

Assist. Prof. Dr. Abbas O. Farhan Al-Janabi
College of Anbar Medicine,
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Medical Mycology

Cutaneous Mycoses

Cutaneous mycoses are caused by fungi that infect only the superficial keratinized tissue (**skin, hair, and nails**). The most important of these are the **dermatophytes**, a group of about 40 related fungi that belong to **three genera: microsporium, trichophyton, and epidermophyton**. **Dermatophytes are probably restricted to the nonviable skin because most are unable to grow at 37 °C or in the presence of serum.**

Dermatophytoses are among the most prevalent infections in the world. Although they can be persistent and troublesome, they are not debilitating or life-threatening—yet millions of dollars are expended annually in their treatment. Being **superficial, dermatophyte (ringworm) infections** have been recognized since antiquity. **In skin they are diagnosed by the presence of hyaline, septate, branching hyphae or chains of arthroconidia.** In culture, the many species are closely related and often difficult to identify. They are speciated on the basis of subtle differences in the appearance of the colonies and microscopic morphology as well as a few vitamin requirements. Despite their similarities in morphology, nutritional requirements, surface antigens, and other features, many species have developed keratinases, elastases, and other enzymes that enable them to be quite host-specific. For some species of dermatophytes, a sexual reproductive state has been discovered, and **all dermatophytes with a sexual form produce ascospores** and belong to the teleomorphic genus arthroderma.

Dermatophytes are classified as geophilic, zoophilic, or anthropophilic depending on whether their usual habitat is soil, animals, or humans. Several dermatophytes that normally reside in soil or are associated with particular animal species are still able to cause human infections. In general, as a species evolves from habitation in soil to a specific animal or human host, it loses the ability to produce asexual conidia and to reproduce sexually.

Anthropophilic species, which cause the greatest number of human infections, cause relatively mild and chronic infections in humans, produce few conidia in culture, and may be difficult to eradicate. Conversely, geophilic and zoophilic dermatophytes, being less adapted to human hosts, produce more acute inflammatory infections that tend to resolve more quickly. Dermatophytes are acquired by contact with contaminated soil or with infected animals or humans.

Some anthropophilic species are geographically restricted, but others, such as *Epidermophyton floccosum*, *Trichophyton mentagrophytes* var *interdigitale*, *T rubrum*, and *T tonsurans*, are globally distributed. The most common geophilic species causing human infections is *Microsporum gypseum*.

Cosmopolitan zoophilic species (and their natural hosts) include *Microsporum canis* (dogs and cats), *Microsporum gallinae* (fowl), *Microsporum nanum* (pigs), *Trichophyton equinum* (horses), and *Trichophyton verrucosum* (cattle).

Morphology & Identification

Dermatophytes are identified by their colonial appearance and microscopic morphology after growth for 2 weeks at 25 °C on Sabouraud's dextrose agar. Trichophyton species, which may infect hair, skin, or nails, develop cylindric, smooth-walled macroconidia and characteristic microconidia). Depending on the variety, colonies of *T mentagrophytes* may be cottony to granular;

both types display abundant grape-like clusters of spherical microconidia on terminal branches. Coiled or spiral hyphae are

commonly found in primary isolates.

The typical colony of *T rubrum* has a white,

cottony surface and a deep red, nondiffusible pigment when viewed from the reverse side of the colony. The microconidia are small and piriform (pear-shaped) Fig.(1). *T tonsurans* produces a flat, powdery to velvety colony on the obverse surface that becomes reddish-brown on reverse; the microconidia are mostly elongate

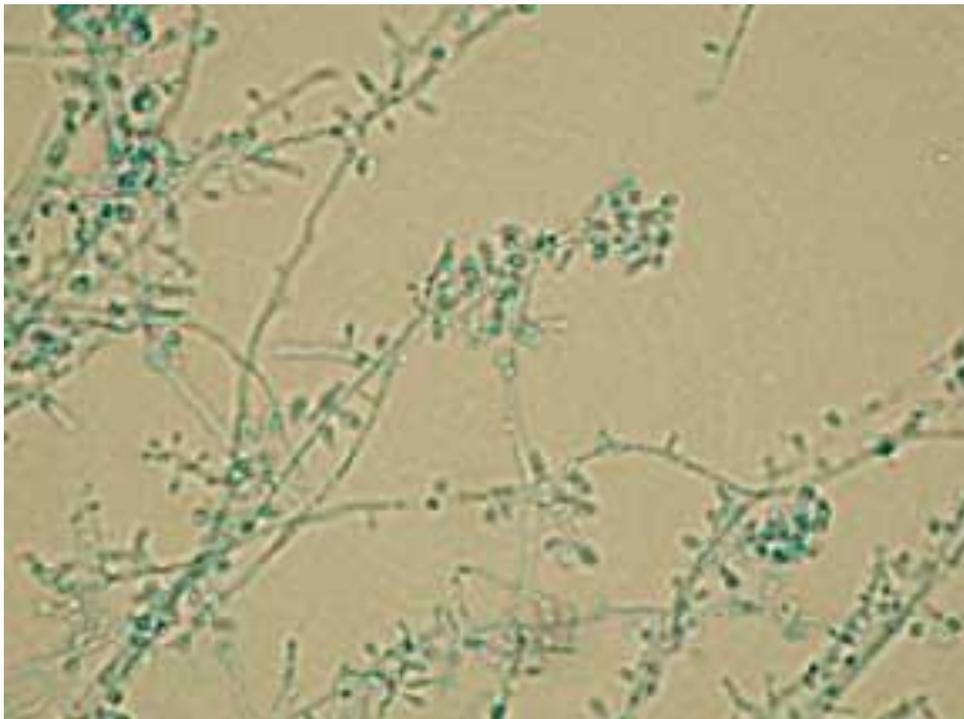


Fig. (1) *Trichophyton rubrum*

Microsporum species tend to produce distinctive multicellular macroconidia with echinulate walls .Both types of conidia are borne singly in these genera. *M canis* forms a colony with a white cottony surface and a deep yellow color on reverse; the thick-walled, 8- to 15-celled macroconidia frequently have curved or hooked tips Fig. . *M gypseum* produces a tan, powdery colony and abundant thin-walled,

four- to six-celled macroconidia. Microsporum species infect only hair and skin.



Fig.(2) *Microsporium canis*

***Epidermophyton floccosum*, which is the only pathogen in this genus, produces only macroconidia, which are smooth-walled, clavate, two- to four-celled, and formed in groups of two or three . The colonies are usually flat and velvety with a tan to olive-green tinge. *E. floccosum* infects the skin and nails but not the air Fig.(3).**

In addition to gross and microscopic morphology, a few nutritional or other tests, such as growth at 37 °C or a test for in vitro hair perforation, are useful in differentiating certain species.

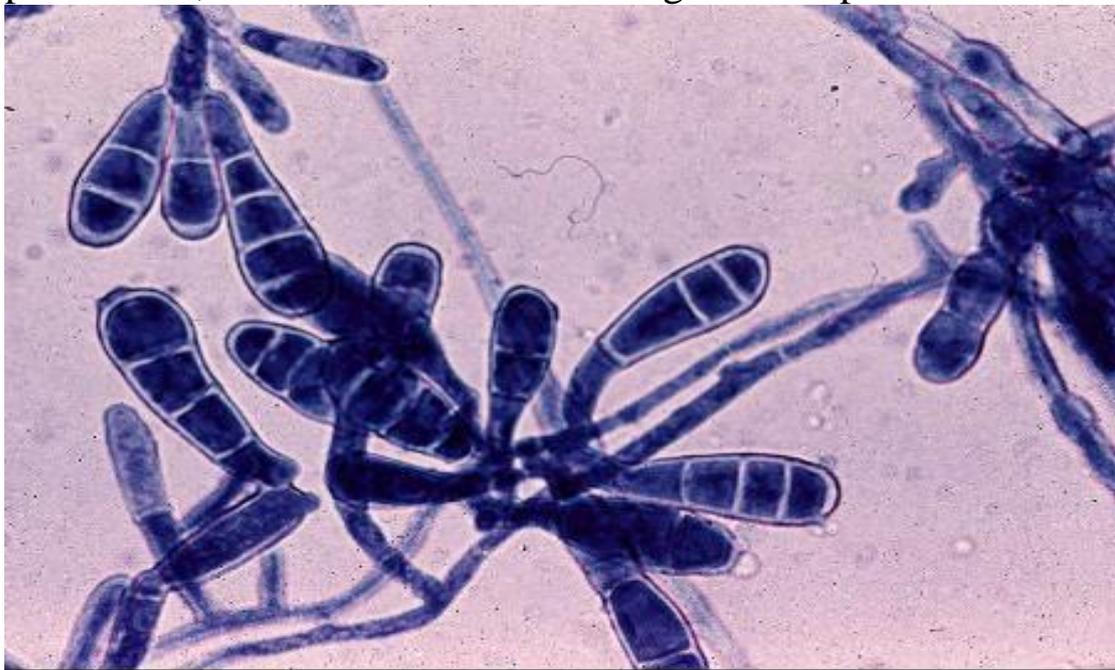


Fig.(3) *Epidermatophyton floccosum*

Epidemiology & Immunity

Dermatophyte infections begin in the skin after trauma and contact. There is evidence that host susceptibility may be enhanced by moisture, warmth, specific skin chemistry, composition of sebum and perspiration, youth, heavy exposure, and genetic predisposition. The incidence is higher in hot, humid climates and under crowded living conditions. Wearing shoes provides warmth and moisture, a setting for infections of the feet.

The source of infection is soil or an infected animal in the case of geophilic and zoophilic dermatophytes, respectively. The conidia can remain viable for long periods. Anthropophilic species may be transmitted by direct contact or through fomites, such as contaminated towels, clothing, shared shower stalls, and similar examples.

Trichophytin is a crude antigen preparation that can be used to detect immediate- or delayed-type hypersensitivity to dermatophytic antigens. Many patients who develop chronic, noninflammatory dermatophyte infections have poor cell-mediated immune responses to dermatophyte antigen.

These patients often are atopic and have immediate-type hypersensitivity and elevated IgE concentrations. In the normal host, immunity to dermatophytosis varies in duration and degree depending on the host, the site, and the species of fungus causing the infection.

Clinical Findings

Dermatophyte infections were mistakenly termed ringworm or tinea because of the raised circular lesions. The clinical forms are based on the site of involvement. A single species is able to cause more than one type of clinical infection. Conversely, a single clinical form, such as tinea corporis, may be caused by more than one dermatophyte species.

Tinea Pedis (Athlete's Foot)

Tinea pedis is the most prevalent of all dermatophytoses. It usually occurs as a chronic infection of the toe webs. Other varieties are the vesicular, ulcerative, and moccasin types, with hyperkeratosis of the sole. Initially, there is itching between the toes and the development of small vesicles that rupture and discharge a thin fluid. The skin of the toe webs becomes macerated and peels, whereupon cracks appear that are prone to develop secondary bacterial infection. When the fungal infection becomes chronic, peeling and cracking of the skin are the principal manifestations, accompanied by pain and pruritus.

Tinea Unguium (Onychomycosis)



Nail infection may follow prolonged tinea pedis. With hyphal invasion, the nails become yellow, brittle, thickened, and crumbly. One or more nails of the feet or hands may be involved.

Tinea Corporis, Tinea Cruris, and Tinea Manus



Dermatophytosis of the glabrous skin commonly gives rise to the annular lesions of ringworm, with a clearing, scaly center surrounded by a red advancing border that may be dry or vesicular. The dermatophyte grows only within dead, keratinized tissue, but fungal metabolites, enzymes, and antigens diffuse through the viable layers of the epidermis to

cause erythema, vesicle formation, and pruritus. **Infections with geophilic and zoophilic dermatophytes produce more irritants and are more inflammatory than anthropophilic species.** As hyphae age, they often form chains of arthroconidia. The lesions expand centrifugally and active hyphal growth is at the periphery, which is the most likely region from which to obtain material for diagnosis. Penetration into the newly forming stratum corneum of the thicker plantar and palmar surfaces accounts for the persistent infections at those sites. **When the infection occurs in the groin area, it is called tinea cruris, or jock itch.** Most such infections involve males and present as **dry, itchy lesions** that often start on the scrotum and spread to the groin. **Tinea manus** refers to **ringworm of the hands or fingers.** Dry scaly lesions may involve one or both hands, single fingers, or two or more fingers.

Tinea Capitis and Tinea Barbae

Tinea capitis is dermatophytosis or ringworm of the scalp and hair. The infection begins with hyphal invasion of the skin of the scalp, with subsequent spread down the keratinized wall of the hair follicle. **Infection of the hair takes place just above the hair root.** The hyphae grow downward on the nonliving portion of the hair and at the same rate as the hair grows upward. **The infection produces dull gray, circular patches of alopecia, scaling, and itching. As the hair grows out of the follicle, the hyphae of microsporum species produce a chain of spores that form a sheath around the hair shaft (ectothrix).**

These spores impart a greenish to silvery fluorescence when the hairs are examined under Wood's light (365 nm). In contrast, ***T tonsurans*, the chief cause of "black dot" tinea capitis, produces spores within the hair shaft (endothrix).** These hairs do not fluoresce; they are weakened and typically break easily at the follicular opening. In prepubescent children, epidemic tinea capitis is usually self-limiting.

Zoophilic species may induce a severe combined inflammatory and hypersensitivity reaction called a **kerion.** Another manifestation of

tinea capitis is favus, an acute inflammatory infection of the hair follicle caused by *T schoenleinii*, which leads to the formation of scutula (crusts) around the follicle. In favic hairs, the hyphae do not form spores but can be found within the hair shaft. Tinea barbae involves the bearded region.

Especially when a zoophilic dermatophyte is involved, a highly inflammatory reaction may be elicited that closely resembles pyogenic infection.

Trichophytid Reaction

In the course of dermatophytosis, the individual may become hypersensitive to constituents or products of the fungus and may develop allergic manifestations—called dermatophytids (usually vesicles)—elsewhere on the body, most often on the hands. The trichophytin skin test is markedly positive in such persons.

Diagnostic Laboratory Tests Specimens

Specimens consist of scrapings from both the skin and the nails plus hairs plucked from involved areas. **Microsporum-infected hairs fluoresce under Wood's light in a darkened room.**

Microscopic Examination

Specimens are placed on a slide in a drop of **10–20% potassium hydroxide**, with or without calcofluor white, which is a nonspecific fungal cell wall stain viewed with a fluorescent microscope. A coverslip is added, and the specimen is examined immediately and again after 20 minutes. In skin or nails, regardless of the infecting species, **branching hyphae or chains of arthroconidia (arthrospores)**. **In hairs, most microsporum species form dense sheaths of spores around the hair (ectothrix). *T tonsurans* and *T violaceum* are noted for producing arthroconidia inside the hair shaft (endothrix).**

Culture

The identification of dermatophyte species requires cultures. Specimens are inoculated onto inhibitory mold agar or Sabouraud's agar slants containing cycloheximide and chloramphenicol to suppress mold and bacterial growth, incubated for 1–3 weeks at room temperature, and further examined in slide cultures if necessary. Species are identified on the basis of colonial morphology (growth rate, surface texture, and any pigmentation), microscopic morphology (**macroconidia, microconidia**), and, in some cases, nutritional requirements.

Treatment

Therapy consists of thorough removal of infected and dead epithelial structures and application of a topical antifungal chemical or antibiotic. **To prevent reinfection, the area should be kept dry, and sources of infection,** such as an infected pet or shared bathing facilities, should be avoided.

Tinea Capitis

Scalp infections are treated with griseofulvin for 4–6 weeks. Frequent shampoos and miconazole cream or other topical antifungal agents may be effective if used for weeks.

Alternatively, ketoconazole, itraconazole, and terbinafine are all quite effective.

Tinea Corporis, Tinea Pedis, and Related Infections



The most effective drugs are **itraconazole** and **terbinafine**. However, a number of topical preparations may be used, such as **miconazole nitrate**, **tolnaftate**, and **clotrimazole**. If applied for at

least 2–4 weeks, the cure rates are usually 70–100%. Treatment should be continued for 1–2 weeks after clearing of the lesions. For troublesome cases, a short course of oral griseofulvin can be administered

Tinea Unguium Nail infections are the most difficult to treat, **often requiring months of oral itraconazole or terbinafine as well as surgical removal of the nail. Relapses are common.**