

CURRENT MEDICAL CLASSIFICATION OF FUNGI INVOLVED IN HUMAN PATHOLOGY: REVIEW OF LITERATURE

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Summary

With high frequency amongst the population, clinical polymorphism and their great contagiousness, mycotic diseases represent an important chapter of medical pathology and a public health problem.

Out of the over 100,000 species of existing microscopic fungi, about one hundred are pathogenic to humans.

From a medical point of view, the fungi are grouped into: dermatophytes, levuriform yeasts or fungi, dimorphic fungi (in vivo lesion form, in vitro filamentous form), opportunistic fungi (pathogens under certain circumstances), actinomycetes (filamentous gram positive bacteria, which produce pseudomycoses).

Key words: fungi, mycosis, yeasts, dermatophytes, mycotoxicosis, fungal allergies.

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Introduction

Lower species, fungi are spread over stretched geographical areas. Out of the approximately 100,000 species of highlighted microscopic fungi, 100 only are pathogenic to humans [1]. The pathology developed in humans involves various clinical aspects after requiring multiple differential diagnosis [2,3,4]. By the irrational prescription and abuse of antibiotics, by the increasingly frequent use of corticosteroids and immunosuppressive therapies, the frequency of this pathology is steadily increasing, favoring the ease of spreading fungi through air, water, soil and objects [5,6,7]. High contagiousness and increased migration of the population are key factors in the spread of the disease.

The systemic biology was intuited by Aristotle, the notion of the reign being proposed for the first time in 1735 by Carl Linné which classifies the organisms in two regnum: animals

and plants, omitting the classification of microorganisms. In 1866 Ernst Haeckel created the 3rd reign, Protista, which included microorganisms and protozoa.

The history of microorganisms biology has evolved into various evolutionary stages, so in 2004 Thomas Cavalier-Smith proposes grouping of organisms and microorganisms in 6 regnum: Bacteria, Protozoa, Chromista, Plants, Fungi, Animalia. [1,8].

In classical taxonomy the reign is the highest level of classification of living organisms, according to their common characteristics and in modern taxonomy it's the second highest taxonomic rank of the scientific classification, located between the domain and incrementation. Within a reign, organisms and microorganisms are grouped in increments, classes, orders, families, genres, species with their taxonomic units.

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Fungi belong to the Fungi kingdom (Regnum Fungorum or Mycota), with 7 phylum Ascomycota, Basidiomycota, Blastocladiomycota, Chytridiomycota, Entomophthoromycota, Glomeromycota, Zygomycota. They are eukaryotic, unicellular or multicellular containing the cytoplasm and the nucleus, but also a rich enzymatic device through which they can digest and use substances from the exterior environment, thus making biosynthesis in particular, toxins and antibiotics. They are made of a network called mycelium, composed of branching, mycelium filaments or thread-like hyphae. Mycelium filaments contain protoplasm and nucleus, the contents being separated by transvers lines into a series of cells called mycelium cells. At the periphery the filaments have a membrane composed of pseudo cellulose. Sometimes mycelium is formed by myelinated filaments segmented by dividing walls that have central pores which allow the passage of nutrients from one segment to another. Other myceliums are made up of unsealed filaments, with multi nuclear cytoplasm and bordering is late in the disappearing elements. There are also described myceliums which are formed from pseudo mycelium, made from elongated cells connected one to another without any communication between them [9,10]. Fungal agents presenting one of the three types of mycelium described were grouped by Silva Lacaz and Grigoriu under the name of eumycete [1,11]. Lack of chlorophyll and therefore incapable of photosynthesis they are inferior heterotrophic plants bound to live a saprophytic life. They are generally aerobic. The optimal development temperature is between 20°C and 37°C (Celsius degrees). The development is stimulated by moisture, the dry environment leading to the development of conservation elements (chlamidospores). The optimal pH is around 7. The light inhibits the development of most of the spores and it favors the growth of certain species [8-10]. Fungi which are human pathogens are mostly saprophytes of the external environment with the exception of the anthropophilic dermatophytes and interior environment saprophytes of the digestive track and vaginal cavity [12].

The classification of fungi

Over time several classifications have been proposed for a number of reasons, criticized from other perspectives.

Alexopoulos grouped the eumycetes in four classes: ascomycete, basidiomycete, phycomycete and deuteromycete.

Ainsworth et al. classified this type of fungi in myxomycota with 3 classes (acrasiomycetes, myxomycetes, plasmodiophoromycetes) and eumycota with 5 classes (mastigomycetes, zygomycetes, ascomycetes, basidiomycetes and deuteromycetes).

Vanbreuseghen et al. proposed to group mycete in 6 classes: archimycetes (not pathogen for humans), myxomycetes (not pathogen for humans), phycomycetes, ascomycetes, basidiomycetes, adelomycetes.

A useful classification in medical practice is the one realized by Grigoriu et al. which grouped the eumycete in four classes: zygomycete, ascomycete, basidiomycete, adelomycete [1]. *Zygomycete* are the ethiological agents (*Apo-physomyces*, *Lichtheimia*, *Mucor*, *Saksenaea*, *Rhizomucor*, *Rhizopus*, *Entomophthorales*, *Cunninghamella*, *Saksenaea* et al.) of a profound serious mycosis: mucormycosis and zygomycosis. *Ascomycete* includes dermatophytes and certain pathogenic yeasts for humans. *Basidiomycetes* contain few pathogenic fungi for humans: *Cryptococcus*, *Trichosporon*, *Malassezia*. *Adelomycetes* also called imperfect fungi include microscopic mushroom organisms that do not show sexual reproduction [13,14].

Another classification groups fungi in 4 classes: *Phycomycetes* (including parasites of plants and genus *Mucor*); *Ascomycetes* (includes *Saccharomyces*, *Aspergillus* and *Penicillium*); *Basidiomycetes* (with pathogenic and conditionally pathogenic fungi for humans); *Adelomycetes*, imperfect fungi (includes all pathogenic fungi) [15-17].

According to the morphological aspect, the fungi are divided into filamentous fungi or moulds formed from a thallus or mycelium (*Penicillium*, *Mucor*, *Aspergillus*, *Epidermophyton*) and yeasts or lees which are unicellular fungi (*Saccharomyces* and *Candida*). There are also disruptive fungi that pass from the leech to the filament depending on the environment

(*Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomycetes dermatidis*) [1,15,16].

From a medical point of view, fungi are grouped into 4 classes: dermatophytes, yeasts or yeast fungus, dimorphic fungi, non pathogenic fungi, which in some circumstances become pathogenic, called "opportunistic" [1,10,17].

Previously included amongst the fungi, *Actinomyces* are considered now filamentous bacteria, or intermediate forms of evolution between bacteria and fungi [18].

Dermatophytes are a group of fungi with lower pathogenic potential for humans and animals but with a great capacity to adapt to environmental conditions. The first classification was made by Sabouraud in 1910, grouping dermatophytes in 4 genres: *Achorion* (flavus agent), *Microsporum*, *Trichophyton*, *Epidermophyton*. In present the used classification is the one proposed by Emmons in 1934, which was later accepted by Negroni (1942) and Ajello (1968) grouping dermatophytes in 3 genres: *Trichophyton*, *Microsporum* and *Epidermophyton* [1,8].

There are more than 26 species belonging to the *Trichophyton* Genus, 19 of which are described by Grigoriu [1] (*Tr. violaceum*, *Tr. soudanense*, *Tr. tonsurans*, *Tr. yaoundei*, *Tr. megninii*, *T. rrodhaini*, *Tr. schoenleinii*, *Tr. erinacei*, *Tr. concentricum*, *Tr. simii*, *Tr. interdigitale*, *Tr. ajelloi*, *Tr. rubrum*, *Tr. terrestre*, *Tr. mentagrophytes*, *Tr. phaseoliforme*, *Tr. quinckeanum*, *Tr. equinum*, *Tr. verrucosum*) and other accepted *Arthrodermataceae* (dermatophytes) from *Trichophyton* Genus species: *Tr. africanum*, *Tr. areolatum*, *Tr. balcanicum*, *Tr. batonrougei*, *Tr. benhamiae*, *Tr. brumptii*, *Tr. bullosum*, *Tr. candelabrum*, *Tr. cerebriforme*, *Tr. circonvolutum*, *Tr. denticulatum*, *Tr. depressum*, *Tr. eriotrephon*, *Tr. europaeum*, *Tr. farinulentum*, *Tr. fischeri*, *Tr. flavescens*, *Tr. floriforme*, *Tr. fluviomuniense*, *Tr. fuligineum*, *Tr. glabrum*, *Tr. gloriae*, *Tr. gourvilii*, *Tr. guzzonii*, *Tr. immergens*, *Tr. indicum*, *Tr. indotineae*, *Tr. japonicum*, *Tr. kanei*, *Tr. krajdenii*, *Tr. kuryangei*, *Tr. longifusum*, *Tr. louisianicum*, *Tr. mariatii*, *Tr. milochevitchii*, *Tr. multicolor*, *Tr. oceanicum*, *Tr. ochoterenai*, *Tr. olexae*, *Tr. pedis*, *Tr. persicum*, *Tr. plurizoniforme*, *Tr. pratense*, *Tr. proliferans*, *Tr. pseudotonsurans*, *Tr. purpureum*, *Tr. radicosum*, *Tr. raubitschekii*, *Tr. rotundum*, *Tr. sabouraudii*, *Tr. sarkisovii*, *Tr. spadix*, *Tr. spiraliforme*,

Tr. teheraniense, *Tr. tenuishyphum*, *Tr. vanbreuseghemii* et al. [13,14, 19-21].

Microsporum Genus also includes several species: *M. amazonicum*, *M. appendiculatum*, *M. audouinii*, *M. boullardii*, *M. langeronii*, *M. duboisii*, *M. ferrugineum*, *M. rivalieri*, *M. distortum*, *M. canis*, *M. canis* var. *distortum*, *M. equinum*, *M. gallinae*, *M. fulvum*, *M. persicolor*, *M. nanum*, *M. gypseum*, *M. cookie*, *M. praecox*, *M. ripariae*, *M. rivalieri* [13,14, 21-23].

Epidermophyton Genus includes very few species, the most known being *Ep. floccosum* (*Ep. album*, *Ep. angustisporum*, *Ep. inguinale*, *Ep. densenae*, *Ep. flavum*, *Ep. griseum*, *Ep. macrosporicum*, *Ep. niveum*, *Ep. planum*, *Ep. plicarum*, *Ep. repens*, *Ep. salmoneum*, *Ep. sartoryi*, *Ep. variable*). [13,14,24-26]

Lees or yeast fungus represent a heterogeneous group of fungi which are a bit confusing: imperfect fungi, deuteromycete, adelomycete or ascomycete. Some cells can develop pseudofilaments and others, rarely, true filaments. They are saprophytes of the outside environment and may become pathogenic to humans. They were grouped in 2 families in 1952 by Lodder and Kreger-van Rij: *Cryptococcoideae* and *Trichosporoideae*. The *Cryptococcoideae* family includes the following Families: *Cryptococcus* (species *Cr. neoformans*), *Torulopsis* (species *Tor. glabrata*), *Pityrosporum* (*P. ovale*, *P. orbiculare*, *Malassezia pachydermatis* also named *P. canis*), *Candida* (*C. aaseri*, *C. adriatica*, *C. agrestis*, *C. akabanensis*, *C. alai*, *C. albicans*, *C. alcophila*, *C. andamanensis*, *C. anglica*, *C. argentea*, *C. atlantica*, *C. berkhoutiae*, *C. bracarensis*, *C. dendrica*, *C. dubliniensis*, *C. endomychidarum*, *C. ezoensis*, *C. fabianii*, *C. glabrata*, *C. guilliermondii*, *C. krusei*, *C. lusitaniae*, *C. mesenterica*, *C. parapsilosis*, *C. pseudotropicalis*, *C. railenensis*, *C. stellatoidea*, *C. tolerans*, *C. tropicalis*, *C. versatilis* et al.).

The *Trichosporoideae* family includes species *Trichosporon* as a minor component of the microflora of human normal skin and widely distributed in the environment: *T. ovoides*, *T. inkin*, *T. asahii*, *T. cutaneum*, *T. asteroides*, *T. mucoides*, *T. faecale*, *T. dermatitis*, *T. domesticum*, *T. loubieri*, *T. jirovecii*, *T. mycotoxinovorans*. Occasionally, particularly in circumstances of high humidity, *Trichosporon ovoides* (scalp) or *Trichosporon inkin* (pubis) can proliferate, causing an unpleasant,

but harmless hair condition known as tinea blanca. [13-15,27-34]

Pathogenic fungi can produce in humans mycosis (fungal infections caused by the presence of fungi in or on the human body), mycotoxicosis (produced by the ingestion of aliments contaminated with toxic metabolites of fungi) and fungal allergies [15,35].

Medical mycology studies only microscopic fungi which can cause disease in humans, named mycosis.

From the clinical point of view, mycosis are divided into 3 categories [36-41]:

I. *Superficial fungal infections (superficial Mycosis, Dermatomycosis):*

A. Dermatophytes:

- Epidermophyton (skin dermatitis);
- Tinea tonsurans (microsporia, black dot *Trichophyton* infection), favus, kerion celsi of the scalp and chin;
- Dermatophytic onychomycosis

B. Keratomycosis: superficial dermatomycosis (pityriasis versicolor, erythrasma)

C. Candidal mycosis

II. Subcutaneous fungal infections affecting the skin and subcutaneous tissue with possible lymphatic interest: sporotrichosis (*Sporothrix schenckii*), micetom (*Madurella mycetomatis*) [42-46].

III. *Deep fungal infections (systemic or visceral) initially classified by the etiological agents in [47-50]:*

1. Mycosis caused by yeasts: candidomycosis (bronhopneumonia, pneumonia, enteritis, endocarditis, meningitis, erythrocytosis, septicemia etc.), cryptococcosis, geotrichoza, other mycosis caused by yeasts (lobomycosis or amazon blastomycosis).
2. Mycosis caused by filamentous fungi: aspergillosis, penicillosis, mucormycosis, other mycosis caused by filamentous fungi.

3. Mycosis caused by dimorphic fungi: north american blastomycosis, coccidioidomycosis, histoplasmosis, sporotrichosis.

In 2002, under the international consensus EORTC& IFIG (European Organization for Research and Treatment of Cancer & Invasive Fungal Infections Group), invasive or systemic fungal infections were divided in 2 [15,16,51-55]:

1. Fungemia – the presence of at least a positive haemoculture in the presence of clinical signs and symptoms compatible with the identified fungus.

2. Invasive fungal infection – the detection of fungi in a physiological sterile site in the present of fungal or radiological signs compatible with the identified fungus, divided in 2:

– endemic invasive fungal infections or pulmonary damage (coccidioidomycosis, paracoccidioidomycosis, histoplasmosis, penicilliosis) and

– invasive opportunistic fungal infections (systemic candidiasis, invasive aspergillosis, cryptococcosis, mucormycosis, hyalohyphomycosis, pneumonia with *Pneumocystis carinii*, systemic infections with *Trichosporum* spp., *Malassezia furfur*).

3. Disseminated fungal infection – the presence of fungi in 2 or more physiologically sterile organs or sites and located at a variable distance.

Conclusions

Due to the importance of the diseases they cause to humans, fungi have been an interesting and important field of study since antiquity. The new methods of scientific research have allowed the identification of new species, a better knowledge of their morphological and physiological characteristics, but also of the diseases produced. Thus, the high frequency among the population, the clinical polymorphism and their high contagiousness, mycotic diseases of the skin, mucous membranes and other organs and systems represent an important chapter of medical pathology and a public health problem.

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Conflict of interest
NONE DECLARED

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