Accurate diagnosis is critical to establishing an effective treatment plan.

By Raza Aly, PhD
Dermatologists are generally well-equipped to manage dermatophyte infections of the skin and nails. Yet when it comes to certain patient presentations, management can be challenging. Recalcitrant and/or recurrent dermatophytosis can be frustrating for patients as well as the clinicians who treat them.

In order to achieve optimal results in management of dermatophytosis, accurate diagnosis, appropriate therapy selection, and proper post-treatment habits are essential. The following is a review of some important diagnostic and therapeutic considerations for clinicians managing fungal infections.

Tinea Pedis: Clinical Presentation
Dermatophytes are able to survive only within dead keratinized tissue, yet not all dermatophyte species demonstrate the ability to invade keratinized hair, the nail bed, or the nail plate. Though dermatophyte invasion is limited to the stratum corneum, the inflammatory response to infection involves both dermal and epidermal layers.

Unlike other mycotic infections, dermatophytosis is communicable. In addition to spread of disease to other hosts, individuals may reintroduce the causative organism from infected clothing, such as footwear, or from contact with infected individuals in the community.

Infection of the feet, affecting up to 70 percent of the population, is the most common form of superficial fungal infection. The major etiological agent implicated in tinea pedis is *Trichophyton rubrum*. Tinea pedis is generally more frequent among those who frequent swimming pools or use public or community bathing facilities, such as in health clubs, prisons, army camps, boarding schools, etc. Additionally, though tinea pedis occurs in women and children, it occurs with much greater frequency in men. Three main clinical presentations of tinea pedis exist.

**Vesiculobullous Type.** This clinical presentation may be most challenging, simply because some cases marked by severe inflammatory response can be incapacitating. Secondary bacterial pyoderma or cellulitis are possible.

The presentation is characterized by the emergence of intense vesicular infections that result in vesicles and bullae in clusters. Essentially, the presentation represents an allergic contact dermatitis: Vigorous T-cell response to fungal antigen produces an inflammatory response that in the acute stage may produce cellulitis, lymphangitis, and adenopathy.

**Interdigital Type.** The most common type of tinea pedis, interdigital type ranges from relatively asymptomatic mild scaling to exudative, macerated, malodorous conditions.

Research reveals that an overgrowth of bacterial species may accompany the more exudative processes and contribute to the clinical picture. Species such as *Brevibacterium epidermidis*, *Corynebacterium minutissimum*, *Micrococcus sedentarius*, *Pseudomonas* and *Proteus* species, and *Staphylococcus aureus*—many of which are resistant to penicillin and its derivatives—have been identified within the interdigital spaces of affected individuals. The initial dermatophyte infection can lead to degradation of the stratum corneum and enhanced opportunities for invasion by these bacteria. Simultaneously, the infective dermatophytes produce penicillin- and streptomycin-like antibiotics, which may actually enhance the proliferation of these resistant bacteria.

As the bacteria proliferate, they induce inflammation, with some producing malodorous and fungicidal thioesters. Resultant dermatophytosis complex is characterized by a macerated, malodorous, symptomatic presentation significantly different from the scaling associated with dermatophytosis simplex.

**Plantar Moccasin Type.** Research shows that the delayed-type hypersensitivity response that the body normally mounts to eliminate fungi is absent among many patients affected by moccasin type tinea pedis. This may be related to a defect in cell-mediated immunity.

Additionally, many affected patients have a family or personal history of atopy.

The presentation is minimally inflammatory, characterized by dull erythema, dryness, scaling, and hyperkeratosis. Distribution is over the entire plantar skin of both feet, either in sandal or moccasin pattern. Of note, some patients present with one hand affected by similar scaling.

Tinea Pedis: Diagnosis and Treatment
Goals of therapy must include both clinical and mycological cure. Confirmation of fungal infection—as well as mycologic cure—is possible through microscopic evaluation of KOH slide preparations (Chlorazol E staining specific for fungal cell walls is useful) and cultures. As noted in Table 1, nondermatophytes may be implicated in cutaneous infections of the foot, however, *Scytalidium* related infections are rare in the US.

**Vesiculobullous Type.** The acute nature of the dermatitis directs treatment. Topical antifungal therapy (allylamines) combined with adjunctive use of topical corticosteroids and compresses, such as Burow’s solution, help yield more rapid control of symptoms.

**Interdigital Type.** For less symptomatic presentations, topical allylamines, imidazoles, and ciclopirox are useful. Broad-spectrum topical antifungal agents are first-line options for management of macerated, erosive presentations, due to the likely involvement of bacteria. The imidazoles and ciclopirox have anticandidal and antibacterial activity. Some cases of dermatophytosis complex warrant introduction of a separate antibacterial agent.
Plantar Moccasin Type. Failure to identify and treat co-existent nail infection permits reinfection. Due to the high incidence of co-existent nail involvement and the thickness of the stratum corneum, combined topical and systemic therapy is generally indicated. Topical therapy can be continued long-term following itraconazole or oral terbinafine therapy to help prevent recurrence.

Onychomycosis
While molds and yeasts may contribute to some cases of onychomycosis, the majority (more than 90 percent) of cases are caused by dermatophytes. Three clinical types exist, defined by the route through which the organism invades the nail and subsequent clinical appearance.

Distal lateral subungual onychomycosis develops when the fungus enters via the lateral nail groove and distal subungual area. Superficial white onychomycosis is the result of infection via the dorsal surface of the nail plate.

Proximal white subungual onychomycosis, which is rare in the general population but may occur in immunocompromised patients such as those with AIDS, develops following infection of the undersurface of the proximal nail fold. The nail fold remains normal in this presentation. Inflammation may indicate chronic paronychia with secondary nail involvement.

Importantly, presence of the characteristic dystrophic nails of onychomycosis is not sufficient to render the diagnosis. Furthermore, clinical patterns do not aid identification of specific causative organisms. The clinician must confirm the diagnosis of onychomycosis and attempt to identify causative organisms through direct examination and/or culture. Making the appropriate diagnosis aids treatment selection and enhances outcomes.

Direct microscopic examination or nail materials on a KOH slide using 15-20% KOH in dimethyl sulfoxide is the easiest method to confirm dermatophyte infection. Chlorazol E stain specific for fungus cell walls will aid evaluation.

Identification of specific causative organisms requires use of culture. Several appropriate media are available commercially. However, since non-dermatophytes may rarely be involved (just as in tinea pedis) include media with and without cycloheximide. Media without cycloheximide will encourage isolation of non-dermatophyte pathogens.

The benefit of direct examination or culture depends on the quality of the sample. For distal subungual onychomycosis, use a small 1ml curette to obtain a specimen from the onychomycotic border. This is where the highest number of viable hyphae exist.

In the case of proximal white subungual onychomycosis, use a No. 15 blade scalpel to remove superficial layers of the nail, then use a curette to remove samples from the infected area.

For superficial white onychomycosis, scrape the affected nail with a No. 15 blade scalpel to obtain sample materials.

Onychomycosis: Medical Treatment
Reported cure rates with oral therapy are as high as 82 percent, but in our experience in one cohort, they were roughly 65 percent. Nonetheless, oral therapy is indicated for a majority of patients. Newer agents provide rapid penetration into the nail via the nail bed and strong incorporation into matrix tissue.
Active agents remain in the nail for varying time durations after discontinuation of therapy, allowing continued improvement and antifungal effect. Note that the nail will not appear normal upon completion of the treatment course, but clinical improvement will continue to develop over time.

Table 2 reviews some important considerations regarding selection of an oral therapy. Of all the antifungal agents, itraconazole has the broadest spectrum of effect (active against dermatophytes, *Candida*, and some nondermatophyte molds). Recommended dosage is usually 200mg BID without food for one week a month. For toenail onychomycosis, provide three to four months of therapy; for fingernails, treatment is for one to two months.

Terbinafine demonstrates *in vivo* activity against dermatophytes, some species of *Candida*, and some molds. Within one to three weeks of therapy, terbinafine is detectable in the nail plate. It persists up to four months following discontinuation of therapy. For toenail infections, a 12-week course of 250mg once daily is effective. For fingernail infections, the duration of therapy is halved to six weeks.

Fluconazole will require more long-term therapy, though evidence supports the use of a 150-300mg once-weekly pulse dose, especially useful for patients taking multiple medications. Active against *Candida* and other yeasts, fluconazole has been used among HIV-infected patients.

There is continued interest in the development of effective combination regimens to manage onychomycosis. Incomplete response, non-response, and relapse are all possible with oral therapy.

**A Show of Hands**

Discussion of tinea pedis and toenail onychomycosis often overlooks the reality of tinea manuum and fingernail onychomycosis. Palmar tinea manuum, like plantar tinea pedis, tends to be non-inflammatory—marked by scaling and pruritis, and caused by *T. rubrum*. Unlike tinea pedis, it is usually unilateral, though it commonly develops in conjunction with bilateral tinea pedis. Bilateral tinea manuum, in fact, may be a clue to *S. hyalinum* or *S. dimidiatum* infection.

Dorsal tinea manuum is a more inflammatory presentation, similar to vesiculobullous tinea pedis, that is more common in individuals who work with animals, such as veterinarians, groomers, etc. Dermatophytes such as *T. mentagrophytes*, *T. verrucosum*, or *M. Canis* are often implicated.

Strategies for diagnosis and treatment of tinea manuum or fingernail onychomycosis are similar to those for the associated foot infections. As noted in the text, systemic treatment durations for fingernail disease are about half that for toenail involvement.

Superficial white onychomycosis (left). Proximal subungual onychomycosis (middle). Distal subungual onychomycosis infected with *T. rubrum* for three years (right).
### Table 1. Causative Organisms Associated with Dermatophyte Infections

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Interdigital type</th>
<th>Moccasin type</th>
<th>Vesiculobullous type</th>
<th>Onychomycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dermatophytes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Trichophyton rubrum</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Trichophyton mentagrophytes var.</td>
<td>X (downy)</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Trichophyton mentagrophytes var.</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Trichophyton mentagrophytes var.</td>
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<tr>
<td>Epidermophyton floccosum</td>
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<tr>
<td><strong>Nondermatophytes</strong></td>
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<tr>
<td>Aspergillus spp</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Scopulariopsis brevicaulis</td>
<td></td>
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<td></td>
<td>X</td>
</tr>
<tr>
<td>Fusarium spp</td>
<td>X (rare)</td>
<td>X (rare)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Acremonium spp</td>
<td>X (rare)</td>
<td>X (rare)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Scytalidium dimidiatum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scytalidium hyalinum</td>
<td>X (rare)</td>
<td>X (rare)</td>
<td></td>
<td>X</td>
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<tr>
<td><strong>Yeast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td>X (rare)</td>
<td>X (rare)</td>
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<td>X</td>
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</tbody>
</table>

Note: Bacteria alone can cause interdigital tinea pedis.

### Table 2. Oral Antifungals for Onychomycosis

<table>
<thead>
<tr>
<th>Antifungals</th>
<th>Potential Drug Interactions</th>
<th>Potential Adverse Effects</th>
<th>Recommended Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itraconazole</td>
<td>Enzyme-inducing drugs: rifampin, isoniazid, phenobarbital, phenytoin. Oral hypoglycemic agents, warfarin, digoxin, terfenadine, astemizole, cyclosporine, histamine type 2 (H2) receptor antagonists</td>
<td>Embryotoxicity, GI disturbance, rash, pruritus, hypokalemia, reversible telogen effluvium, very rare hepatotoxicity</td>
<td>Fingernail: 200mg BID for 1 week/month x 2 pulses OR 200mg QD x 6 weeks</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>Rifampin, histamine type 2 (H2) receptor antagonists</td>
<td>GI disturbance, taste disturbance, rare hepatobiliary dysfunction</td>
<td>Fingernail: 250mg QD for 6 weeks</td>
</tr>
<tr>
<td>Fluconazole (unapproved indication)</td>
<td>Warfarin, hypoglycemics, thiazides, phenytoin, rifampin, cyclosporine, theophylline</td>
<td>GI disturbances, rare hepatotoxicity</td>
<td>Toenail: 250mg QD for 3 months</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Fingernail: 150-300mg once per week x 6 months or until clear</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Toenail: 150-300mg once per week x 9 to 12 months or until clear</td>
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</tbody>
</table>
Dermatophyte Infections

**Table 3. Prevention Strategies**

One critical but often overlooked element of patient management is prevention of reinfection. Clinicians should arm patients with effective strategies to prevent recurrence of fungal infections. Occlusion (particularly occlusive footwear) plays a significant role in the development of fungal infections, giving rise to the adage, ‘tinea pedis follows in the footsteps of shoe-wearing nations.’ With this in mind.

**Patients seeking to prevent reinfection should:**
- Wear non-occlusive footwear, such as sandals, or no footwear when possible.
- Thoroughly drying the feet and interdigital spaces prior to putting on socks and shoes.
- Wear cotton absorbent socks. Wash these in hot water.
- Consider using absorbent foot powders to minimize moisture.
- Replace ‘infected’ footwear with new shoes, once onychomycosis or tinea pedis is cleared. This is especially important for those prone to relapses.

**Clinicians confronted with relapsing fungal infections should:**
- Ensure proper fit of footwear to minimize trauma. Trauma increases the risk of infection.
- Consider prophylactic antifungal therapy (for those prone to relapses): Apply Lamisil cream or lotion daily for one week per month.
- Wear shower shoes at the pool, gym or any other common bathing areas.

Management of fungal infections of the feet and hands tends to be relatively straightforward. However, coexistent infection by non-dermatophytes or yeast can complicate therapy. Establishing the diagnosis and identifying causative organisms through direct examination and culture permits the dermatologist to establish an effective treatment regimen.

Many cases of tinea pedis and tinea manuum will respond to topical allylamines and benzylamines, which offer in vitro fungicidal activity and short treatment duration. The development of newer oral azoles and allylamine antifungal agents offers enhanced approaches to skin infections and better, more convenient interventions for nail infections.

Avoidance of reinfection, through treatment of footwear, use of antifungal foot powders, and avoidance of potentially contaminated surfaces (wearing shower shoes, avoiding public baths, etc.) is important. Additionally, some patients will benefit from long-term intermittent topical therapy to help prevent reinfection or treat it before it becomes clinically troublesome.

For more on fungal infections of the skin, consult Atlas of Infections of the Skin, Maibach HI & Aly R, Eds. (Churchill Livingstone 1999) and Cutaneous Infection and Therapy, Aly R, Beutner KR, and Maibach H, Eds (Dekker 1997), from which some of the above material was adapted.

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