13 Clinical Aspects of Dermatophyte Infections

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I. Introduction

Infections caused by dermatophytes are termed dermatophytoses, tinea or ringworm. They are among the most common and widespread endemic infectious diseases (Rippon 1988; Kates et al. 1990; Odom 1993; Gupta et al. 2003). In some geographic areas or environments more than 30% of the population is affected (Rippon 1985; Noguchi et al. 1995). Therefore, dermatophytoses pose a considerable worldwide health problem. In most cases dermatophytoses in humans remain superficial infections, restricted to the skin, nails, and hair (Ogawa et al.1998). These infections often lead to skin lesions, which are uncomfortable but not life-threatening. However, infections of deeper structures like subcutaneous soft tissue can occur under conducive conditions. The relationship between the pathogen and the human host depends very much on the species of dermatophyte involved and on the patient's immunocompetence, general health, and living conditions. Dermatophytoses provide a fascinating model for the interaction between highly specialized fungi and host defense. Because the skin is uniquely accessible to examination with the naked eye, a trained observer can examine this fungal battlefield without additional technical devices.

In the following chapter, after a short look at the dermatophytes as medically important fungi, some of the known mechanisms involved in dermatophyte infections are discussed in order to help better understand the development and pathogenesis of dermatophyte infections. The clinical aspects of the most common and characteristic types of dermatophytoses (or forms of tinea) are covered, followed by a review of their epidemiological aspects. Finally, general principles of treatment are described.

II. Dermatophytes

The term dermatophyte is defined primarily by functional characteristics and not by strict taxonomical criteria. A dermatophyte is a hyalohyphomycete that can degrade keratin and consequently cause communicable skin infections in humans and/or animals (generally mammals; Weitzman and Summerbell 1995; Weitzman and Padhye 1996). Keratin is the main constituent of the outermost layer of human skin, the stratum corneum, as well as hair and nails in humans, and hooves, fur, and feathers in animals. An intact stratum corneum is usually a sufficient protective barrier against microorganisms, but highly specialized keratinophilic dermatophytes can invade this outer shield of the skin and cause infections.

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The different species of dermatophytes are morphologically and physiologically very closely related (de Vroey 1985; Matsumoto and Ajello 1987). Comparisons of ribosomal RNA genes in fact indicate that they are monophyletic in origin and that radiation began only about 50×10^6 years ago. This means that the evolution of dermatophytes occurred synchronously with the evolution of their mammalian hosts (Harmsen et al. 1995). Clonal lineages can even be found in the medically relevant and host-associated dermatophytes, and such lineages are capable of maintaining populations and undergoing further evolutionary developments (Gräser et al. 2006).

Phylogenetic studies have suggested that dermatophytes developed from non-pathogenic, soil-colonizing fungi into species specialized for particular human or animal hosts as their ecological niche (Gräser et al. 1999). Better dermatophyte adaptation to the human host is generally accompanied by a reduced capability to produce spores like macroconidia and differentiated hyphal elements (Summerbell 2000). Interestingly, a strictly anthropophilic dermatophyte, *Trichophyton rubrum* (Fig. 13.1) is currently the most prevalent cause of dermatophyte infections of hairless skin (Sinski and Kelley 1991; Aly et al. 1994; Chinelli et al. 2003; Foster et al. 2004) and another strictly anthropophilic species, *T. tonsurans*, is the most common cause of dermatophyte scalp infections in large parts of the world (Babel et al. 1990; Foster et al. 2004).

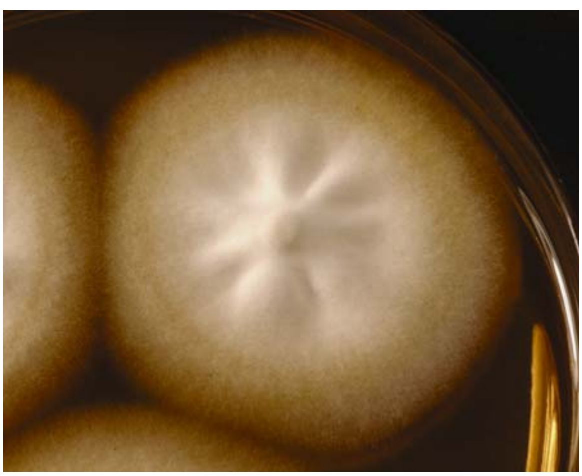

Fig. 13.1. *Trichophyton rubrum* on Sabouraud agar. This species is the most common dermatophyte worldwide. The thallus has a characteristic surface profile

The exact classification of dermatophytes is hampered by the fact that their pathogenic growth phase (which occurs in human skin) differs from the saprophytic phase obtained in vitro. As saprophytes, dermatophytes reproduce asexually in an anamorphic state by producing vegetative spores (conidia). In some species, however, teleomorphic states have been discovered that reproduce sexually (Takashio 1979). These teleomorphic states, or perfect forms, turned out to be members of the Subphylum Ascomycotina, Order Onygenales, Family Arthrodermataceae, Genus *Arthroderma* (Matsumoto and Ajello 87). The dualism of anamorphic and teleomorphic states has led, on the one hand, to a classification system based on anamorph states, and on the other hand, to a valid taxonomic classification based on teleomorphic states (Simpanya 2000). In recent years, genetic methods have generated a wealth of additional information pertaining to species differentiation of dermatophytes (De Hoog et al. 1998; Harmsen et al.1999; Summerbell et al. 1999). This on-going research, which has led to revisions of the classification, is continually evolving and being refined (Gräser 2001).This dynamic field of investigation is, however, beyond the scope of this clinically-focused chapter.

A nomenclature adequately reflecting the medically important features of separate species is required for clinical purposes. From a clinician's point of view, all strains of a distinct species should be characterized by species-related associations with particular diseases (e.g., infections of the nails or the scalp), host adaptation (e.g., adaptation to humans, or distinct species of animals like cats or mice), and epidemiology (i.e., geographic distribution). A strictly biological approach, generally emphasizing purely taxonomic aspects, does not always achieve this aim. The problem is that some genetically very closely related dermatophytes have long been viewed as distinct species because of their association with different clinical settings. Therefore, it remains an unsolved problem how to define dermatophyte species in a way that each recognized species is in congruence with both distinctive medically important characteristics and also a taxonomic system based on evolutionary data. The clinician must be able to correlate an infection with its causative agent. The identification of a specific pathogenic species should allow meaningful clinical conclusions on how the pathogen was likely acquired and what kind of infection it usually causes. In contrast, taxonomic perfection is less relevant in a clinical context. Dermatophytes isolated from skin infections are usually identified by culture techniques that only allow growth of their anamorphic state. All this explains why clinicians are accustomed to applying the classification system that is based on the anamorphic states and why clinicians continue to distinguish some morphologically divergent variants of now genetically unified species that are of interest with regard to differences in distribution, ecology or pathogenicity. The names of the anamorphic states are therefore used in this chapter on the clinical aspects of dermatophyte infections.

The anamorphic states of the dermatophytes belong to three genera: *Trichophyton*, *Microsporum* and *Epidermophyton*, which are easily distinguished by their morphological criteria (Weitzman and Summerbell 1995). All dermatophytes grow in filamentous form on standard mycological media like Sabouraud agar or Kimmig agar, developing dense mycelial thalli and vegetative spores (conidia). The genus *Trichophyton* (Figs. 13.1–13.3) characteristically produces small monocellular club-shaped microconidia, which are borne laterally on the hyphae. Thin- and smooth-walled multicellular macroconidia are often additionally found, although these can be quite rare. These macroconidia are club-shaped and usually not clustered. *Micosporum* species (Fig. 13.4) also have micro- and macroconidia, but the latter are rough-walled, with spindle-shaped walls thicker than those of *T. macroconidia*. The genus *Epidermophyton* does not produce microconidia, but forms multicellular macroconidia instead. These are club-shaped, thin- and smooth-walled, and arranged in bundles. The only clinically relevant species of this genus is *E. floccosum* (Fig. 13.5).

All dermatophytes grow within infected tissue by forming hyphae, allowing them to spread and penetrate adjacent host cells. In older hyphae transverse septa can lead to the separation of fungal cells that then develop thickened walls.

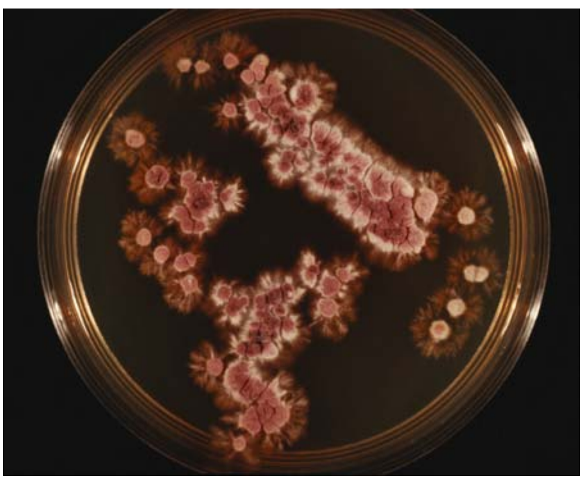

Fig. 13.2. *Trichophyton violaceum* on Sabouraud agar. The name of this anthropophilic species is explained by its strong red, or violaceous, pigmentation

Fig. 13.3. *Trichophyton mentagrophytes* on Sabouraud agar. The variant shown has a granular surface and is often associated with animals

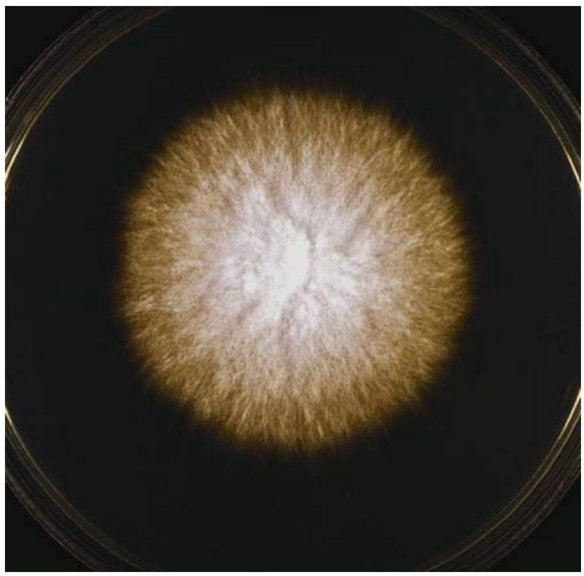

Fig. 13.4. *Microsporum canis* on Sabouraud agar. Cats are important hosts of this zoophilic dermatophyte. It is a common pathogen in scalp infection (tinea capitis) of children

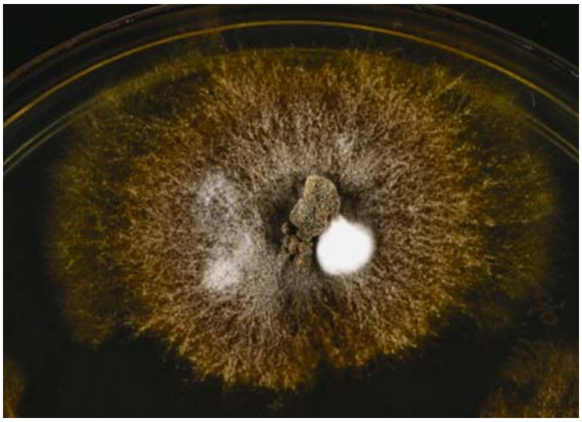

Fig. 13.5. *Epidermophyton floccosum* on Sabouraud agar. The name refers to the white mycelial balls that often occur on the surface of older thalli. This strictly anthropophilic dermatophyte is a common cause of crural infections (tinea cruris)

Finally the hyphae disintegrate into chains of single cells called arthrospores. Arthrospores are robust and resistant to environmental noxa like cold, dryness or UV radiation (Hashimoto and Blumenthal 1978). Even under unfavorable conditions arthrospores can remain viable and virulent for a long time, making them important for the distribution of dermatophytes. Dermatophytes infecting hair can form spores located either within the hair (endothrix) or covering the hair in a sleeve-like manner (ectothrix). These spores are also important propagules for fungal distribution.

According to their phylogenetic development, the main habitat of distinct dermatophyte species can be soil, animals, or humans, so that geophilic, zoophilic and anthropophilic species of dermatophytes must be distinguished (Summerbell 2000; Table 13.1). However, many dermatophytes not primarily adapted can cause human skin infections under conducive conditions. From a clinical point of view, this distinction is of interest because geophilic and zoophilic species tend to trigger more inflammatory lesions in humans than anthropophilic species (Blank et al. 1969; Grigoriu et al. 1984; Brasch 1990a–c) and because knowledge of the ecological group is necessary to identify and eradicate possible sources of infection. For example, cattle are the most common reservoir for *T. verrucosum*, whereas cats are common hosts of *M. canis*. Furthermore, some species or variants of dermatophytes are only endemic in certain geographical areas. Knowledge of geographical distribution is often helpful, although any species can

Table 13.1. Dermatophytes (anamorph species) according to Summerbell and Kane (1997), De Hoog et al. (2000), Brasch and Gräser (2005a, b)

Anthropophilic dermatophytes	Main geographic areas of distribution
Trichophyton concentricum	Pacific Islands, Southeast Asia, Central America
T. interdigitale	Worldwide
T. rubrum	Worldwide
former *T. megninii*	Portugal, Spain, Sardinia, Burundi
var. *kanei*	North America, Europe, Africa
var. *krajdenii*	North America, Europe
var. *raubitschekii*	Asia, Mediterranean, Africa, North America
T. schönleinii	Eurasia, North Africa
T. tonsurans	Worldwide
T. violaceum	Eastern Europe, Northern Africa, Central America
former *T. gourvilii*	West and Central Africa
former *T. soudanense*	Africa
former *T. yaoundei*	Central and Southeast Africa
Microsporum audouinii	Worldwide
M. ferrugineum	Asia, Eastern Europe, Africa
Epidermophyton floccosum	Worldwide
Zoophilic dermatophytes	Main host animals
Trichophyton erinacei	Hedgehogs
T. mentagrophytes	Rodents and other animals
T. simii	Monkeys
T. tonsurans	
i.e., former *T. equinum*	Horses
T. verrucosum	Cattle and other animals
Microsporum amazonicum	Rats
M. canis	Cats, dogs, and other animals
M. gallinae	Fowl, birds
M. nanum	Pigs
M. persicolor	Voles
M. praecox	Horses
Geophilic dermatophytes	
Trichophyton ajelloi	
T. eboreum	
T. flavescens	
T. gloriae	
T. phaseoliforme	
T. terrestre	
T. thuringiense	
T. vanbreuseghemii	
Microsporum cookei	
M. fulvum	
M. gypseum	
M. racemosum	

now be encountered at any location due to global travel and tourism (Brasch and Gräser 2005a, b).

Identification of dermatophyte species begins with the clinical assessment of an infection, taking epidemiological considerations, potential means of acquisition, localization of the infection, and the type of tinea into account. Examination under long-wave ultraviolet light (Wood light) is helpful in detecting certain dermatophyte species (e.g., *M. canis*), which can produce fluorescent metabolites. Infected superficial tissue (hair, nails, scrapings from flaky skin) is then collected from appropriate sites. In many cases, fungal elements can be microscopically detected in KOH-mounts of such specimens. Furthermore, cultures are grown from the collected material at room temperature or at 26–28 °C on mycological agars with supplementary antibiotics to prevent bacterial overgrowth and cycloheximide to suppress molds. The cultures are then identified by their macroscopic morphology, microscopic characteristics of fungal elements, and physiological characteristics (Brasch 1990a–c, 2004; Meinhof 1990). Genetic analyses and other innovative methods like MALDI-TOF are increasingly being used in specialized laboratories. The currently recognized distinct species of dermatophytes are listed in Table 13.1 (Summerbell and Kane 1997; De Hoog et al. 2000; Brasch and Gräser 2005a, b).

III. Dermatophytoses

A. Pathophysiology

Dermatophyte infections (tinea, ringworm) are transmitted by infectious particles, mostly arthrospores (or other spores or hyphal fragments) formed within infected tissue (Richardson 1990; Tsuboi et al. 1994; Rashid 2001). Transmission can occur directly from human or animal to human, or indirectly via contaminated objects such as hairbrushes, towels, pillows, furniture, floors, or objects in contact with animals like fences or blankets. Germination of adherent spores can be observed one day after inoculation, followed by penetration of hyphae after three days (Duek et al. 2004). However, it often takes two weeks or more until a lesion becomes clinically apparent.

The kind of infection that develops in an individual subject depends on the inoculation site, the fungal species involved, and on the host response, which is related to age, gender, immunocompetence, general health, and possibly to genetic disposition (Brasch 1990a–c; Faergemann et al. 2005). Dermatophyte infections generally remain restricted to keratinized tissue (Tsuboi et al. 1994; Ogawa et al. 1998). It can be said that zoophilic and geophilic species cause more acute and inflammatory infections than anthropophilic species, that immunodeficiency or otherwise compromised general health leads to more severe or chronic infections, and that invasion of non-viable tissues (nails, hair) tends to produce persistent infections. For example, an infection caused by *T. verrucosum* is usually much more inflammatory than an infection with *T. rubrum*, infections in AIDS patients are much more refractory than comparable infections in otherwise healthy individuals, and a dermatophyte infection of a nail has a much higher tendency to become chronic than an infection of facial skin.

Inoculation of infectious dermatophyte elements into the skin and adherence of such propagules to the stratum corneum are promoted by defects in the stratum corneum, occlusion, and moist skin. If the transmitted fungal propagules are left undisturbed with sufficient time for attachment (Zurita and Hay 1987) and growth (Aljabre et al.1993; Tsuboi et al. 1994), hyphae begin to spread radially within the stratum corneum. UV exposure may potentially promote the downward growth of dermatophytes (Brasch and Menz 1995). Dermatophytes are well equipped with a spectrum of enzymes, enabling them to penetrate the stratum corneum and digest keratins (Day et al. 1968; Cheung and Maniotis 1973; Apodaca and McKerrow 1989; Summerbell 2000; Viani et al. 2001; Jousson et al. 2004; Kaufman et al. 2005), lipids (Nobre and Viegas 1972; Das and Banerjee 1977; Hellgren and Vincent 1980) and other substrates (Hankin and Anagnostakis 1975; Hopsu-Havu and Tunnela 1976; Calvo et al. 1985; Brasch et al. 1991; Brasch and Zaldua 1994). Keratinolytic proteases appear relevant for their ability to utilize keratin (Ferreira-Nozawa et al. 2006). The epidermal barrier is markedly impaired by fungal invasion of the skin (Jensen et al. 2007). Other pathogenic factors of dermatophytes include xanthomegnin as a toxin (Gupta et al. 2000), mannans as immunosuppressive agents (Dahl 1994; Dahl and Grando 1994), hemagglutinins (Bouchara et al. 1987), and trigger factors for cooperative hemolytic reactions (Schaufuss et al. 2005). Antibiotic substances synthesized by dermatophytes (Youssef et al. 1978; Lappin-Scott et al. 1985) may help them to compete with bacteria. The inflammatory skin response triggered by the spreading dermatophytes is greatest at the advancing margin of the fungal invasion and can be recognized by marked erythema, scaling, and palpable infiltration of the skin, sometimes accompanied by pustules. The accentuated inflammatory rim of the skin lesions often has an arched or circular shape, explaining the use of the term "ringworm" to describe dermatophytoses.

This fungal invasion activates the host's defense mechanisms (Wagner and Sohnle 1995). The inflammatory response comprises innate immunity and, if previous sensitization had occurred, immunological mechanisms as well (Jones 1986; Martínez Roig and Torres Rodriguez 1987; Tagami et al. 1989, Calderon 1989; Brasch et al. 1993; Dahl 1994). Neutrophilic granulocytes and macrophages are attracted and activated by complement-dependent and complement-independent mechanisms (Sato 1983; Swan et al. 1983; Davies and Zaini 1984; Dahl and Carpenter 1986; Suite et al. 1987; Brasch et al. 1991; Kahlke et al. 1996; Campos et al. 2005). The significant increase in epidermal proliferation (Berk et al. 1976; Jensen et al. 2007) is thought to help slough the fungus from the skin surface. Serum factors like transferrin and fatty acids of the skin may help suppress infections by binding iron necessary for fungal growth (King et al. 1975) or by having antimycotic effects (Nathanson 1960; Carlisle et al. 1974; Das and Banerjee 1982; Garg and Müller 1993; Brasch and Friege 1994). Keratinocytes and infiltrating mononuclear cells are activated to release inflammatory cytokines like interferon-gamma, plus a broad panel of interleukins (Miyata et al. 1996; Koga et al. 2001; Nakamura et al. 2002; Shiraki et al. 2006a, b). Cytokines and interleukins are cellular mediators that can activate and regulate defense mechanisms. Epidermal keratinocytes can also express so-called defensins as antimicrobial peptides; human beta-defensin 2 has been detected in dermatophyte-infected skin (Kawai et al. 2006; Jensen et al. 2007). Langerhans cells play a decisive role in the initiation of epidermal cellular immune defense and accumulate at the site of infection (Emtestam et al. 1985; Brasch et al. 1993). Furthermore, lymphocytes invade the lesional skin and are activated (Brasch and Sterry 1992). These mechanisms contribute to a delayed, T cell-mediated immune response that develops during dermatophyte infections (Svejgaard 1986a, b) and is decisive for healing (Dahl 1985; Jones 1993; Dahl 1994). In contrast, a Th2 reponse appears to provide no protection (Leibovici et al. 1995). The terminal hair follicles of the scalp are the main habitat of dermatophytes infecting the scalp. They are connected to the sebaceous glands, forming so-called pilosebaceous units that decisively contribute to the endocrine functions of the skin by producing and metabolizing steroid hormones (Zouboulis 2000). Human steroid hormones encountered in this highly differentiated and distinct environment may have effects on dermatophytes dependening on the fungal species (Chattaway and Townsley 1962; Schär et al. 1986; Brasch and Gottkehaskamp1992; Brasch and Flader 1996; Brasch 1997; Brasch et al. 2002). Since steroid hormones are regulated differently in men and women, they may contribute to gender-related resistances to certain fungal infections (Stevens 1989). In most cases the combined effects of defense mechanisms lead to at least some temporary clearing in the central areas of infected skin, which may, however, be followed by new waves of invasion. This process can be mirrored in characteristic skin lesions (Fig. 13.6). Chronic infections are common with anthropophilic strains.

Antibodies against dermatophyte products were detected under suitable conditions in the blood and tissue of individuals with dermatophyte infections (Holden et al. 1981; Honbo et al. 1984; Svejgaard 1986a, b; Calderon et al. 1987; Lee et al. 1988) and blood cells and skin were shown to specifically respond to dermatophyte compounds (Espiritu et al. 1988; Koga et al. 1993). Such circulating cells and agents may explain hematogeneously elicited sterile skin reactions observed in patients with inflammatory dermatophytoses in

Fig. 13.6. Tinea lesions on glabrous skin with marked erythematous rings and concentric areas of clearing between them

non-infected skin, otherwise known as dermatophytids (Grappel et al. 1974).

B. Clinical Manifestations

As discussed above, dermatophyte infections begin with the adherence of contagious particles to the outmost layer or the epidermis (stratum corneum) or with the inoculation of infectious propagules into the epidermis. Hyphae then spread within the superficial epidermal layers and cause an inflammatory infection. This process can occur at any site on the skin surface, including nails and hair. The disease remains confined to the superficial skin in most cases and is called dermatophytosis, ringworm, or tinea. The latter name is usually supplemented by a Latin term designating the affected site, for example, tinea manuum for infection of the hand or tinea capitis for infection of the scalp. The disease is called tinea profunda when the dermis is invaded. In very rare cases extracutaneous dermatophyte infections have even been proven. Although the occurrence of systemically elicited sterile skin reactions triggered by dermatophyte infections at a distant site is named trichophytid or dermatophytid, the existence of such reactions is generally not acknowledged.

1. Tinea Pedis and Tinea Manuum

Tinea pedis is a dermatophyte infection of the skin of the feet, generally beginning in the toe webs (Fig. 13.7) and often affecting the soles. Tinea pedis is the most common fungal infection worldwide (Masri-Fridling 1996) and has an extremely high prevalence in shoe-wearing populations. Constricting footwear promotes perspiration of the feet and mechanical friction of the skin, followed by interdigital skin maceration, which offers ideal conditions for dermatophyte invasion. Certain professions (miners, athletes, soldiers) are particularly vulnerable to tinea pedis, otherwise known as athletes' foot, due to their high degree of physical activity and their wearing of tight boots or shoes. Individuals living and working in close conditions and sharing bathing facilities have a high risk of foot contact with dermatophyte-contaminated material. Under such conditions, tinea pedum is endemic, affecting nearly 100% of the individuals, even leading to considerable disability in some cases (Götz and Hantschke 1965; Allen and Taplin 1973).

Tinea pedis is most often caused by *T. rubrum*, *T. interdigitale*, variants of *T. mentagrophytes* (Brasch 2001) or other anthropophilic dermatophytes. These species generally lead to aphlegmasic and persistant, chronic lesions. However, geophilic species are also occasionally found due to exposure to contaminated soil and zoophilic species can trigger severe inflammatory infections.

Tinea pedis generally begins within the narrow interdigital space of the toe webs, often as a lesion between digits four and five (Fig. 13.7). It is characterized by itching, scaling, and maceration of the skin. It can spread to the soles and dorsal sides of the feet (Fig. 13.8). Infections of the plantar skin, characterized by dry scaling and often barely recognized as an infection by the host, are particularly likely to become chronic ("moccasin"-type tinea pedis). Scales containing contagious arthrospores are shed and thereby contribute to the further distribution of the disease. However, acute inflammatory courses can also be seen which are associated

Fig. 13.7. Tinea pedis, interdigital form. Maceration and fissuring of the skin are typical features

Fig. 13.8. Tinea pedis. The skin shows inflammation accompanied by erythema and scaling

Fig. 13.9. Tinea manum. There is a sharply defined inflammatory response on the palmar skin spreading from the thenar area

with vesicles, pustules, and weeping, erosive lesions. Significant work absence may become necessary, with secondary bacterial infection a common complication in such cases (Leyden 1994). Longstanding tinea pedum is often associated with infection of the toenails (onychomycosis; Szepietowski et al. 2006) and is considered a major fungus reservoir that may lead to infection of other body areas (Daniel and Jellinek 2006). Tinea manuum is a dermatophytosis of the hand (Fig. 13.9). Tinea manuum is much less frequently encountered than tinea pedis (Blank and Mann 1975) and can often be attributed to autoinoculation of fungi from the feet to a hand. The synchronous infection of both feet and one hand ("two feet – one hand syndrome") is a rather common condition, with lesions on the feet normally preceding the infection of the hand (Daniel et al. 1997). Tinea manuum is most often due to *T. rubrum* (Arenas 1991), but zoophilic and geophilic species can also be found, particularly following exposure to animals or soil.

2. Onychomycosis

A fungal infection of the nails is called onychomycosis. When the fungus is a dermatophyte, this condition is named tinea unguium. Onychomycosis is an endemic and extremely common disease in developed countries (Roberts 1992; Perea et al. 2000; Effendy et al. 2005; Szepietowski et al. 2006). It has been estimated that up to 30% of dermatological patients in Germany, 15–20% of people between 40 and 60 years of age in the United States (Zaias 1985) and 8.4% of the entire population in Finland (Heikkilä and Stunn 1995) suffer from onychmycosis with dermatophytes as the main agents. The prevalence of onychomycosis in Europe, mostly due to dermatophytes, has been estimated at approximately 25% (Hay 2005). Dermatophytes can penetrate the nail plate and form mycelium and arthrospores within the nail (Rashid et al.1995; Scherer and Scherer 2004). Tinea unguium is typically seen in older patients and is comparatively rare in children (Philpot and Shuttleworth 1989). Predisposing factors include impaired blood circulation in the toes, endocrine disorders like diabetes mellitus, neurological abnormalities, a compromised immune system, and slow nail growth. Toenails are infected much more often than fingernails. Most cases of onychomycosis worldwide are caused by anthropophilic dermatophytes, predominantly *T. rubrum* (Gupta and Ryder 2004), although almost all other dermatophytes can also be found.

Depending on the route of fungal invasion and the part of the nail involved, different types of onychomycosis can be distinguished (Baran et al. 1998). The most frequent type is distal and lateral subungual onychomycosis, mainly due to *T. rubrum*. Fungal penetration begins with the inoculation of infectious material under the free distal or lateral part of the nail plate. From there the fungus grows proximally through the nail, leading to thickening, yellow discoloration, disintegration of the nail plate, and distal onycholysis (Fig. 13.10). Superficial white onychomycosis begins with invasion of the dorsal nail plate, resulting in a white and roughened nail surface. In

Fig. 13.10. Onychomycosis (tinea unguis). The distal two-thirds of this toenail show discoloration and destruction, as well as a early stage of distal onycholysis. The proximal part of the nail is less severely affected

addition to *T. rubrum*, *T. interdigitale* is often found. Proximal subungual onychomycosis is associated with fungal paronychia at the primary site of infection. In endonyx onychomycosis the nail plate shows lamellar splitting, due to fungal destruction of deep as well as superficial nail parts and a diffuse milky-white discoloration (Tosti et al. 1999). *T. soudanense* and *T. violaceum* are encountered. Finally, complete invasion of the nail results in total destruction of the nail, known as dystrophic onychomycosis. Onychomycosis is usually a chronic disease with little prospect of spontaneous resolution. As the nail plate is not accessible to cellular host defense, it provides a relatively safe habitat for fungi. Accordingly, inflammation is not a feature of onychomycosis.

3. Tinea Capitis and Tinea Barbae

Dermatophyte infections of the scalp and localized hair follicles are termed tinea capitis. Tinea capitis is a significant worldwide problem. It is usually caused by anthropophilic or zoophilic dermatophytes, depending on the country in which it is encountered (Elewski 1996; Aly et al. 2000; Gupta and Summerbell 2000). In tinea barbae the dermatophyte infection affects the bearded areas of the face and neck. The scalp and beard areas have a very high density of terminal hair follicles and associated sebaceous glands. The activity and proliferation of these pilosebaceous units is regulated by steroid hormones and undergoes considerable changes during puberty. The pilosebaceous units can, in fact, be seen as a cutaneous endocrine organ, producing hormones with in situ effects ("intracrinology"; Courchay et al.1996; Kintz et al. 1999; Labrie et al. 2000). This means that epithelial proliferation, including hair growth as well as the activity of sebaceous glands, is different in skin areas with hair follicles than in areas without. The particular ecological characteristics of the hair follicles are likely explanations for some distinctive features of tinea capitis and tinea barbae. Dermatophytes are susceptible to fatty acids and can bind and respond to certain steroid hormones (Capek and Simek 1971; Clemons et al. 1988; Brasch and Gottkehaskamp 1992; Brasch and Flader 1996; Hernández-Hernández et al. 1999; Brasch et al. 2002). It is not surprising therefore, that tinea capitis is an age-dependent infection. Tinea capitis is typically a pediatric disorder and represents one of the most common infectious diseases in children (Elewski 1996; Alvarez and Silverberg 2006). Tinea capitis often resolves in puberty and is therefore much less frequently seen in adults. In contrast, tinea barbae, confined to adult males, is less often seen than tinea capitis.

Different species of dermatophytes are the predominant pathogens in tinea capitis in distinct geographical areas. In the Americas *T. tonsurans* is already the most common species and continues to increase in incidence (Babel et al. 1990; Foster et al. 2004), while *T. violaceum* is widespread in Africa, and *M. canis* is found most frequently in Northern Europe.

Fungal invasion of the hair causes disintegration and breakage, producing patchy areas of hair stumps or intrafollicular black debris (black dot ringworm; Fig. 13.11). Hyphal elements transform into arthrospores (Okuda et al. 1988, 1989) and, depending on the fungal species, spores accumulate within the hair (endothrix) or as sheaths on the

Fig. 13.11. Tinea capitis caused by anthropophilic *Trichophyton violaceum*. Patchy areas with scaling and hair stumps but without much inflammation are typical for this infection

outside of the hair shafts (ectothrix). *T. schoenleinii* can form endothrix mycelia. This species typically causes heavily crusted scalp lesions (kerion) covered with so-called scutula; this peculiar type of tinea capitis is termed favus. Zoophilic agents like *M. canis* are often acquired from animals like cats and dogs. Subsequent child to child transmission can lead to epidemic outbreaks of tinea capitis in schools. The zoophilic species often cause inflammatory infections with folliculitis and pustules and even regional lymphadenopathy (Fig. 13.12), whereas infections with anthropophilic species are normally mild with only slight erythema (Fig. 13.11). These infections can take chronic courses and persist into adulthood. Under suitable conditions anthropophilic dermatophytes can even exist in an asymptomatic state on the scalp of carriers (Sharma et al. 1988). It is noteworthy that the most common dermatophyte worldwide, *T. rubrum*, only very exceptionally causes scalp infection, similar to *E. floccosum*.

Involvement of the deeper parts of the hair follicles and the dermis is common in tinea barbae (De Lacerda et al. 1981; Bonifaz et al. 2003). Tinea barbae results in often strongly inflammatory and suppurative pustular lesions (Fig. 13.13) accompanied by painful swelling of the draining lymph nodes and even general malaise, especially if zoophilic dermatophytes are involved (Sabota et al. 1996). Hairs are loose and can easily be removed, and purulent material can be discharged. Occupational exposure to infected animals should always be considered

Fig. 13.12. Tinea capitis caused by zoophilic *Microsporum canis*. This is an inflammatory lesion accompanied by loss of hair, erythematous swelling, scaling and crusts

Fig. 13.13. Tinea barbae. The development of strongly inflammatory and suppurative pustular lesions is a typical feature often misdiagnosed as a bacterial infection

in tinea barbae (Rutecki et al. 2000), particularly cattle that may be carriers of *T. verrucosum* (Sabota et al. 1996). An old term for such purulent and inflammatory lesions is sycosis barbae. This type of infection is often initially misdiagnosed as a bacterial disease and is unsuccessfully treated with antibiotics (Roman et al. 2001). Such insufficiently treated lesions ultimately heal with scarring and permanent loss of hair.

4. Tinea Corporis

Dermatophytosis of the glabrous skin is called tinea corporis. Tinea corporis can be directly transmitted between humans. Direct physical contact, such as intimate contact or contact during sports, enables direct transmission to occur. Outbreaks of tinea corporis, referred to as tinea gladiatorum, have been observed among wrestlers and judokas, due to *T. verrucosum* (Frisk et al. 1966) and particularly *T. tonsurans* (Cohen and Schmidt 1992; Hradil et al. 1995; Brasch et al. 1999; Esteve et al. 2006; Shiraki et al. 2006a, b). However, most cases of tinea corporis are probably caused by self-infection through autoinnoculation of fungi from tinea unguium or tinea pedis, or by indirect transmission. *T. rubrum* is the main agent of tinea corporis and can cause chronic and persistent infections (Kemna and Elewski 1996). Reduced general health and impaired immunity are predisposing factors.

A typical lesion of tinea corporis originates from the centrifugal spreading of the fungus within the superficial epidermis, leading to the development of annular and sharply marginated erythematous plaques with raised and scaling borders, and incomplete central clearing in most cases (Fig. 13.14). Multiple lesions can give rise to extensive confluent patterns (Fig. 13.15). The degree of inflammation varies according to the fungal species and the host response. In severe cases, mostly due to geophilic or zoophilic dermatophytes, vesicles, pustules, and folliculitis are seen; anthropophilic species may trigger only mild erythema and scaling (Fig. 13.16).

5. Tinea Cruris

Tinea cruris is a dermatophyte infection of the groin, perineum and perianal region (Fig. 13.17). The prevalent pathogens are *T. rubrum* (Silva-Tavares et al. 2001) and *E. floccosum*. Predisposing factors are perspiration, occlusion and restricted hygiene (e.g., in certain communities, dormitories, etc.). It is noteworthy that tinea cruris is mainly found in men, particularly tinea cruris caused by *E. floccosum* (Dvorak and Otcenasek 1969; Blank and Mann 1975; Alteras and Feuerman 1983). This is possibly related to the susceptibility of the fungi to androgenic hormones (Chattaway and Townskey 1962; Schär et al. 1986; Brasch and Gottkehaskamp 1992; Brasch and Flader 1996; Brasch 1997; Brasch et al. 2002). Serum testosterone levels were found to be significantly lower in patients with Epidermophyton floccosum infections than in controls (Hashemi et al. 2004). Infections in females are comparatively rare, with *E. floccosum* identified in only one out of seven female prostitutes, already at high occupational risk of acquiring the infection through direct contact with their clients (Otero et al. 2002). Many patients with tinea cruris also suffer from tinea pedum or onychomycosis (Alteras 1968).

Clinical lesions in tinea cruris are similar to those in tinea corporis. Rather sharply delineated

Fig. 13.15. Tinea corporis spreading on the trunk

Fig. 13.14. Tinea corporis on the neck with confluent circinate lesions

Fig. 13.16. Tinea corporis, a chronic type of infection caused by anthropophilic *Trichophyton rubrum* that triggers only discrete inflammation

Fig. 13.17. Tinea cruris. This is a typical chronic infection with only minor inflammation and some hyperpigmentation caused by anthropophilic *Epidermophyton floccosum*

erythematous and scaling plaques extend with progressive and accentuated borders (Fig. 13.17). Acute inflammation can lead to vesicles and pustules, while chronic lesions often develop hyperpigmentation. Maceration can occur in the inguinal folds. The scrotum is often involved. Although patients may experience itching, the infection often remains unnoticed.

6. Deep Infections

Although dermatophytes are specialized on superficial infections, deep infections (tinea profunda) can occur preferentially with anthropophilic species and when the host is immunocompromised (Meinhof et al. 1976; Smith et al. 2001). These lesions cannot be clinically diagnosed with certainty and the fungus must be confirmed through histology and culture of biopsy material taken from the organ involved (Squeo et al. 1998; Fig. 13.18). Suppurative nodular eruptions can be caused by perforating granulomas (Majocchi's granuloma) within the deep reticular dermis (Padilha-Goncalves 1980; Kinbara et al. 1981; Chastain et al. 2001). The terms dermatophyte pseudomycetoma (Ajello et al. 1980) or mycetoma (West and Kwon-Chung 1988) have been applied in cases showing discharge of whitish-yellow grains composed of hyphae from subcutaneous tissue. Even systemic dissemination of dermatophytes has been seen in very rare cases with lymph node involvement (Tejasvi et al. 2005) and infection of bone, CNS, and other organs (Hironaga et al. 1983; Hofmann 1994).

Fig. 13.18. Tinea profunda on the forearm. The erythematous nodular swelling indicates an infection of the dermis

7. Dermatophytids

Dermatophytids are secondary inflammatory reactions of the skin at sites distant from the skin area infected with the dermatophyte. In particular, strongly inflammatory tinea lesions are viewed as elicitors of dermatophytids. Dermatophytid reactions may be triggered by an immune response carried by circulating antigens, T cells and antibodies. They can manifest as clinically heterogeneous efflorescences, including papules, vesicles, urticae, erythema nodosum-like eruptions, and erythema annulare (El-Mofty and Nada 1965; Veien et al. 1994; Iglesias et al. 1994; Gianni et al. 1996; Romano et al. 2006). Although there are many reports of such reactions in the literature the general concept of such "id"-reactions is not unanimously endorsed by all dermatologists and each case of a suspected dermatophytid must be critically confirmed (Kaaman and Torssander 1983).

IV. Epidemiology

Although dermatophytes are cosmopolitan fungi, certain species are more likely to be found in specific geographic areas and some species are more likely to be associated with particular forms of tinea. It has long been recognized, however, that such associations are not permanent and can change considerably in the course of time (Rippon 1985). Monitoring of these changing ecological and epidemiological patterns and surveying of factors influencing dermatophyte transmission are not only helpful for better understanding of the natural history of dermatophytes but also for the correct assessment of their current roles in diseases. Precise information regarding the present distribution of dermatophytes, their transmission and spreading and their relation to general disease patterns is essential for the planning of disease control measures. Epidemiological studies on dermatophytoses have therefore been conducted in many parts of the world. In the following, the up-to-date epidemiological findings pertaining to the most important species of dermatophytes and their related diseases are reviewed.

In **Italy** a study of the fungi responsible for skin mycoses showed that *M. canis* was the most common dermatophyte, followed by *T. rubrum*, *T. mentagrophytes* and *E. floccosum*. Tinea corporis was the most common mycosis, followed by tinea unguis, tinea capitis and tinea pedis. Men were chiefly carriers of tinea cruris and tinea pedis, women of tinea corporis, and children and adolescents of tinea capitis. Several examples are known of infection transmission via interhuman contact, via human–animal contact, and from soil (Filipello Marchisio et al. 1996).

In **Northern Greece** similar results were found in a study of dermatophytoses due to *T. rubrum* during 1981–1990. During this decade *T. rubrum* was the most frequent causative agent of dermatophyte infections in Northern Greece, especially in cases of tinea pedis, tinea cruris, tinea corporis, and tinea unguium, as well as dermatophytosis of the hands. In women tinea pedis and toenail infections prevailed, wherease men were particularly infected in the groin, hands, and face. Chronic follicular dermatophytosis of the lower legs was also present in women, while tinea corporis and fingernail infections showed no significant sex-related differences (Devliotou-Panagiotidou et al. 1992).

In **Central Poland** 7393 cases of dermatophytosis were studied in 1998, including 2204 (29.8%) cases of tinea glabrosa. Etiological factors in descending order were: *M. canis* (23.5%), *T. mentagrophytes* var. *granulosum* (21.6%), *T. rubrum* (17.8%), *T. tonsurans* (10.4%), *T. mentagrophytes* var. *quinckeanum* (6.0%), *M. gypseum* (5.3%), *T. violaceum* (3.7%), *T. mentagrophytes* var. *interdigitale* (2.3%), *M. equinum* (0.7%), *T. verrucosum* (0.4%), *Trichophyton* sp. (0.4%) and *M. cookei* (0.14%). At present tinea of the glabrous skin is the dominant clinical form of dermatophyte infections of skin and skin-appendages in Central Poland (Jeske et al. 1999).

In the general population of **Spain** the prevalence and risk factors of tinea unguium and tinea pedis were investigated in the year 2000. The prevalence of tinea unguium was 2.8% (4% for men, 1.7% for women), and the prevalence of tinea pedis was 2.9% (4.2% for men, 1.7% for women). The etiological agents of tinea unguium were identified as *T. rubrum* (82.1%), followed by *T. mentagrophytes* var. *interdigitale* (14.3%) and *T. tonsurans* (3.5%). *T. rubrum* (44.8%) and *T. mentagrophytes* (44.8%), followed by *E. floccosum* (7%) and *T. tonsurans* (3.4%), were the organisms isolated from patients with tinea pedis. The percentage of subjects suffering from both diseases was 1.1% (1.7% of men, 0.6% of women). In a multivariate logistic regression analysis, age [relative risk (RR) 1.03] and gender (RR 2.50) were independent risk factors for tinea unguium, while only gender (RR 2.65) was predictive for occurrence of tinea pedis. In both analyses, the presence of one of the two conditions was associated with a higher risk of other disease (RR >25; Perea et al. 2000).

In **Switzerland** the dermatophytes are important because 5–10% of dermatological consultations are related to mycotic infections. During an eight-year period (1993–2000) a study was conducted to obtain information about the prevailing species of dermatophytes in the southwest of Switzerland and their patterns of infection. A dermatophyte was detected in 4193 cultures out of a total of 33 725. *T. rubrum* was the most frequently isolated species, accounting for 62.5% of the strains, followed by *T. mentagrophytes* (24.5%) and *M. canis* (5.0%). The relative frequency of isolation of distinct dermatophyte species depends on the frequency of different types of tinea found in different countries, among other factors. The Swiss study reveals the importance of *T. rubrum*, the noteworthy frequency of *M. canis* in the native Swiss population, and the appearance of new species among immigrants (Monod et al. 2002).

In **Slovenia** dermatophyte infections were studied during the period 1995–2002. A total number of 42 494 samples were collected from 33 974 patients suspected of having dermatomycoses. 71.2% positive cultures could be identified. *M. canis* was the most frequenty isolated dermatophyte (46.8%), followed by *T. rubrum* (36.7%), *T. mentagrophytes* var. *interdigitale* (7.9%), and *T. mentagrophytes* var. *mentagrophytes* (4.9%). Less frequently isolated were *M. gypseum*, *T. verrucosum*, *E. floccosum*, *T. tonsurans*, and *T. violaceum*. The most common dermatophyte infections included tinea corporis, onychomycosis, tinea pedis, and tinea faciei. Zoophilic dermatophytes were most commonly recovered from children and adolescents with tinea capitis, tinea corporis, and tinea faciei. Anthropophilic species were identified mostly in adults with tinea pedis, onychomycosis, and tinea inguinalis. During the period studied, a decline in the rate of *M. canis* infection could be recorded, while infections produced by *T. rubrum* increased in frequency (Dolenc-Volj 2005).

In southern Iran the prevalence of dermatophytes was found to be 13.5%, and an incidence of 10.6 per 100 000 person-years was registered over a period of three years (1999–2001). *E. floccosum* was the most frequently isolated dermatophyte (31.4%), followed by *T. rubrum* (18.3%) and *M. gypseum* (4.1%). *E. floccosum* was the most commonly isolated dermatophyte in the age group 20–29 years (30.2%). Tinea corporis (31.4%) was the most common type of infection, followed by tinea cruris (20.7%), tinea manuum (15.4%), tinea capitis (12.4%), tinea pedis (10.6%), tinea faciei (7.1%), and tinea unguium (2.4%). The rates of all types of tinea were higher in males than in females. The anthrophilic species *E. floccosum* was the most common agent of tinea. The most prevalent fungal infection was tinea corporis caused by *E. floccosum* (Falahati et al. 2003).

In the same area of Iran a group of children aged ≤16 years suspected to have dermatophyte infections was examined over a period of three years (1999–2001). The incidence rate of dermatophytoses was 6.6 per 100 000 person-years. *T. violaceum* was the most frequent isolate (28.3%), followed by *M. canis* (15.1%), *E. floccosum* (15.1%), *T. rubrum* (13.2%), *T. mentagrophytes* (11.3%), *M. gypseum* (7.5%), and *T. verrucosum* (5.7%). Tinea capitis (39.6%) was the most common type of infection, followed by tinea corporis (30.2%), tinea faciei (18.9%), and tinea manuum (7.5%; Rastegar Lari et al. 2003).

In **Jordan** a similar spectrum of dermatophytes was found during 1997–1998. The frequencies of etiological agents isolated from patients were as follows: *T. mentagrophytes* var. *interdigitale* (32.7%), *T. rubrum* (28.6%), *E. floccosum* (20.1%), *M. canis* (11.1%), *T. schoenleinii* (4%), *T. verrucosum* (2%), *T. violaceum* (1%), and *M. gypseum* (0.5%). The most common superficial mycotic infection was tinea pedis (35.2%), followed by tinea capitis (23.1%), tinea unguium (21.6%), and tinea corporis (10.6%). Men were mainly affected by tinea cruris and tinea pedis, while women suffered from tinea pedis, tinea unguium, and tinea capitis (Abu-Elteen et al. 2004).

During the period 2003–2004 the first epidemiologic study was conducted in **Algeria**. A total of 1300 male subjects were clinically examined. Clinical diagnosis for tinea pedis and onychomycosis was suspected in 249 and 72 subjects, and confirmed in 197 and 60 cases, respectively. The yeast species *Candida parapsilosis* and the dermatophyte *T. rubrum* were shown to be the most common pathogens in both tinea pedis (*C. parapsilosis* 20.4%; *T. rubrum* 17%) and onychomycosis (*T. rubrum* 35%; *C. parapsilosis* 28.3% Djeridane et al. 2006).

In **Mexico** a total number of 2397 cases of dermatophytoses with superficial cutaneous lesions were reviewed between the years 1978 and 1990. The total numbers of cases were as follows: 726 tinea pedis (30.3%), 613 tinea unguium (25.6%), 441 tinea capitis (18.4%), 395 tinea corporis (16.5%), and 222 tinea cruris (9.3%). The most commonly isolated dermatophyte species was *T. rubrum* (45%), followed by *T. mentagrophytes* (23.7%), *T. tonsurans* (21%), *M. canis* (7.1%), and *E. floccosum* (2.5%). Less frequently *M. audouinii*, *M. gypseum*, *T. violaceum*, and *T. verrucosum* were isolated. Most of the cases were observed in the warmest months of the year (from March to September), and were equally distributed in both genders, except for tinea cruris which was more prevalent in men (3.5:1 ratio; Welsh et al. 2006). Table 13.2 gives an overview of the prevalence of dermatophyte species in different countries (Monod et al. 2002).

In **summary**, these recent epidemiological studies reveal the following facts. Some general trends have become apparent within the last decades. The spectrum of dermatophytes causing skin lesions has changed within the past 70 years. Before the Second World War, especially in Germany, *M. audouinii* and *E. floccosum* were most frequently found. Since the middle of the past century, *T. rubrum* has become the most frequently isolated dermatophyte, accounting for 80–90% of all strains isolated, followed by *T. mentagrophytes*. *T. rubrum* is the most common cause of tinea pedis, nail infections, tinea cruris, and tinea corporis worldwide. Although the incidence of tinea capitis is declining in developing nations, tinea pedis and onychomycosis are becoming more common. This development is typical for Central and Northern Europe and is connected with the increase in the incidence of tinea pedis. In contrast, zoophilic dermatophytes, such as *M. canis* and *T. verrucosum*, are now the most frequently isolated dermatophytes in Southern Europe and in the Middle East and North Africa. The increasing use of athletic

Table 13.2. Prevalence (%) of dermatophyte species in different countries (according to Monod et al. 2002, and references listed in that paper). In this table some old names of dermatophytes are listed that, according to current opinion, do not describe separate species (see Table 13.1): *Trichophyton soudanense* and *T. gourvilii* are now considered to be *T. violaceum*; *T. equinum* is now considered to be *T. tonsurans*. + Only very low numbers of isolates

	Switzerland (Lausanne)	Holland (Leiden)	Germany (Würzburg)	Finland (Oulu)	Poland (Gdansk)	Spain (Galicia)	Italy (Rome)	Greece (Crete)	Iran	USA	USA
	1993–2000	1972–1992	1976–1985	1982–1995	1984–1995	1951–1987	1985–1993	1992–1996	1986–1991	1993–1995	1985–1987
Epidermophyton floccosum	1.0	6.0	2.7	4.4	9.5	11.8	9.3	7.6	14.9	1.1	2.0
Microsporum canis	5.0	1.2	1.2	0.1	27.8	25.5	50.0	25.0	19.4	3.3	4.0
M. gypseum	0.2	0.2	+			5.2	2.3	0.3		0.4	0.6
M. nanum										+	+
M. ferrugineum		0.1									+
M. gallinae			+						0.2		
Trichophyton mentagrophytes	24.6	21.4	19.6	24.2	41.6	21.4	10.6	17.8	20.6	8.5	6.0
T. rubrum	62.1	64.2	73.9	67.5	15.5	24.6	27.0	44.4	16.5	41.3	54.8
T. soudanense	1.6					0.1				+	+
T. violaceum	1.7	0.5	+	0.3	0.3	1.2	0.6	3.1	8.7	0.2	0.08
T. verrucosum	1.3	2.5	1.0	3.2	1.0	3.1	+	1.8	11.5	0.3	0.2
T. tonsurans	0.1		0.2		4.3	3.9	0.16		1.3	44.9	31.3
T. gourvilii	+										
T. schoenleinii		0.3	+			2.5			5.5	+	+
T. terrestre			0.8	0.06							+
T. equinum						0.1					
T. erinacei									0.8		
T. concentricum										+	
Total number of strains analyzed in the study	4193	7111	8973	1543	1544	3351	2823	327	7712	26 815	14 696

shoes by both men and women and the popularity of communal bathing may be contributing factors. In contrast, the anthropophilic agents of scalp infections appear to have been eradicated in developing countries. The exception is *T. tonsurans*-related tinea capitis in North America. *M. canis* is a prevalent agent of tinea capitis in many parts of the world, and this could be related to a close association of humans with their pets. *T. violaceum* is endemic in certain parts of Eastern Europe, Africa, Asia, and South America, but not in North America (Aly 1994; Foster et al. 2004).

These epidemiological findings do not confirm the assumption that patients are genetically predisposed to *T. rubrum* infection in a dominant autosomal pattern (Seebacher 2003a–c).

V. Treatment

Once a dermatophyte is identified as the causal agent of a skin infection, adequate treatment is no longer problematic due to modern and effective antimycotic drugs. However, in many parts of the world, particularly Africa and Asia, such medications are either too expensive or are not available to patients in need. Dermatophytoses are therefore insufficiently treated with traditional methods in many populations, or simply remain untreated. In countries with highly developed medical systems, sufficient treatment is not impaired by a lack of resources. Here, difficulties in eradicating endemic dermatophyte infections and preventing their further spread are mainly due to the fact that wearing of shoes is unavoidable, living in close communities is common, the number of individuals with predisposing factors (old age, reduced immunocompetence, etc.) is increasing, and hygiene is often neglected.

All individuals, regardless of their circumstances, are equally affected by one relevant thereapeutic problem: dermatophytes can colonize nails and hair and often do so. In these habitats dermatophytes cannot be reached by defending host cells of innate or acquired immunity or by antimycotic serum factors or immunoglobulines. In addition, they can form resistant and dormant arthrospores in these niches. Tinea of nails and hair therefore requires particular treatment measures.

In the following some basic agents and principles of treatment are described. For more detailed information the current dermatological literature should be consulted (Gupta et al. 1998; Roberts et al. 2003; Kyle and Dahl 2004; Baran and Kaoukhov 2005; Borgers et al. 2005; Seebacher et al. 2006).

A. Topical Treatment

Superficial dermatophytoses not involving hair and nails, such as tinea corporis, tinea cruris, and tinea faciei, can be adequately treated with topical drugs (Kyle and Dahl 2004) if the lesions are not too extensive. Topical treatment can also be used for onychomycosis, if it is of superficial type or if no more than the distal half of the nail plate is infected. The base used for application of the antimycotic agent can be an ointment, cream, lotion, lacquer, or spray. It should be chosen according to the body site affected and the condition of the skin. Azoles (Hantschke and Reichenberger 1980; Gutierrez 1994), hydroxypyridones (Dittmar 1981; Hänel et al. 1988), allylamines (Balfour and Faulds 1992; Korting et al. 2001), and morpholines (Reinel and Clarke 1992; Zaug and Bergstraesser 1992) have all been proven effective. These agents must be applied once or twice daily for a sufficient period of time to an area exceeding the clinically visible lesion. The azoles are considered fungistatic, whereas hydroxypyridones and allylamines can be fungicidal, so that shorter treatment periods can be justified with the latter agents (Kyle and Dahl 2004).

B. Systemic Treatment

Systemic treatment is usually recommended for superficial tinea when it is widespread or recurrent, or when immunocompromised patients are affected. It should generally be combined with topical treatment. Tinea capitis and tinea profunda usually require systemic treatment. Onychomycosis also requires systemic treatment when more than the distal halves of a few nails are involved, and is usually combined with topical treatment. Well tested antimycotic substances for oral administration in dermatophytoses are griseofulvin, azoles, and allylamines (Reichenberger and Götz 1962; Niewerth and Korting 2000; Bell-Syer et al. 2003; Fleece et al. 2004; Borgers et al. 2005; Dasghaib et al. 2005). Griseofulvin is the oldest agent with a narrow spectrum comprising only dermatophytes. It interferes with the cellular microtubular system and has a fungistatic effect.

Azoles (ketoconazole, fluconazole, itraconazole) inhibit the fungal biosynthesis of ergosterol, which is an essential compound of the fungal cellular membranes. The effect is a fungistatic one. Griseofulvin and the oldest azole, ketoconazole, are gradually being replaced by the newer agents. Griseofulvin is considered less effective in most cases than terbinafine (Bell-Syer et al. 2002). Terbinafine, an allylamine, inhibits fungal ergosterol synthesis as well, but allylamines also initiate a toxic effect and can be fungicidal. The choice of a particular agent in a given situation depends on the type of tinea, potential contraindications for a particular drug and on interactions with the patient's other medications (Back et al. 1992).

Clinically relevant dermatophyte resistance to these substances is currently a rare exception. The ongoing development of new antimycotic agents aims to reduce interactions with other drugs, to eliminate side-effects and to increase fungicidal effects.

C. Special Treatment Aspects of Distinct Forms of Tinea

Tinea capitis is characterized by the formation of arthrospores around and/or within the hair. Cutting of the infected hair helps to rapidly eradicate this source of further fungal distribution. An additional topical treatment is generally recommended and helps stop infectiousness and shorten treatment time. Systemic treatment must normally be continued for several weeks. Tinea capitis due to *M. canis* may be less responsive to terbinafine in children (Baudraz-Rosselet et al.1996) because of reduced drug delivery via their not yet developed sebaceous glands (Fleece et al. 2004). Tinea capitis predominantly affects children. Modern drugs, however, have usually only been tested in adults and are often not yet officially approved for use in children in some countries (Seebacher 2006). These legal issues must also be considered in treatment.

Onychomycosis poses a considerable problem due to the arthrospores in the air-filled cavities of the keratotic material (Effendy and Strassman1999). Arthrospores in these cavities are inaccessible and often resistant to medications in their resting phase (Seebacher 2003a–c). Therefore, clipping of the nails and mechanical or chemical removal of infected nail parts is recommended. Antimycotics should by topically applied with use of solutions or lacquers that enhance drug penetration into the nails (Seebacher 2003a–c). Systemic treatment must be performed for several months, depending on the growth rate of he nails (Iorizzo et al. 2005; Gupta and Tu 2006). Accordingly, toenails require longer treament periods than fingernails. Different modes of intermittent drug application have been developed to reduce the total amount of drug necessary for treatment (Ginter and De Doncker 1998; Evans and Sigurgeirsson 1999). Despite these intensive therapeutic efforts, long-term cure of onychomycosis cannot always be achieved (Epstein 1998; Sigurgeirsson et al. 2002).

Tinea profunda always requires systemic therapy. In such cases potential immunosuppression of the patient must be considered and may necessitate a considerably prolonged treatment period.

D. Hygiene

Antifungal treatment of a patient must be accompanied by measures to prevent reinfection and further distribution of the disease. Since the infectious fungal propagules shed with scales, hair or other particles from tinea lesions remain infectious for a long time, care must be taken to eliminate such materials from the environment (Gupta et al. 2001; Tanaka et al. 2006). Clothing, shoes, home textiles, personal care items, and floors likely to be contaminated must be sufficiently cleaned and disinfected. The source of an infection, the reservoir of the dermatophyte, should be tracked down whenever possible. Depending on the species of dermatophyte in question, family members, other individuals within shared communities, pets, or other animals must be checked for tinea and treated, if necessary.

VI. Conclusions

Infections caused by dermatophytes are termed dermatophytoses, tinea, or ringworm. A dermatophyte is a hyalohyphomycete that can degrade keratin and can cause communicable skin infections in humans and/or animals. Dermatophytoses result from the interaction between these highly specialized fungi and the host defence. All over the world dermatophytoses are among the most common and widespread endemic infectious diseases. Dermatophytoses are typically superficial infections restricted to the skin and its appendages.

Dermatophytes probably developed from non-pathogenic, soil-colonizing fungi into species specialized for particular animal or human hosts as their ecological niche. Accordingly, geophilic, zoophilic, and anthropophilic species are recognized. Most of the dermatophyte species have no known sexual reproduction. Their taxonomy continues to be a matter of debate and recent genetic analyses led to some shifts in nomenclature. The anamorphic asexual states of the dermatophytes belong to three genera (*Trichophyton*, *Microsporum*, *Epidermophyton*) which can easily be distinguished by morphological criteria that are mainly based on the form of conidia. The type of dermatophytosis can give a first clue which pathogenic species may be involved. However, species identification needs a pure culture to assess morphologic and physiologic characteristics. In addition, genetic analyses are gaining increasing importance.

Transmission of dermatophytes (mostly by arthrospores as propagules) can occur directly from human or animal to human, or indirectly via contaminated objects. Usually it takes two weeks or longer until a lesion becomes clinically apparent. The kind of infection that develops depends on the inoculation site, the fungal species involved, and the host response, which is related to age, gender, immunocompetence, general health, and possibly to the genetic disposition of the host. If the transmitted fungal propagules are left undisturbed with sufficient time to attach to the skin of a new host, hyphae begin to spread radially within the stratum corneum. This triggers an inflammatory skin response which is most intense at the advancing margin of the fungal invasion and can clinically be recognized by marked erythema, scaling, and palpable infiltration of the skin, sometimes accompanied by pustules. The accentuated inflammatory rim of the skin lesions often has an arched or circular shape, explaining the term "ringworm" to describe dermatophytoses. Hair follicles, hair shafts, and nails can also be invaded, leading to different patterns of infection. Usually an immunologic host response develops over time.

Tinea pedis is a dermatophyte infection of the skin of the feet that generally starts in the toe webs and often reaches the soles. It is the most common fungal infection worldwide and has an extremely high prevalence in shoe-wearing populations. An infection of the nails by a dermatophyte is named tinea unguium. The nails of the feet are affected most frequently. It is an endemic and very common disease in developed countries. Dermatophyte infections of the scalp and its hair follicles are termed tinea capitis. Tinea capitis is a significant worldwide problem and represents one of the most common infectious diseases in children. Dermatophytosis of the glabrous skin is called tinea corporis. It is mainly caused by *Trichophyton rubrum*. Tinea cruris is a dermatophyte infection of the groin, perineum, and perianal regions. Although dermatophytes are specialists for superficial infections, infections of subcutaneous tissue (tinea profunda) can occur, especially when the host is immunocompromised.

Dermatophytes are cosmopolitan fungi but certain species are more likely to be found in specific geographic areas and some species are more likely to be associated with particular forms of tinea. *T. rubrum* is the most common cause of tinea pedis, nail infections, tinea cruris, and tinea corporis worldwide, followed by *T. mentagrophytes* in Northern Europe. In some countries, however, other species, like *Microsporum canis* or *T. tonsurans*, are isolated more often and some dermatophytes, like *T. violaceum* or *M. audouinii*, preferentially cause tinea capitis or tinea inguinalis (*Epidermophyton floccosum*).

A panel of modern antimycotic agents is available for the treatment of dermatophytoses. Superficial infections of small skin areas can be adequately treated by topical application of such substances in a suitable vehicle. However, widespread infections and infections that involve hair follicles or large parts of the nails require systemic therapy. For topical application hydroxypyridones, allylamines, morpholines, and azoles are preferred agents. For systemic treatment griseofulvin, azoles, and allylamines are approved drugs. Different treatment schemes and periods are recommended for the distinct agents and types of infection, and for the choice in an individual case possible side-effects and drug interactions need to be considered. A combined topical and systemic treatment is often advisable. Removal of infected tissue like nail material can be helpful to shorten therapy and hygienic measures are necessary to prevent reinfections.

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