

## Cutaneous and nail candidiasis

- It presents as an erythema associated with a creamy whitish coating, at the bottom of a usually fissured fold.
- The lesions are often pruritic and can become superinfected or eczematous.
- Candida intertrigo can occur at any age but is more prevalent in obese, diabetic, and elderly individuals.
- Two types of intertrigo can be distinguished:

- intertrigo of large folds (inguinal, axillary, abdominal, submammary, intergluteal, etc.)
- intertrigo of small folds (hands and feet)(Fig. 11).

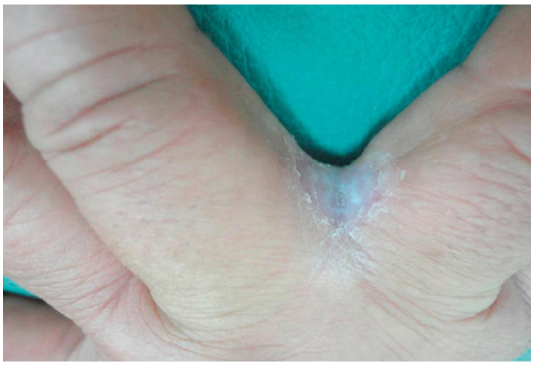

Figure 11: Candidal interdigital infection[18]

Figure 12: Candidal onychomycosis [18]

**Candidal onychomycosis** , Unlike dermatophytes, lesions are primarily located on the fingernails.

- **Paronychia:** inflammation of the nail fold.
- **Onychia:** beginning at the proximal border (often linked to glove wearing => maceration + detergents)(Fig. 12)

**Oral candidiasis** is a common fungal infection caused by *Candida albicans*. It often appears as small, white spots or patches on the tongue, inner cheeks, and palate. These patches can be creamy and adherent to the mucosa. In severe cases,the infection can spread to the corners of the mouth (angular cheilitis)(Fig. 13;14) and even the esophagus[17].

Fig .13. Angular cheilitis due to Candida [19]

Fig. 14. Oral candidiasis [19]

## Genital Candidiasis

Note that genital candidiasis is not considered a sexually transmitted infection (STI). However, a case of candidiasis in a man should prompt a search for a female partner carrying genital candidiasis[17].

- **Vaginal:** Frequent and recurrent: white coating, abundant vaginal discharge, vaginal itching (especially for albicans and glabrata). Treatment is difficult.
- **Balanitis:** Involvement of the foreskin then the glans, less frequent, white coating, itching (initially, then burning sensation), sometimes associated with urethritis. Recurrent in diabetics and the elderly.

## B. Deep Candidiasis

Invasive, systemic or disseminated(Fig.15) [20]

- Nosocomial infections (surgery, immunosuppressive treatment)
- Cause: Dissemination via the bloodstream of yeasts of endogenous origin (digestive mucosa) or exogenous origin (catheter, prosthesis, dental care).
- Irritation upon passage through mucous membranes
- Dissemination via the bloodstream (= fungemia)
- Departure of spores to various tissues.

1. **Candida septicemia or fungemia**
    - Nonspecific symptoms: fever (resistant to antipyretics) in patients with risk factors (immunocompromised,neutropenic, with venous lines)
2. **Secondary localizations (after fungemia)**
    - The most common:
        - Eye (chorioretinitis)
        - Urinary tract (hematuria, cystitis, fungal renal abscess)
        - Heart (endocarditis)
        - Bones, joints, liver, spleen, lungs
3. **Deep localizations of non-systemic origin**
    - Due to surgery: peritonitis (intestinal surgery), cholecystitis.

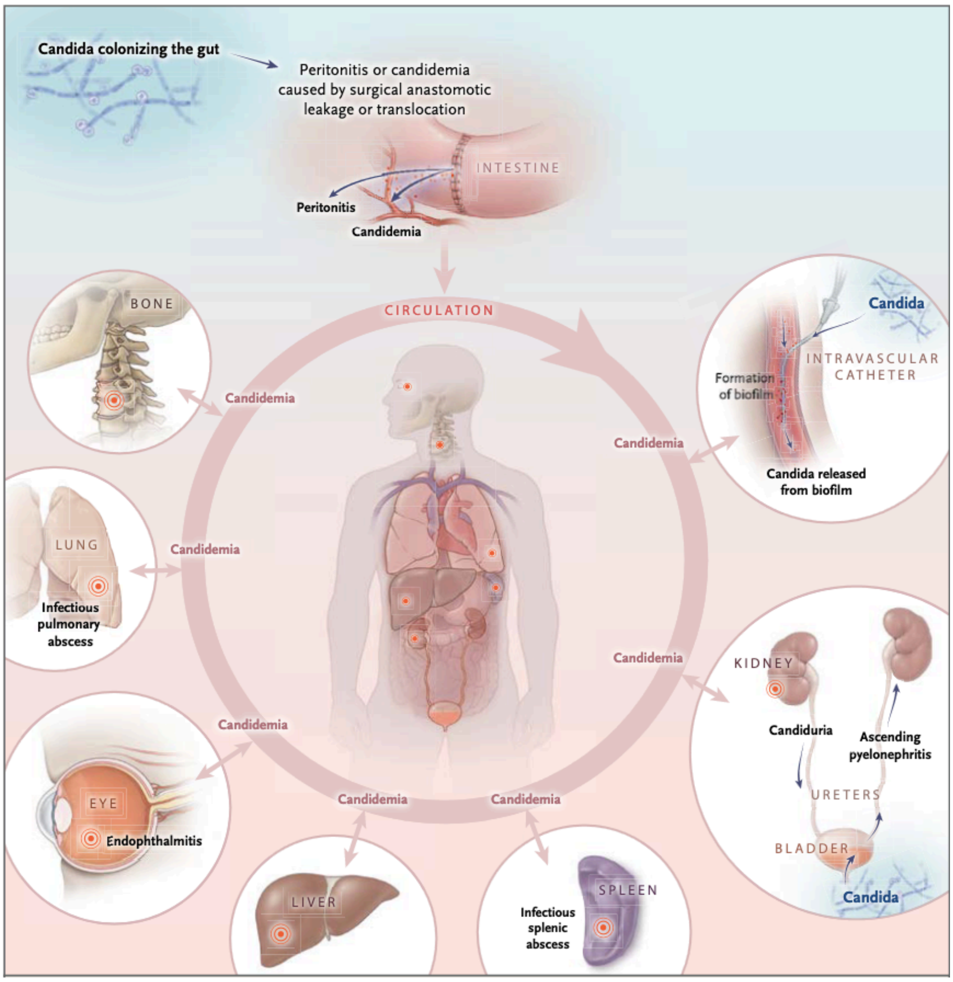


Fig. 15. Pathogenesis of Invasive Candidiasis [20]

## B. Laboratory diagnosis

### 1. Specimen Collection and Direct Examination

Depending on the symptoms [21]:

- **Skin and nails:** Scrapings (curette, nail clippers)
- **Mucosal lesions:** Swabs (Fig. 16)
- **BAL (Bronchoalveolar lavage), CSF (Cerebrospinal fluid);** organ biopsies
- **Urine, stool:** sterile container without fixative
- **Blood cultures:** 8-20 ml of blood on specific media: Sabouraud, automated systems (Bactec)

All biopsies undergo mycological and histological examination. Specimens are collected before any specific treatment and in sterile containers.

For the interpretation **[21]**:

- **Sterile sites (blood, CSF, etc.):** any deep specimen without contact with mucous membranes or ambient air; confirms the diagnosis of mycosis.

- **Sites normally colonized by yeasts:** mouth, trachea, sputum, stool, urine in catheterized patients:
    - **Budding:** multidirectional for albicans, uni for glabrata. The presence of pseudohyphae is quite characteristic of albicans.
    - **Abundance:** confirms the diagnosis. If numerous, indicates infection. Be careful not to confuse it with commensalism.

**2. Culture**

**Types of Media that can be used in culture are:**

- **Sabouraud + antibiotic:** colonies in 24-48 hours.
- **Chromogenic for albicans** due to the presence of a specific coloration.
- **For blood culture:** Search for chlamydospores (resistance spores, refractive, quite specific to albicans) on poor media PCB (potato, carrot, bile), RAT (rice, agar, tween).

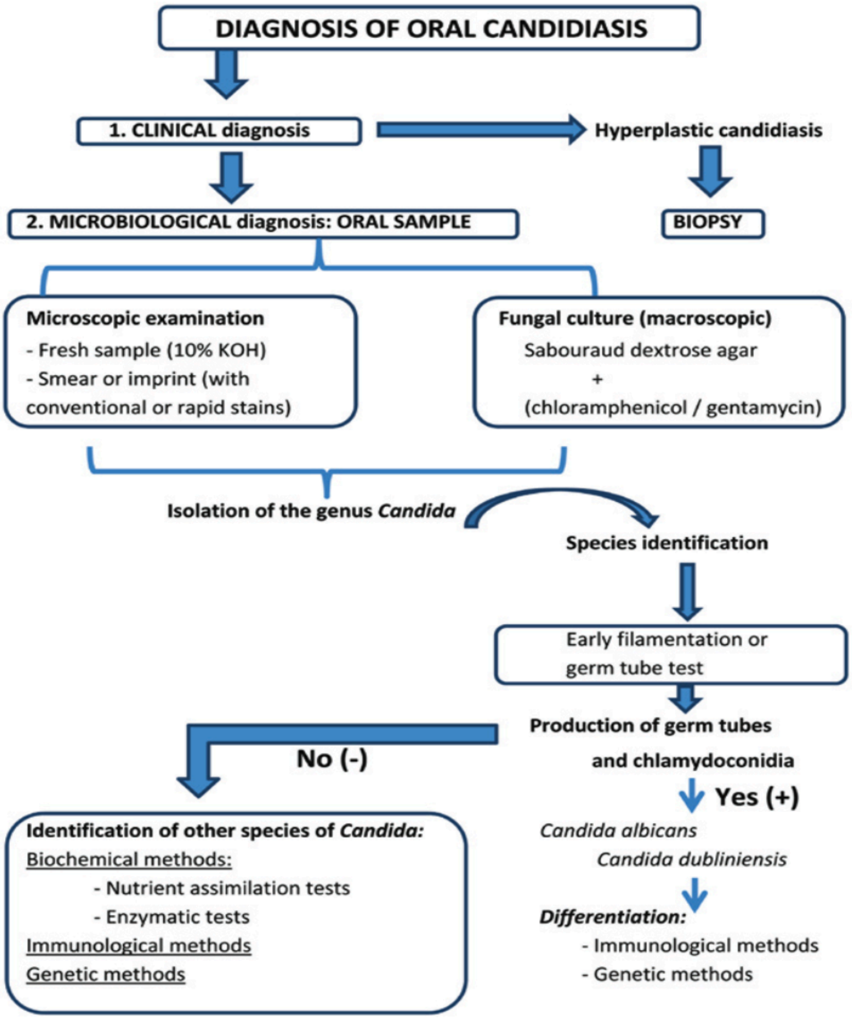


Fig. 16. Diagnosis of oral candidiasis. [20]

### B. Immunological Diagnosis

- **Antibody search:** by immunofluorescence, ELISA or immunoprecipitation. IgM (difficult in immunocompromised patients) and IgG + followed by kinetics (to avoid confusion with commensalism).
- **Search for circulating antigens:** search for the antigen released by yeasts.[21]

### C. Other examinations

For the screening of invasive candidiasis: Histological diagnosis (biopsy) and molecular diagnosis (fungemia) Antifungal agents.[21]

## III.1. 5. Treatment

- Only justified if a lesion is present.
- Must be comprehensive: both etiological and symptomatic.

### A. Superficial Candidiasis

- **Cutaneous:** Topical imidazole antifungals (formulation adapted to the location).
- **Onychomycosis:** + Ketoconazole (Nizoral®) or Terbinafine, administered systemically.
- **Digestive:** Amphotericin B or Nystatin (Mycostatin®).
- **Oropharyngeal and Esophageal:** Mainly for HIV patients. Local treatment with Miconazole (Loramyc®) and systemic treatment with Posaconazole (Noxafil®) as first-line, Fluconazole, Itraconazole (Sporanox®) if strains are sensitive.
- **Genital:** Topical imidazoles. Systemic treatment with Fluconazole.

### B. Visceral Candidiasis

- **Systemic antifungals:**
  - **Fluconazole:** Oral or IV depending on the patient's condition, if the strain is sensitive.
  - **Voriconazole:** If fluconazole is ineffective. Oral or IV.
  - **Amphotericin B:** IV with or without Flucytosine (Ancotil®). Lipid formulations (Ambisome®).
  - **Caspofungin:** Cancidas®, IV, many interactions.

Adhere to the duration of treatment, even after improvement (recurrences are frequent for interdigital plantar and nail infections) .[21].

## III.1. 6. Prophylaxis General Rules:

- Stop smoking and alcohol consumption.
- Perfect oral hygiene after each meal. Use bicarbonate toothpaste, and in case of glossitis, brush the tongue. Mouthwash: chlorhexidine (excellent antifungal) in the morning and at noon.
- Dental care (cavities, scaling).
- Avoid eating between meals, especially sweets.

- Adaptation and hygiene of dentures, remove the denture at night and maintain the denture.
- Follow the same routine as brushing teeth: after meals and at bedtime, clean with a hard brush, toothpaste, or a special denture cleaner; store the denture in 0.1% chlorhexidine solution.

## III.2. Dermatophytosis

## III.2. 1. Definition and etiology

Dermatophytosis is a contagious fungal infection caused by organisms called dermatophytes. These specific types of fungi are within the genera Microsporum, Trichophyton, and Epidermophyton. These fungi are characterized by their ability to digest keratin, a protein found in the outer layers of skin, hair, and nails [22]

- Microsporum and Trichophyton can infect both humans and animals.
- Epidermophyton primarily affects humans, with E. *floccosum* being the most common species associated with disease.

It's important to note that some fungi within these genera, often referred to as dermatophytosis, are primarily found in the environment and rarely, if ever, cause infections. Examples include T. terrestre. Also, dermatophytes can be categorized based on their preferred hosts[22] (table 5)

- **Anthropophilic:** These fungi primarily infect humans.
- **Zoophilic:** These fungi primarily infect animals but can also infect humans.
- **Geophilic:** These fungi typically reside in the environment but can occasionally infect both humans and animals.

While most dermatophyte infections are superficial and self-limiting, they can cause discomfort, disfigurement, and economic losses, especially in livestock. In rare cases, the infection can spread to deeper tissues, particularly in individuals with weakened immune systems. [22]

Table 5. Current synopsis of dermatophyte species and congeners: ecological classification, host [24]

| Anthrophilic species (area of endemicity) | Zoophilic species (typical host) | Geophilic species |
|---|---|---|
| *E. floccosum* | *M. canis* (cat, dog) | *E. stockdaleae* |
| *M. audouinii* (Africa) | *M. equinum* (horse) | *M. amazonicum* |
| *M. ferrugineum* (East Asia, East Europe) | *M. gallinae* (fowl) | *Microsporum* anamorph of *A. cookiellum* |
| *T. concentricum* (Southeast Asia, Melanesia, Amazon area, Central America, Mexico) | *M. persicolor* (vole) | *M. boullardii* |
| *T. gourvilii* (Central Africa) | *T. equinum* (horse) | *M. cookei* |
| *T. kanei* | *T. mentagrophytes* (two sibling species and variants; rodents, rabbit, hedgehog) | *M. gypseum* (complex of three species) |
| *T. megninii* (Portugal, Sardinia) | *T. sarkisorii* (Bactrian camel) | *M. nanum* |
| *T. mentagrophytes* (complex of two species) | *T. simii* (monkey, fowl) | *M. praecox* |
| *T. raubitschekii* (Asia, Africa, Mediterranean) | *T. verrucosum* (cattle, sheep, dromedary) | *M. racemosum* |
| *T. rubrum* | | *M. ripariae* |
| *T. schoenleinii* | | *M. vanbreuseghemii* |
| *T. soudanense* (Subsaharan Africa) | | *T. ajelloi* |
| *T. tonsurans* | | *T. flavescens* |
| *T. violaceum* (North Africa, Middle East, Mediterranean) | | *T. gloriae, T. longifusum* |
| *T. yaoundei* (Central Africa) | | *T. phaseoliforme*, *T. terrestre* (complex of three species), *T. vanbreuseghemii* |

## III.2. 2. Contributing Factors

- **Heat, humidity, and maceration:** These conditions create an ideal environment for fungi to thrive.
- **Occlusive protective gear:** Items like boxing gloves or rubber gloves can trap moisture against the skin, leading to maceration and increasing the risk of infection.
- **Friction from footwear:** Friction can cause small cuts in the skin, providing an entry point for dermatophytes. Poor hygiene in public places like swimming pools or gyms can also facilitate the spread of infection.
- **Domestic animals:** Frequent and close contact with pets can increase the risk of transmission.
- **Immunological factors:** Conditions that weaken the immune system, such as HIV/AIDS, corticosteroid use, immunosuppressive therapy, or chemotherapy, make individuals more susceptible to fungal infections.
- **Hormonal factors:** Ringworm is more common in children and often resolves spontaneously during adolescence.[23]

## III.2. 3. Diagnosis

## A. Clinical aspects

## 1. The epidermophytes.

The fungus emits filaments in a centrifugal pattern, creating a round, erythematous, and scaly lesion with a clear border, known as circinate epidermophytosis (Fig. 17;18). The erythematous-squamous patches extend eccentrically, forming a ring shape(Fig. 19;20;21;22; 23)[23].

- The fungus is active at the periphery of the lesion.
- These lesions can be singular or multiple.
- They can appear on any skin region.
- All dermatophytes can be responsible.

Fig. 17. Interdigital tinea - initial lesion with discrete extension to the dorsum of the foot, and later lesion with pearly white thickening at the base of the fold. [23]

Fig. 18: Dermatophytosis of hairless skin: rounded lesion with vesicular border[25]

## **Regarding hair and fur**: tinea

When one of the mycelial filaments encounters a hair follicle opening, it penetrates the inner sheath and the hair itself to seek out young keratin. The fungus enters through the follicular opening and advances toward the hair follicle. [23]
The dermatophyte's progression occurs in the opposite direction of hair growth.This process weakens the hair or fur, eventually causing it to break at its base (ringworm). This breakage allows the fungus to spread in the surroundings, with the hair or fur serving as a reservoir of infectious elements that can remain active for several months, or even years[24].

1. **Microsporic ringworm tinea**
   caused by dermatophytes of the genus *Microsporum*:

   - *M. canis* +++ (cosmopolitan)
   - *M. audouinii* (Africa)
   - *M. ferrugineum* (Far East)

2. **Trichophytic ringworm**
   Caused by contagious anthropophilic species:
   - *T. violaceum* +++
   - *T. tonsurans*
   - *T. soudanense*
3. **Favic Ringworm or Favus**
   Caused by *T. schoenleinii*; anthropophilic
   Rare (affects children and adults)

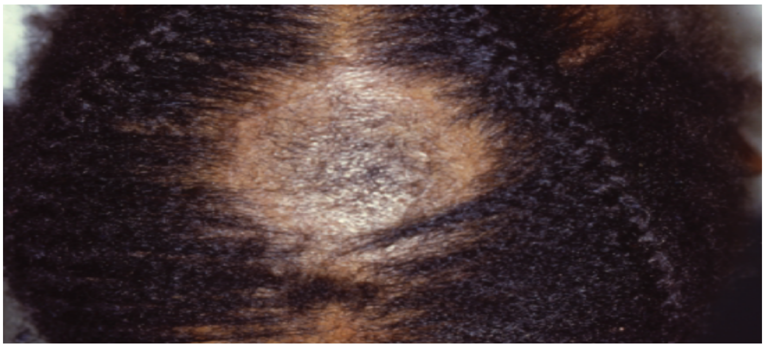
Fig. 19. Microsporic tinea capitis

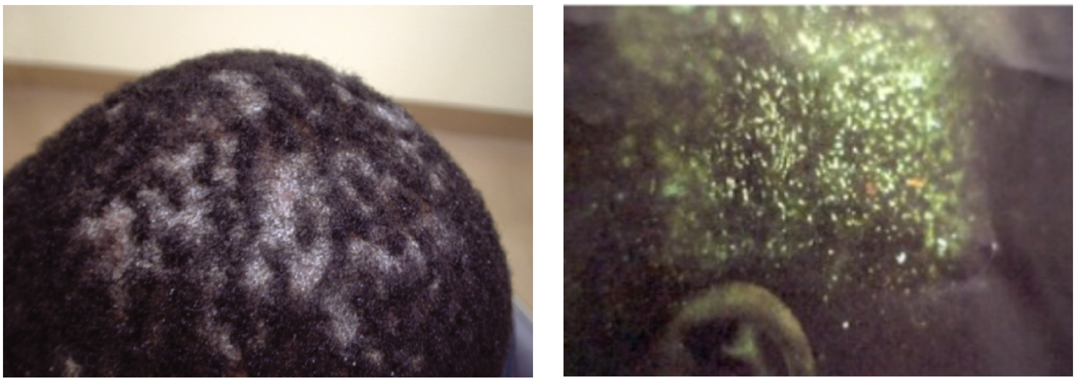
Fig 20. Trichophytic tinea capitis


Fig**. 21.** Inflammatory tinea **ou** kerion


Fig. 22. Sycosis

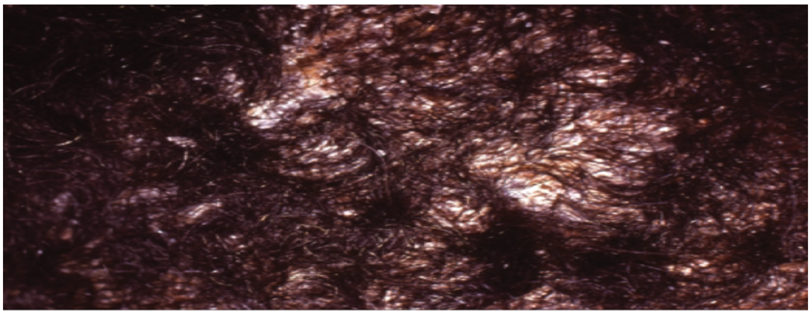
Fig. 23. Favus tinea

## Onychomycosis caused by dermatophytes

Infection penetrates through the free edge, progresses towards the matrix along the lateral groove. Proliferation occurs inside where keratin is less resistant (Fig. 24). [(24).]
The most common causative agents are[(23).]:

- *T. rubrum*
- *T. interdigitale*
  Nail mycoses that progress from the base of the nail to the free edge are primarily due to yeasts. Dermatophytes can also attack the nail plate, causing superficial leukonychia. These are white spots of variable size, with a powdery appearance.

Fig 24 . onychomycosis [(23).]

## B. Laboratory diagnostic

In Mycological, there is No serology. PCR allows differentiation at the genus level but not yet at the species level.

1. **Sample Collection**[(23).]:
   - The quality of the sample determines the result.
   - It should be done at the onset of the infection and without any ongoing treatment (caution with self-medication: often requires long treatment. There is a risk of relapse if not properly managed).
   - For scalp ringworm, the sample collection will be preceded by an examination under a Wood's lamp in a completely dark room (Fig. 25). A green fluorescence will guide the diagnosis towards a microsporic ringworm or favus.

   - **Locations**:
     - **Skin and nails**: Active areas of lesions (keratin destruction, often under the nails).
     - **Hair**:
       - UV positive for microsporic and favus ringworms.
       - UV negative for trichophytic ringworms.
     - Also, collect scales, and for a kerion, the pus (using a swab).

Finally, the sample collection will be accompanied by an interview with the patient to determine their origin and lifestyle (habitat, occupation, hobbies, pets, etc.), as well as to identify any possible contributing factors (underlying conditions, medications, etc.) [(23).].

Fig. 25. Scalp examination under Wood's lamp. [(23).]

## 2. Sampling method

### a. Equipment

A minimal set of sterile instruments is required for collecting dermatophyte samples (Fig. 25): Brocq curette or Vidal scraper, scissors, vaccinostyle, and swabs. Tweezers are additionally needed for folliculitis, tinea capitis,and sycosis. For the latter two conditions, a sterile carpet square can also be used. Sterile polystyrene or, preferably, glass Petri dishes (due to reduced static electricity) are used to collect scales, nail fragments, hair, or fur. [(23).]

### b. Sampling Procedures

Each lesion should be sampled separately using sterile instruments (Fig. 26;27; 28)[(23).]

- **Skin Lesions:** Scrape the lesion's periphery (the inflamed border) with a curette, scraper, or scalpel. Then,swab the area with a sterile, moistened cotton swab.
- **Folliculitis and Sycosis:** Remove hairs with tweezers and swab the base of the hair follicle and any oozing areas.
- **Onychomycosis:** Scrape the nail bed underneath and trim the section of the nail that is damaged. Scrape the nail's surface if you have leukonychia (white patches on the nail).
- **Tinea Capitis:** Examine the scalp under a Wood's lamp for fluorescence. Collect scales, broken hairs, and crusts using a curette and tweezers. Swab the area. For eeAile carpet square can be pressed onto the scalp.
- **Int for epidemiological studiesertrigo:** Scrape the periphery of the lesion and swab the edges.

Fig. 26. Equipment required for sampling dermatophytes. (23).

Fig. 27. Sampling of an intertrigo intertrigo with extension to the sole. (23).

Fig 28. Sampling of an intertrigo intertrigo with extension to the sole. (23).

**2. Culture**:

- **Media**:
    - Sabouraud with chloramphenicol (and/or gentamicin).
    - Sabouraud with chloramphenicol and cycloheximide to prevent contamination by environmental fungi.
- Incubation at 25 to 30°C for at least 4 weeks.
- Regular observation is necessary (don't wait the full 4 weeks): examining the cultures' macroscopic and microscopic characteristics(Table 6). [(23).]

T**able 6.** Sequence of procedures for the identification of dermatophytes in pure culture (27)

| Procedure |
|---|
| 1. Examine the colony for color of the surface and reverse, topography, texture, and rate of growth. Proceed to step 2. |
| 2. Prepare teased mounts and search for identifying microscopic morphology, especially presence, appearance, and arrangement of macroconidia and microconidia. If results are inconclusive, proceed to step 3. |
| 3. Prepare and examine slide culture for characteristic morphology as indicated above if teased mounts do not provide sufficient information. Consider special medium if sporulation is absent (potato glucose agar, Sabouraud glucose agar plus 3 to 5% NaCl, or lactrimel). If results are inconclusive, proceed to step 4. |
| 4. Perform as many of the physiological tests listed below as necessary for identification |
| a. Urease |
| b. Nutritional requirement if a *Trichophyton* sp. is suspected |
| c. Growth on rice grains if a *Microsporum* sp. is suspected |
| d. In vitro hair perforation |
| e. Temperature tolerance and/or optimum temperature of growth |
| f. Special media to differentiate *T. mentagrophytes* from *M. persicolor* (131), *T. rubrum* from *T. mentagrophytes* (240), and *T. soudanense* from *M. ferrugineum* (193, 273) |
| g. Mating studies to be performed in reference laboratories |

[a] It may be necessary to incubate culture on brain heart infusion agar or similar medium to determine absence of bacterial contamination before proceeding to step 4. Procedures are adapted from Weitzman and Kane (270).

## III.2. 4. Treatment

Most of the time, treatments are topical, involving antifungal creams, gels, or lotions (with various active ingredients like azoles, terbinafine, ciclopiroxolamine, or tolnaftate). It's essential to also address the environment: socks (with antifungal powder), shoes (with spray), slippers (with spray) to prevent a second infection[(24).].

Don't forget about the shower and bathtub (avoid bath mats and treat the shower/tub once a week with a bleach sponge to destroy spores). For widespread infections, oral treatment with Griseofulvin may be prescribed.

If the dermatophyte originates from an animal (e.g., M. canis), it's crucial to treat the animal (take it to the vet) as it may be a carrier (especially cats), otherwise, the infection will persist[(25).]

***A. Ringworm****:*

- Griseofulvin: Systemic treatment for 6-8 weeks.
- Ketoconazole: Oral treatment for extensive or resistant skin and mucosal infections (also available as a topical treatment like Ketoderm®).
- Terbinafine: Not for children.
- Topical treatment: Imidazoles in lotion form.

- Inflammatory ringworm: Anti-inflammatory and anti-infective treatment before specific antifungal therapy.
- Infected children: Anthropophilic species may require school eradication.

***B. Epidermophytes***:

- Limited circinate herpes and intertrigo: Topical treatment with imidazoles for 3 weeks (long-term treatment, regular application is crucial), ciclopiroxolamine (Mycoster) for 3 weeks, or terbinafine for 1 week. For extensive or recurring lesions, oral treatment for 1 to 3 months may be necessary, possibly combined with topical therapy:
  - Griseofulvin: Especially for children.
  - Terbinafine: Broad-spectrum, for adults.
  - Itraconazole: Not for onychomycosis.
  - Ketoconazole: Used less frequently.
- Athlete's foot: Must address predisposing factors, such as reducing maceration, providing hygiene advice, and disinfecting areas prone to reinfection.

***C. Onychomycosis***:

- Due to the longer and more difficult treatment for nails:
  - Distal involvement: Without matrix involvement, local treatment for 3-9 months:
    - Amorolfine (Loceryl®)
    - Ciclopirox
    - Bifonazole (Amycor® Onychoset® then Amycor)
  - Proximal or total involvement:
    - Ketoconazole: 6-12 months.
    - Terbinafine: 3-6 months.
    - Griseofulvin: 6-12 months.

## III.2. 5. PROPHYLAXIS:

- Complete the full duration of treatment, even after improvement (recurrences are common for interdigital and nail infections).
- Minimize contamination: Thorough washing and drying after workouts and showers.
- Change socks daily.
- Do not share towels.
- Avoid walking barefoot on floors (wear pool shoes).
- Be mindful of floor mats.
- Conduct an epidemiological investigation to identify the source of the contamination (ringworm). [24].

## References


1. Sridhar Rao Pn, 2006; Introduction to mycology. www. microrao.com. 9pp
2. Chabasse D, Guiguen CL, Contet-Audonneau N. 1999. Mycologie Médicale. Masson, Paris : 1-78 ;
3. Macmillan https://www.macmillanhighered.com/BrainHoney/Resource/6716/digital_first_content/trunk/test/hillis2e/hillis2e_ch22_4.html consult in jan 2024
4. Kavanagh K., Khaled H. Abu-Elteen, C. Bachewich, V Bugeja, 2005. Fungi Biology and Applications, John Wiley & Sons Ltd,
5. Walker, 1998 *in* Kavanagh K., Khaled H. Abu-Elteen, C. Bachewich, V Bugeja, Fungi Biology and Applications, John Wiley & Sons Ltd,
6. Chermette R, Bussieras J. 1993. Parasitologie Vétérinaire, Mycologie. Service De Parasitologie. Ecole Nationale Vétérinaire D'alfort. 11-157 ;
7. Botton B., Breton A., collectif. larpent, J-P., 1990. Moisissures utiles et nuisibles importance industrielle, 2e ed . rev et compétée . ed, Dunod, Paris.
8. Roland , J-C., Roland, F., El Maarouf-Bouteau., H., 2008. Atlas biologie végétale. Dunod, DL 2008., Paris. France.
9. Urmila Rana, Pooja Juyal, Kanchan Joshi, Pritee Pant, Shalini Rawat, Shalabh Gupta .; 2021; Fungi, Lichen, Viruses, and Bacteria., Mscbot-501, Department Of Botany School Of Sciences Uttarakhand Open University. 264pp
10. Renu Negi, Rajan Kumar Gupta Kapil Khulbe, Nisha Mishra, Pooja Juyal, Reeta Sachan, Saurabh Guleri, Snehalata Bhandari, 2023Microbiology, Mycology And Plant Pathology, Bscbo-101 , School Of Sciences Department Of Botany Uttarakhand Open University, 286pp
11. -Ripert C. 2013.Mycologie médicale. Tec & doc-Lavoisier. Paris.
12. Hochfeld, W.L. (2006). Producing Biomolecular Substances with Fermenters, Bioreactors, and Biomolecular Synthesizers (1st ed.). CRC Press. https://doi.org/10.1201/9781420021318
13. Sivakumar N.., 2019. Bioprocess Technology., M.Sc ., Ii-Semester., 441 School of Biotechnology, Madurai Kamaraj University, Madurai -21. 366pp https://mis.alagappauniversity.ac.in/siteAdmin/dde-admin/uploads/4/PG_M.Sc._Microbiology_364%2041_Bioprocess%20Technology-English_9699.pdf
14. *Tortora Gerard J. - Funke Berdell R. - Case Christine L.* 2012., Introduction à la microbiologie . *Erpi* 2e éd. 630pp
15. Kumar S., 2012; Textbook of microbiology, Jaypee Brothers Medical Publishers (P) Ltd *First Edition:* 2012. 784pp
16. Musy-Preault C. (1994). Les maladies de la peau : acné, eczéma, mycose, herpès, allergies solaires. Collection: santé. Albin Michel S.A. Paris. pages 69-81.
17. Martins, N. Ferreira I, Barros L , Silva S , Henriques M,* (2014). Candidiasis: Predisposing Factors, Prevention, Diagnosis and Alternative Treatment. Mycopathologia pp 1-43 https://www.academia.edu/92735177/Candidiasis_Predisposing_Factors_Prevention_Diagnosis_and_Alternative_Treatment
18. Mokni M., Dupin N et Del Giudice P. (2014). Dermatologie infectieuse. Elsevier Masson SAS. 331 pages
19. Bouchara J-P., Pihet M., De Gentile L et Chabasse D. (2010). Les levures et levuroses. Cahier de bioformation Biologie médicale. N° 44. Pages 14-34.
20. Coronado-Castellote L, Jiménez-Soriano Y. 2013; Clinical and microbiological diagnosis of oral candidiasis. J Clin Exp Dent. 5(5):e279-86. http://www.medicinaoral.com/odo/volumenes/v5i5/jcedv5i5p279.pdf
21. Bouonda Tamo SP. 2020. Candida Infections: Clinical Features, Diagnosis and Treatment. Infect Dis Clin Microbiol; 2: 91-102. DOI: 10.36519/idcm.2020.0006
22. CFSPH (the center for food security and public health) : 2013. Dermatophytosis Ringworm, Tinea, Last Updated: March 2013 https://www.cfsph.iastate.edu/Factsheets/pdfs/dermatophytosis.pdf
23. Chabass D., Bouchara JP., de Gentile L., Brun S., Cimon B., Penn P., 2004, CAHIER DE formation en biologie medicale ; les dermatophytoes N°31la Version Numerique Des Cahiers Bioforma 258pp
24. Chabasse D. and Contet-Audonneau N.. 2011, Dermatophytes et dermatophytoses. EMC – Maladies infectieuses, Elsevier Masson, 9782842995089. 10.1016/S1166-8598(11)56491-9. hal-03333816 https://univ-angers.hal.science/hal-03333816/document
25. Zagnoli A, Chevalier B, Sassolas B., 2005. Dermatophyties et dermatophytes. EMC (Elsevier Masson SAS, Paris), Pédiatrie, 4-110-A-10,