Medical Mycology

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Are eukaryotes that grow in two basic forms, a yeasts and molds (or moulds).

Growth in the mold form occurs by production of multicellular filamentous colonies. These colonies consist of branching tubules called hyphae. The mass of intertwined hyphae that accumulates during active growth is a mycelium.

In the reproductive phase, fungi may undergo either asexual or sexual reproduction. **Asexual reproduction** involves the generation of spores; **sexual reproduction** requires specific cellular structures that are used for taxonomic differentiation.
Classification of Mycoses

The clinical nomenclatures used for the mycoses are based on the

A. Site of the infection

Mycoses are classified as
1- Superficial (are generally limited to the outer layers of the skin and hair.
2- Cutaneous (are located deeper in the epidermis, hair and nails.
3- Subcutaneous (involve the dermis, subcutaneous tissues and muscle).

infections (generally originating in the lungs and other organs).

B. Route of acquisition of the pathogen

1. Exogenous (routes of entry for exogenous fungi include airborne, cutaneous)
2. Endogenous (endogenous infection involves colonization by a member of the normal flora or reactivation of a previous infection).

C. Type of virulence exhibited by the fungus.

1. Primary pathogens can establish infections in normal hosts.
2. Opportunistic pathogens cause disease in individuals with compromised host defense mechanisms.
**Hypae** (threads) making up a **mycelium**

**Yeasts**

Many pathogenic fungi are **dimorphic**, forming hyphae at ambient temperatures but yeasts at body temperature.
There are five types of mycoses to describe, in two main categories:

**Skin mycoses**
- 1. Superficial mycoses
- 2. Cutaneous mycoses
- 3. Subcutaneous mycoses

**Systemic mycoses**

Systemic mycoses due to primary (usually dimorphic) pathogens
Systemic mycoses due to opportunistic pathogen.
Superficial mycoses

- Defined as fungal infections of the skin and hair that invade only the most superficial layers and cause little or no inflammatory response.
- These fungi have ability to produce keratinase, which allows them to metabolize and live on human keratin tissue like skin, nail and hair.
- Are a major cause of morbidity in the world, particularly in the tropics, where heat and humidity provide the ideal conditions for the growth of fungi.
- Direct contact is sufficient to transmit the infection from a contaminated surface or host to another.
Superficial Mycoses

Superficial Mycoses include the following fungal infections and their etiological agent:

- Pityriasis versicolor النخالية المبرقشة (Malassezia furfur)
- Tinea nigra السعفة السوداء (Phaeoannellomyces werneckii)
- Black piedra البيصرية السوداء (Piedraia hortae),
- White piedra البيصرية البيضاء (Trichosporon beigeli)
**Pityriasis versicolor**
- is a common superficial mycosis
- is characterized by hypopigmentation or hyperpigmentation of skin of the neck, shoulders, chest, and back.
- is due to *Malassezia furfur* which involves only the superficial keratin layer.

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

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

**White piedra**
- Due to *Trichosporon beigelii*
- Is characterized by a soft, friable, nodule of the distal ends of hair shafts.
Pityriasis versicolor
Hypopigmented macules

Tinea nigra
Black macules

**White piedra**
*Trichosporon asahii*

Nodules with mycelia

**Black piedra**
*Piedraia hortae*

Nodules of spore
black piedra

White piedra

Pityriasis versicolor

Tinea Nigra
**Cutaneous mycoses (Dermatophytes)**

- There are three genera of fungi that commonly cause disease in the on-living tissues of skin, hair, or nails of people and animals, by growing in a zone just above where the protein keratin is deposited.

These three genera are

- **Microsporum**
- **Trichophyton**
- **Epidermophyton**

- These fungi all have the ability to degrade keratin and grow as non-invasive saprotrophs on skin and its appendages

- Their growth causes irritation and inflammation of underlying epithelial cells, this being an allergic reaction that may result in death of these cells

- Contagious-direct or indirect contact
Tinea faciei: Face excluding beard & moustache

Tinea capitis: scalp

Tinea versicolour; back, chest, shoulders

Ringworm: whole body

Tinea mannum Hand

Tinea pedis “athletes foot” foot

Tinea corporis; a ringworm of arms, legs and trunk

Tinea barbae; beard

Tinea cruris “jock itch”; groin, upper legs
Scalp Ringworm
Tinea capitis

Ringworm of beard area
Tinea barbae or Barber’s itch

Tinea versicolor

Ringworm of the body
Tinea corporis

Ringworm of the toes
Tinea pedis or Athlete’s foot
Tinea pedis - athlete's foot
**Cutaneous Mycosis:** Obligate Parasitic Fungi (dermatophytes), attack the outer surface of humans

- **Soil fungi:** thermal dimorphic, adaptations to human body
- **Opportunistic saprobes:** attack people with compromised immune systems
- Secrete keratinase, an enzyme that degrades keratin.
- Infection is transmitted by direct contact or contact with infected hair (hair salon) or cells (shower floors).
  - Cause common tinea (ringworm), which is a very common fungal infection of the skin. Tinea is often called "ringworm" because the rash is circular, with a ring-like appearance
  - Grow only on humans
  - Reservoir not in soil or animals
  - Reservoir in carpets and upholstery for up to two years
Cutaneous mycosis is classified as
a. **Dermatophytoses** (caused by the genera *Epidermophyton*, *Microsporum*, and *Trichophyton*)
b. **Dermatomycoses** (the most common of which are *Candida* spp.)

- The Dermatophytoses are characterized by an anatomic site-specificity according to genera. For example

  * *Epidermophyton* spp. infects only skin and nails, but does not infect hair shafts and follicles
  * *Microsporum* spp. infect hair and skin, but do not involve nails.
  * *Trichophyton* spp. may infect hair, skin, and nails.
Dermatophytosis

- Trichophyton
  - Cylinder

- Microsporum
  - Spindle

- Epidermophyton
  - Club

Dermatomycoses

Candida albicans
Subcutaneous Mycoses
Involves dermis, subcutaneous tissues and may be the muscle. There are three general types of subcutaneous mycoses:

a. Chromoblastomycosis الفطريات الاصطباغية

b. Mycetoma (chronic inflammation of the tissues)

c. Sporotrichosis. (a chronic fungal infection producing nodules and ulcers in the lymph nodes and skin).

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

* Chromoblastomycosis is a subcutaneous mycosis characterized by Verrucoid lesions of the skin افة ثالولية. It is believed to originate in minor trauma to the skin, usually from thorns or splinters
- symptoms often do not appear for years. It is generally limited to the subcutaneous tissue, with no involvement of bone, tendon, or muscle, the lower extremities.
- The most common causes of Chromoblastomycosis are Fonsecaea pedrosoi, Fonsecaea compacta, Cladosporium carionii.
Chromoblastomycosis
Mycetoma is a Suppurative and Granulomatous subcutaneous mycosis, which is destructive of contiguous bone, tendon, and skeletal muscle.
- It is characterized by the presence of draining sinus tracts from which small but grossly visible pigmented grains or granules are extruded.
- The causes of Mycetoma are more diverse but can be classified as Eumycotic Mycetoma (fungi 40%) and Actinomycotic Mycetoma (bacteria, Actinomycetes).
Sporotrichosis
- This infection is due to *Sporothrix schenckii* and involves the subcutaneous tissue at the point of traumatic inoculation.
- The infection usually spreads along cutaneous lymphatic channels of the extremity involved.
Deep Mycoses

Primary versus Opportunistic mycoses
- The Primary pathogenic fungi are able to establish infection in a normal host; whereas, Opportunistic pathogens require a compromised host in order to establish infection (e.g., Cancer, Organ transplantation, Surgery, and AIDS).
- Primary deep pathogens usually gain access to the host via the respiratory tract.
- Opportunistic fungi causing deep mycosis invade via the Respiratory tract, Alimentary tract, or Intravascular devices.

Primary systemic fungal pathogens include:
- *Coccidioides immitis* (*Coccidioidomycosis*)
- *Histoplasma capsulatum* (*cave disease*)
- *Blastomyces dermatitidis* (*Blastomycosis*)
- **Originate in lungs**, phagocytosis by macrophages, spread to many organs.
- Most primary infections are inapparent.
- Progression may produce pulmonary symptoms or ulcerative lesions.
- Host responses produce formation of **fibrous tissue, granulomas and calcified lesions**.
- Normally found in soil, infect via inhalation
**Histoplasmosis** (Cave disease or Ohio valley disease) a disease caused by dimorphic *Histoplasma capsulatum*.
- Characterized by intracellular growth of the pathogen in macrophages and a granulomatous reaction in tissue which may reactivated and cause dissemination of fungi to other tissues (rarely).
- The inoculums is represented principally by *microconidia* that, once inhaled into the alveolar spaces, germinate and then transform into *budding yeast cells*.

**Coccidioidomycosis** (Valley fever), a fungal disease caused by *Coccidioides immitis*. The disease is usually mild, with flu-like symptoms, cough, myalgia, fever, headaches and rashes.
- *C. Immitis* is a dimorphic that grows as a mycelium in the soil and produces a *spherule* form in the host organism

**Blastomycosis** a fungal infection caused by *Blastomyces dermatitidis*. Presented as a flu-like illness with fever, chills, myalgia, headache, and a nonproductive cough which resolves within days, or a chronic illness that mimics tuberculosis or lung cancer, with a skin and bone like lesion
Opportunistic Fungal pathogens include:

- *Cryptococcus neoformans*
- *Candida* spp. (*Candidiasis*)
- *Aspergillus* spp. (*Aspergillosis*)
- *Penicillium marneffei*
- *Zygomycetes* (*Zygomycosis*)
- *Trichosporon beigeli*.

- These organisms generally have a low potential for virulence but can produce severe disease involving a variety of body tissues.
- Mycotic disease is often a consequence of **predisposing factors** including:
  1. Age
  2. Stress
  3. Other pathologic conditions (e.g. cancer, diabetes, AIDS).
**C. albicans** is a member of the indigenous microbial flora of humans.
- Found in the gastrointestinal tract, upper respiratory tract, buccal cavity, and vaginal tract.
- Growth is normally suppressed by other microorganisms found in these areas.
- Alterations of gastrointestinal flora by broad spectrum antibiotics or mucosal injury can lead to gastrointestinal tract invasion.
- Skin and mucus membranes are normally an effective barrier but damage by introduction of catheters or intravascular devices can permit *candida* to enter the bloodstream.

*in vitro* (25 o c): mostly yeast;
*in vivo* (37 o c): yeast, hyphae and pseudohyphae

Two conditions are associated with *C. albicans* (oral and vaginal thrush)
**Vaginal Candidiasis (vaginal thrush)** is the most common clinical infection. Local factors such as pH and glucose concentration (under hormonal control) are of prime importance in the occurrence of vaginal candidiasis. In mouth: normal saliva reduces adhesion (lactoferrin that produce by various secretory fluids has antimicrobial activity, is also protective).

**Risk factor for candidiasis**
1. Post-operative status
2. Cytotoxic cancer
3. Chemotherapy
4. Antibiotic therapy
5. Burns
6. Drug abuse
7. GIT damage.
Some of the tissue responses to fungi infection may be due to the **Mycotoxins**, which are fungal metabolites that are toxic to the host. Some fungi have a variety of virulence factors including

- **LPS-like endotoxins**
- **Hemolysins**
- **Steroid-like toxins** that affect the nervous system
- **Aspergillus** produces a toxin called **Aflatoxin** that has a strong association with **liver cancer**.
- **Aflatoxin**: When contaminated food is processed, Aflatoxins enter the general food supply where they have been found in human foods as well as in feedstocks for agricultural animals.
  - At least 14 different Aflatoxins are produced (b1 is the most toxic).
  - Animals fed contaminated food can pass Aflatoxin into **eggs, milk products, and meat**.
- Children are particularly affected by Aflatoxin exposure, which leads to stunted growth, delayed development, liver damage, and liver cancer.
- Adults have a higher tolerance to exposure, but are also at risk. Aflatoxins are among the most **carcinogenic** substances known
Host defenses

Host defenses against the fungi include nonspecific and specific factors

**Nonspecific defenses** include

1. the skin (lipids, fatty acids, normal flora)
2. Internal factors (mucous membranes, ciliated cells, macrophages)
3. Blood components
4. Temperature
5. Genetic

**Specific defenses** include both

A. **Humoral Immunity** (antibodies may be protective (e.g. antitoxins or opsonins).

B. **Cell-mediated Immunity.** Generally, cell-mediated defenses are probably more important. It is usually T-cell mediated and persons with compromised cell-mediated defenses generally show more disseminated disease
**Epidemiology**

*Dermatophytes* may be communicated from person to person by combs, towels, etc.

*Candida* is a member of the normal vaginal flora; candidiasis is often associated with *diabetes*.

In some cases of mycosis, *Occupation* seems an important contributor. For example, *Sporothrix* is normally found in woody plants; hence, agricultural workers acquire disease more often. Similarly, *Histoplasma* is often found in bird or bat excret; hence caves workers or persons involved in community clean up may acquire more often.
**DIAGNOSIS**

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

**Laboratory**: Treatment of skin scrapings with 10% potassium hydroxide can reveal hyphae or spores. Most fungi can be grown on **Sabouraud's dextrose agar** but they are often very difficult to speciate. **Skin testing** for a delayed hypersensitivity response is useful for epidemiologic purposes but often not for diagnosis.
Germ tube test
Is a screening test which is used to differentiate *candida albicans* from other yeast.
When *candida* is grown in human or sheep serum at 37°C for 3-4 hours, they forms a germ tube, which can be detected with a wet films as filamentous outgrowth extending from yeast cells. It is positive for *candida albicans*.
**CONTROL**

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

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

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