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.
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).

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 1987). 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

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