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Epidemiology and Ecology of Onychomycosis

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Abstract
The epidemiology and ecology of onychomycosis are complex and little understood. Most is known about tinea unguium, dermatophytic nail infection, and its causative agents. This is often categorised according to the precise locus on the nail of the infection. The principal infectious propagules are thought to be the arthroconidia or chlamydospores which form within the solid substratum of invaded nail tissue. The process of infecting new hosts appears to be facilitated by abrasion, moistening and scratching. The role of the non-dermatophyte yeast *Candida* as an agent of onychomycosis per se may have been overestimated. The range of interactions between dermatophytes and non-dermatophytes in nails is complex and poorly understood. There may be at least six distinct ecological categories of non-dermatophyte isolations from nails. It would be of clinical interest to know which species found in mixed infections were never able to advance beyond 'secondary colonisation', as they would not require specific treatment.

The epidemiology and ecology of onychomycosis are surprisingly complex. A number of factors, each simple on its own, come together in this area to form a composite of overlapping probabilities that few understand well. Moreover, the biology of many organisms in nails is poorly known, and theoretically simple methods of clarifying such matters are difficult to co-ordinate with clinical realities.

The best-known aspect of onychomycotic epidemiology is that related to tinea unguium, dermatophytic nail infection, and its causative agents. Less well understood is the epidemiology of non-dermatophytes causing nail infections of various kinds. Least well known, and often a matter for free speculative contention, is the interaction between dermatophytes and non-dermatophytes in nails. These subjects will be addressed in order below.

Dermatophytes as Sole Agents of Tinea unguium

Of the more than 20 dermatophyte species that regularly cause human infections, only a few are significant agents of onychomycosis. The ability to cause this disease is evidently specialised, since there is no known parallel disease affecting keratinous claws or hooves of our non-anthropoid mammalian relatives. Dermatophyte species or variants competent at causing tinea unguium are obligate human pathogens which have lost the ancestral heterothallic sexuality of the dermatophyte group and which, in the 2 most common species, often show degenerate asexual reproduction, with conidia reduced in number or simplified or distorted in form. They exhibit a great deal of variability in colony coloration and microscopic morphology, suggestive

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abundance, may merely signify pockets of saprobic colonisation in nails split or fissured by an unrelated disease process (e.g. dermatophytosis, psoriasis) so that microscopic humid chambers suitable for yeast proliferation have been produced. Non-*C.-albicans Candida* species of the normal skin flora may often be isolated in similar circumstances and may persist over time in these harmless colonisations. Distinction of these colonisations from genuine cases of infection by these fungi (especially *Candida parapsilosis*) can best be accomplished by showing microscopically that some pseudomycelial tissue penetration has been accomplished in the purported infection. (If true mycelia are seen, the possibility of overgrown or senescent dermatophyte material should be strongly considered – see below.)

Approximately 35 non-dermatophyte filamentous fungal species have been shown to be capable of causing or sustaining onychomycosis as sole aetiological agents. In addition, numerous other species have been alleged but not well demonstrated to do so. Most virulent among the well-established agents are *Scytalidium dimidiatum* (synanamorph *Nattrassia mangiferae,* formerly *Hendersonula toruloidea*) and *S. hyalinum*, which appear to be as effective as dermatophytes in infecting heavily keratinised epidermis and nails [9]. These fungi have somewhat distinctive filaments in nail tissue and are rarely or never isolated as contaminants in temperate areas of the world; thus, isolation usually signifies infection, and this can readily be confirmed by direct microscopy. Most dermatomycotic agents, however, are common contaminants associated with feet and nails and only occasionally 'cross over' into aetiological status. The events precipitating such a transition are unknown but may include attenuation of host defences in age (especially in the elderly), nail injury and prior nail infection by a dermatophyte. When, in any case, they are present in nails as sole agents of infection, they may have distinctive elements produced in or from host tissue (e.g. unusual filaments, conidiophores, conidia), in which case infection is easy to confirm, or only indistinctive hyphae in tissue, in which case sole infection may be difficult to confirm except by repeated sampling (see below). Such difficult-to-confirm infections may be seen with selected members of the genera *Scopulariopsis, Fusarium, Aspergillus* and *Alternaria,* as well as with less common fungi.

Complex Relations between Dermatophytes and Non-Dermatophytes, Including Mixed Infections

In an active bacterial infection, it would be almost unthinkable to have entire areas of the affected tissue invested only with dead bacterial cells and no living inoculum. Filamentous fungal colonies, however, are continuous, modular bodies which, like trees with dead limbs, can be seen in the space they occupy either as living or dead forms. The study of onychomycosis is primarily rendered complex by the fact that approximately 20% of all samples from nails invested with dermatophyte filaments happen to include material only from the 'dead branches', or senescent growth fronts, of the somewhere still active dermatophyte colony. (This type of sample yields a negative culture, often misleadingly referred to as 'false-negative' even though the culturing technique reflects the condition of the sample material with impeccable accuracy.) When these dead dermatophyte filaments, seen in direct microscopy, coincide with cultures positive for a fungus growing from contaminating spores or conidia, this is easily misinterpreted as signifying a non-dermatophyte infection, especially if the contaminating inoculum is of a species well known to cause occasional onychomycosis. Similarly, when these dead dermatophyte elements are intermingled with living elements of a co-infecting non-dermatophyte, the diagnosis of a pure non-dermatophyte infection may be incorrectly made. Conversely, the diagnostician may err oppositely when confronted with a genuine non-dermatophyte infection by misinterpreting the non-dermatophyte filaments in the nail as dead dermatophyte filaments, and misattributing the non-dermatophyte culture to contamination. A non-dermatophyte genuinely participating in a mixed infection may similarly be misinterpreted as a contaminant if a dermatophyte grows.

The degree of overlap among these and related possibilities effectively precludes a firm diagnosis of non-dermatophytic or mixed onychomycosis from any single specimen where: (a) a non-dermatophyte known to cause onychomycosis occasionally is isolated in the presence or absence of a dermatophyte and (b) the elements seen in direct microscopy are generic fungal filaments and do not unequivocally confirm or exclude the non-dermatophyte in question. The non-dermatophyte in such cases is an organism only tentatively associated with disease, a situation best clarified using Koch's first postulate of pathogenicity, namely, consistency of association of the putative aetiological agent with the disease [10]. This consistency is demonstrated by examining one or more successive repeat samples from the patient's lesion and finding the same non-dermatophyte

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