Concepts in Onychomycosis Treatment and Recurrence Prevention: An Update
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Abstract
In considering therapy for onychomycosis, the most important factor to take into account is patient selection rather than treatment selection. Patients should be screened and evaluated for the extent of nail involvement, the amount of subungual debris, the degree of dystrophy, their ability and willingness to follow the regimen, and whether comorbidities are present that may affect the efficacy and/or safety of one or more therapies. Onychomycosis is a chronic disease with a high recurrence rate. Common-sense measures to reduce the risk for reinfection include patient education and a clinician-patient team approach to long-term management.

Keywords
Dermatophytes; diabetes; geriatric patients; immunosuppression; onychomycosis; pediatric patients; psoriasis; treatment adherence

A number of patient-specific factors must be considered in the context of onychomycosis treatment, and these fall into two main categories: age related and medically related. Both extremes of the age spectrum—pediatric and geriatric patients—have special problems and needs related specifically to age. In addition, patients with onychomycosis may have medical comorbidities—including diabetes, psoriasis, immunosuppression (acquired or drug-related), and organ transplantation—that can affect treatment choices. In many of these patients, systemic antifungal therapy can be problematic, and topical therapy may be a better first-line choice.

Age-Related Issues in Onychomycosis

Pediatric Population
Among the pediatric population, onychomycosis is seen most commonly in those between 12 and 18 years of age; onychomycosis is uncommon in children under 12 and is relatively rare in those under 6 years of age.1-4 The proposed reasons for the low prevalence of onychomycosis in younger children include faster nail growth, better circulation, less trauma, less exposure to fomites (eg, in gyms or public pools), and a lower incidence of tinea pedis; however, no scientific evidence exists to directly support these theories.

Pediatric patients who develop onychomycosis often have a family history of onychomycosis and/or tinea pedis (caused by Trichophyton rubrum). The probability is high that children who develop onychomycosis have a genetic predisposition to acquire the infection, and their risk for developing an active infection is increased by exposure to dermatophytes and other organisms—eg, wearing occlusive athletic footwear, walking through and showering in locker rooms without footwear, and sharing a household in which others have onychomycosis or tinea pedis.

Geriatric Population
In geriatric patients, an increased risk for onychomycosis arises probably in association with multiple comorbidities, decreased circulation, and accumulated trauma to the nails. Approximately 40% of elderly patients have onychomycosis,1 which may cause pain or affect gait, increasing the risk for falls in this population. Drug-drug interactions are of particular concern in older patients, who typically use several medications concomitantly. If it is physically possible for patients to apply topical antifungals—or if daily assistance is available for applying these medications—the use of yet another systemic medication can be avoided.

Patients should understand that the changes to nails that are associated with aging—such as dystrophy and discoloration—and that are not related to onychomycosis will persist after successful treatment (Figure).6

Comorbidities
Psoriasis
More than 82% of patients with psoriasis have nail abnormalities5; in an estimated 13% to 22% of cases, onychomycosis coexists with psoriatic nail involvement.8 Thus, in a patient with psoriasis and nail involvement, clinicians should recognize the possibility of coexisting dermatophyte, candidal, or mixed dermatophyte/candidal infection.7,8 and, if clinical signs are consistent with onychomycosis, consider obtaining a specimen for a mycologic culture. This is especially important in patients with psoriasis who are being treated with interleukin-17 inhibitors, such as secukinumab, which may increase the risk for yeast infections.11

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Two topical antifungal agents, efinaconazole and tavaborole, have demonstrated good in vitro activity against *Candida* species and nondermatophyte molds such as *Aspergillus* and *Fusarium* spp. However, caution must be exercised when dealing with fungal pathogens, as in vitro susceptibility does not always correlate with in vivo efficacy.

**Diabetes**

An estimated 46% of patients with diabetes have nail abnormalities, and about 50% of these abnormalities are due to onychomycosis; thus, the prevalence of onychomycosis in this population may be as high as 20% to 30%. Onychomycosis also increases the risk of diabetic foot syndrome, a constellation of problems—diabetic neuropathy, macroangiopathy, and the combination of those conditions—which can lead to serious, limb- and life-threatening bacterial infections.

In patients with diabetes who develop onychomycosis, atypical organisms (especially yeasts) may be more commonly seen, although some investigators have found no difference in the types of fungi in this patient population. A mycologic culture is indicated to identify the offending organism in diabetic patients with signs and symptoms of onychomycosis. Efinaconazole and tavaborole have proven efficacy in this population in the pivotal trials.

Onychomycosis also is more common among patients undergoing hemodialysis treatment, not all of whom have diabetes and end-stage renal disease. An estimated 81% to 92% have nail abnormalities; 20% to 31% of these abnormalities are due to onychomycosis, for an onychomycosis prevalence of about 16% to 27% in this population. Duration of hemodialysis is a significant predictor of onychomycosis. The patterns of isolates in these patients seem to mimic what is seen in patients who are not on dialysis, ie, predominantly *T. rubrum* and, occasionally, *Candida* spp and nondermatophyte molds.

**Strategies for Adherence and Preventing Reinfection**

The treatment of onychomycosis is both acute and long-term—and includes the use of medication and infection risk reduction strategies during the initial and any subsequent reinfection episodes, and, long-term, the continuation of risk reduction measures and vigilance for signs of recurrence of onychomycosis and/or tinea pedis, with prompt initiation of treatment.

Recurrence of onychomycosis is common because the propensity to develop these fungal infections in the first place is based largely on autosomal-dominant inheritance. Thus, patients who have had onychomycosis would do well to implement all reasonable measures to reduce the risk for reinfection. Patients should understand that although genetics cannot be changed, behavior can be modified.

**Clinician-Patient Team Effort**

Adherence to onychomycosis treatment can be enhanced with measures such as phone calls, automated phone messages, postcards, and a website that patients can log in to.

**Attention to Footwear**

Patients should absolutely avoid walking barefoot in public areas such as gyms, locker rooms, spas, and public showers and pools. An inexpensive pair of water shoes or rubber sandals can prevent exposure to fungi and other organisms.

If possible and practical, patients should consider discarding...
shoes that have been worn prior to initiation of onychomycosis treatment. An alternative to discarding expensive or relatively new shoes is disinfection in an ozone cabinet (usually found in sports equipment stores) or with the use of ultraviolet C light-generating shoe inserts. These devices have been shown to be active against dermatophytes and Candida spp.\textsuperscript{25-27} Other measures include alternating pairs of shoes daily (allowing fungus-promoting moisture to evaporate) and using medicated powder daily in shoes and socks.

**Application Instructions for Topical Antifungals**

The instructions for applying the different antifungal agents should be simple and clear to patients (see “Using Topical Antifungal Medications: Instructions for Patients,” page S62).

**Nail Polish and Topical Antifungals**

Patients often ask whether they may use nail polish during their treatment with a topical antifungal. The use of nail polish is contraindicated during treatment with ciclopirox; however, recent studies demonstrate that the penetration and efficacy of efinaconazole and tavaborole are not affected when used over nail polish. The penetration studies of efinaconazole were performed with up to three coats of nail polish.\textsuperscript{29} Tavaborole was studied with up to four coats of nail polish.\textsuperscript{29} Advise patients who do want to use polish to test the tackiness of the polished nail surface before putting on socks, stockings, or shoes; color transfer has been seen with some polishes used with these topical antifungals. Thus, although nail polish does not affect the medications, the medications may affect the cosmetic aspects of nail polish.

**Great—But Realistic—Expectations**

Because nails grow slowly, at an average of about 3 mm per month, patients should understand that although treatment may (and should) eliminate the infecting organism, the appearance of the affected nails will not improve until the nail plate grows out. Finger-nails grow out in 3 to 6 months, but complete growth of toenails can take 9 to 18 months.

During this long treatment process, it helps to use or suggest methods for monitoring progress. Pictures taken at regular intervals—as such can be helpful, particularly if the clinician marks the proximal edge of clear nail, at the start of therapy. This allows the patient to more accurately gauge the growth of new nail.

Patients should be told that they can expect improvement in the appearance of the affected nails, but many factors—such as the age of the patient and the extent of infection—may affect the ultimate outcome. However, they must understand that the optimum results can only be expected if the recommended therapy is used in the manner directed and for as long as directed.

**Conclusion**

Onychomycosis is a common fungal infection due principally to dermatophytes; Candida spp and saprophytic fungi account for a smaller number of cases. Comorbid diseases and conditions may affect the prevalence of onychomycosis, and may alter the clinical presentation as well as the causative organism(s)

Pediatric onychomycosis is uncommon, but the possibility of this diagnosis should not be overlooked, particularly in patients with family members who have onychomycosis and/or tinea pedis.

Treatment is feasible with both systemic and topical drugs; the newer topical agents, efinaconazole and tavaborole, have broad in vivo activity and can provide improved clinical efficacy.

The treatment goal of “complete cure”—i.e., complete eradication of organisms and a totally normal appearance of the treated nail—used in clinical trials is a somewhat unrealistic expectation in real-world application.\textsuperscript{6} Instead, treatment success—that is, eradication of the infection, improvement of the appearance of the nail, and, when pain is a symptom, resolution of discomfort—is a more reasonable and achievable, practical goal.

**References**

25. Ghannoun MA, Isham N, Long L. Optimization of an infected shoe model for...


