

## ONYCHOMYCOSIS: Update and Practical Management Protocol

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Onychomycosis is a condition that is very familiar to the podiatric physician. Ongoing research and newer medications will possibly soon revolutionize cutaneous mycotic infection management. It is important for the podiatric physician to be familiar with dermatophyte infections in preparation for these new medications and their potential podiatric applications. The following is a protocol for management of onychomycosis that includes Federal Drug Administration approved medications that have been found to be very beneficial. The office visits are broken down into a management outline for care. The overall management scheme involves: identification of pre-disposing factors, modifying environmental factors, utilizing topical and systemic medications, and a well-informed patient. This outline applies to many conditions, and will provide an overall approach that the podiatric physician and patient can appreciate in an informed and logical process.

### BACK TO BASICS REVIEW

Fungal infections are probably the most common nail affliction, but also the most commonly overlooked by the medical community in general. Onychomycosis, tinea unguium, or mycotic nails generally represent a painful condition due to shoe pressure, and the resultant nail dystrophic changes produced. Occasionally the primary concern is only a cosmetic one. Occupational concerns for those individuals exposed to the environment, or other factors, may likewise produce complaints and concerns from patient and employers alike. Associated tinea pedis, with the nail as a source for reinfection, can cause multiple presenting complaints as well.

Onychomycosis is an infection caused by a dermatophytic fungus an estimated 95% of the time. The few remaining incidences include yeasts and molds. Yeasts rarely cause chronic dystrophy in the feet. Molds have a controversial role, and may primarily be a contaminant for all practical purposes.

*Trichophyton rubrum* (T. rubrum) is the most common fungus, with a greater than 50% incidence. Next, in terms of incidence, is *Trichophyton mentagrophytes* (T. mentag) with nearly 50% incidence as a close second. The clinical presentation of these two species of fungus can be strikingly different. Third is *Epidermophyton floccosum* (E. flocc), representing a 5% incidence.

The differential diagnosis of pedal nail dystrophy includes other noninfectious dermatological conditions such as psoriasis. The presence or history of the classic skin lesions over the extensor surfaces of the arms and legs, as well as the presence of small pits on the surface of the nail, aid in the definitive diagnosis. Trauma to the nail matrix can result in thickening of the nails. The feet are particularly prone to injury, whether occult and obvious, or more subtle from chronic shoe pressure. Clinical history and isolated nail involvement are helpful in identification of this etiology. The diagnosis of eczema and nail dystrophy is well-aided by history as well as associated lesions. Candida, or yeast infection of the pedal nail, presents with maceration and paronychia. A history of yeast infections in other geographic locations or the diagnosis of mucocutaneous candidiasis is obtainable by history or clinical exam.

Dermatophytosis can only infect the dead outer layer of the epidermis and nail. Dermatophytes must feed on the outer keratin layer of the skin or nails. Nails are basically a modification of the stratum corneum or outer layer of the skin. The dermatophytes produce a keratinase or keratolytic enzyme that enables them to feed on the keratin in this area. Skin compromise and weakening, in the presence of the fungal infection, can result in secondary bacterial and yeast infections. The fungus does not invade the skin so deeply as to cause a lethal host response to the fungus, yet the fungus does not invade so little as to become lost in desquamation of the skin.

The dermatophytic fungi thrive at body temperature. A moist environment of 50% humidity, as well as darkness, aid in their growth and proliferation.

The pedal nails grow at 0.01 - 0.05 mm per day. This rate of growth can be modified and reduced by diseases or local skin circulatory and nutritional factors. The hyponychium is the subungual scaling skin under the distal free edge of the nail. This natural keratin build-up from nail growth and skin maturation is an excellent medium for the fungus to grow and thrive on the foot, within the closed confines of shoes.

## DIAGNOSTIC TECHNIQUES

Identification of the fungus prior to treatment, especially if systemic treatment is to be considered, is very important. Potassium hydroxide (KOH) preparations are the Gram's stain of the fungus infection identification process. False negatives may be the result of poor harvesting techniques for those attempting to identify fungal elements in onychomycosis. The fungal elements are best cultured and isolated in onychomycosis in the proximal hyponychium and skin well under the distal free edge of the nail plate, at the nail-nail bed junction. Just as in tinea pedis, the location of the active fungus is near the advancing border, not the centrally cleared area of the lesion. The debris more distally under the nail plate is primarily scaling keratin and callous tissue, and is a poor source of fungus for identification purposes.

The presence of fungal elements or hyphae on KOH aid in identifying a fungus infection, but is not diagnostic. The viability of the fungal element obtained cannot be assured, and contamination may be possible. No specific genera identification can be established by KOH preparation. Fungal cultures are required for specific fungal identification purposes. Positive identification of the fungus by either KOH or culture, correlated with the clinical presentation, aids in the diagnostic process. The KOH preparation can be completed in minutes; the fungal culture requires weeks to complete. Enteric therapy may be started prior to completion of the fungal culture process. The clinical presentation of the type of nail involvement is correlated to aid in fungus genera identification. The differential diagnosis is further aided by associated skin lesions of tinea pedis. Other dermatopathologies, as a differential diagnosis for dystrophic nail conditions, have been reviewed. The presence of tinea pedis, or history of tinea pedis, should be noted by the physician.

Zaias has identified 4 types of onychomycosis. This system has practical application in the clinical setting and is very helpful for fungal genera identification. This classification system also aids in other diagnostic as well as therapeutic considerations. It is vitally important to remember that no one clinical presentation will identify a specific fungus, nor can one be excluded. Also, the more severe the clinical symptoms and signs of a dermatophytosis, the more likely yeast and/or bacteria may be involved.

The four types of onychomycosis Zaias identified are distal subungual onychomycosis (DSO), white superficial onychomycosis (WSO), proximal subungual onychomycosis (PSO), and mucocutaneous candidiasis. The distal subungual onychomycosis (DSO) is the most common presentation. The fungal infection begins in the hyponychium, beneath the distal free edge of the nail. Subungual skin and fungal infiltration of the nail causes scaling and debris build-up beneath the nail. The fungal and keratotic build-up involves both the nail and the skin, and generally cannot be adequately cleansed or removed by the patient. Attempts at removal may result in further inoculation or damage to the nail bed and worsening of the condition. Onycholysis, or loosening of the nail, as a result of this process results in a proximal advancement of the fungus *beneath* the nail plate. The location of the fungus is at the proximal advancing border of the nail and nail-bed junction. The subungual debris feeds, and is a result of, the fungal infection. Clinically, the nail is thickened at its most distal free edge. The entire nail may be involved, in advanced cases to the proximal nail fold. The nail discoloration may be yellowish-brown or grayish-white in color. Symptoms occur as the nail becomes thicker, and is less accommodated (irritated) by shoes.

*T. rubrum* is the most common species involved in this clinical presentation. A moccasin-type scaling and xerotic-type tinea pedis is generally associated with this mycotic nail presentation. The tinea pedis may preclude or follow the nail involvement.

The second type of onychomycosis identified by Zaias is the white superficial onychomycosis (WSO). The fungus invades the nail from above (superficial surface), not from below. A whitish discoloration is evident as a painted-on appearance to the digital nail. Subungual changes are not evident. Patients with this type of onychomycosis may be

more concerned with cosmesis than pain. Gross thickening and dystrophy may not be present. The fungus must invade the nail directly. Special enzymes must be produced by the fungus to enable it to directly obtain access to the nail plate keratin from such a superficial route. *T. mentagrophytes* is commonly associated with this type of onychomycosis. *T. mentagrophytes* typically produces a more aggressive clinical tinea pedis as well with a vesicular and bullous type eruption due to the production of these enzymes. The clinical symptoms of the onychomycosis may be less notable, but the invasive nature of the fungus is greater.

The third type of onychomycosis is proximal subungual onychomycosis (PSO). The infection by the fungus originates at the eponychium of the posterior nail fold, instead of the distal subungual region. The distal nail is clear until late in the disease process. It is a rare presentation and is more importantly associated with severe immunocompromised states, such as those found in HIV patients.

The final or fourth type is mucocutaneous candidiasis or yeast infection. This is rarely noted in the foot as a chronic nail dystrophy problem. Paronychia, as a result of yeast infection in the foot, is much more common as a secondary condition. Secondary paronychia yeast involvement, with other primary dermatophytic infections of the nail, are likewise possible as well.

### PATHOPHYSIOLOGY

The basics of dermatophytic or fungal infections have been reviewed, which will lead to a logical form of management from many fronts. The practitioner must understand the pathophysiology of how the infecting fungal organism affects the nail and surrounding skin. Patient understanding is essential so that the patient can also appreciate the logic of care. This will hopefully aid in compliance and result in an informed patient. Hopefully, the patient can then accept the prolonged treatment that is needed, not only to clear the infecting dermatophytic fungus, but provide maintenance that will prevent recurrence for a patient that may have a life-long predisposition to this condition. Recurrence of the onychomycosis may hopefully be prevented or avoided.

The presence of the dermatophytic fungus and keratin at the right moment, in the right

environment, results in onychomycosis or tinea pedis. The right environment may include maceration, most importantly hereditary predisposition, trauma, or a systemic or local immunocompromised state. The right environment generally exists under the nail and inside shoes. Here, the air is humid, dark, and warm. If this situation is left in the predisposed patient, a tinea pedis or onychomycosis results.

If the fungal elements are exposed to the host cells of the patient, an immune response can develop. Associated histamine release results in vesicular formation and pruritis. Further skin compromise results in secondary yeast and bacterial infections. An exaggerated form of the immune response is the id reaction.

Clinical symptoms are a result of the effects of the fungus on the skin and nails, as well as the fungal-mediated immune response. The clinical signs of onychomycosis result from similar interactions of the fungus and keratin-laden tissues. Treatment is directed at affecting not only the fungal elements themselves through medication, but the environment. Symptoms may need to be addressed through additional medications, either locally or systemically, that mediate the immune response or its effects.

### MANAGEMENT PROTOCOL

The management protocol suggested and discussed here can be applied in principle to many conditions encountered by the podiatric physician. The patient visits are divided into four specific types: initial assessment visit, management visits, reassessment visits, and maintenance visits. Practically speaking, time for the visits can readily be scheduled in the office, based on a specific purpose. This time-line approach to management is easily understood by the patient, and can be divided into regular intervals. The patient is informed prior to treatment of the treatment protocol, due to its prolonged duration. Acceptance or rejection is then best associated with full knowledge of the extended course of the treatment and its implications.

The initial visit includes a history and physical examination, as on any new patient. The diagnosis is aided by KOH and culture harvesting and preparation. Photographs are taken to more accurately monitor progression of the disease, or response to management. Laboratory work is obtained to

establish the pre-treatment renal and kidney function. Treatment is begun and environmental modification measures undertaken. The affected nail is debrided to the nail and nail bed junction, to remove all loosened nail, and expose the skin beneath the nail to topical medication. This likewise alters the subungual environment. The hyponychium is gently curetted and debrided and specimens may be taken for KOH and culture preparations. Efforts at environmental modification for the foot include drying, cooling, and providing light to the affected area as much as possible during the course of the day. This may or may not be possible, depending on the employment status of the patient. Alteration in environment is critical to the overall management and maintenance scheme, to prevent reoccurrence of the condition. A hereditary predisposition is considered one of the primary etiologic factors. Therefore, environment modification may be a lifetime concern for reoccurrence prevention.

Medication is a serious consideration to aid in treatment and clearing of the fungus. "Significant" involvement of the distal subungual type of onychomycosis necessitates oral medication treatment. The only FDA approved drugs for this purpose at the time of this writing, are Griseofulvin and Ketoconazole. Ketoconazole is only indicated in fungal infections unresponsive to Griseofulvin, or in Griseofulvin allergic patients as a second line medication. Griseofulvin, a fungistatic, not fungicidal agent, is the drug of choice. The author prefers Gris-Actin Ultra 330 mg administered 2 times daily. The treatment duration generally approximates a 12-month period. Precautions are many. The effectiveness of birth control pills may be reduced, and precautions should be discussed with women of child-bearing age. Other side effects such as photosensitivity, cephalgia, nausea, and potentiating effects of alcohol, should be reviewed with the patient. Coumadin may need to be adjusted, as the effectiveness is increased in patients taking Griseofulvin. Penicillin allergy is a contraindication, as Griseofulvin is produced from the *Penicillium* mold. It is suggested that the reader refer to pharmacology texts on Griseofulvin for a more thorough review of actions and contraindications.

The minimal DSO and most WSO may be well-managed with topical medications alone. Both conditions lend themselves, with appropriate debridement, to direct application of medication to

the fungal elements. Preparations such as Fungoid Tincture or Gorodochrome, are specifically designed with a vehicle for nail use and should be considered. Creams and lotions which are antifungal in nature are not necessarily designed for nail application. If proper debridement and environmental factors can be controlled, as well as modifications of predisposing factors, the effectiveness of topical medications can be increased.

Management visits following the initial visit are short in duration. They include proximal debridement of the nail and monitoring the effect of treatment. Major decision making is not intended as a purpose for this visit. Problems in treatment are reviewed and discussed, as well as questions concerning the overall management scheme. Reinforcement is helpful during these visits to encourage the patients to continue in their efforts for relief of the condition. Objective review of environmental and medical compliance is observed.

Reassessment visits are decision points at 6- and 12-month intervals to assess response to treatment. Photographs are compared. Laboratory testings to reassess renal and kidney function are performed. Decisions can be made at these visits to proceed with therapy, stop, or modify its application. Any nail unresponsive to treatment by 6 months may be chemically or surgically avulsed. The nail bed may then be treated topically as a new nail regrows. The body has likewise incorporated a degree of Griseofulvin within the dermis. This skin level of medication will assist in clearing of the fungal elements from the nail bed. If permanent dystrophy of the nail is identified, regardless of possible clearing of the fungal elements, then damage to the nail matrix may have occurred by the fungus, and the possibility of total clearing may not be possible. The patient must be informed of the possibility of damage to the nail matrix prior to treatment. Even with the best dermatophytic treatment, permanent damage to the nail plate through the nail matrix may have occurred. This damage may have occurred long before avulsion or the initiation of any treatment program. Oral medications are continued until 8-12 months in pedal nail infections, or until clinical clearing exists.

Maintenance visits involve periodic checks to review post-treatment progress. The topical medication may be applied 2-3 times per week, and all environmental changes are continued to help prevent reoccurrence. Lifestyle changes are important to

maintain the cleared nail in attempts to prevent recurrence. Encouragement, as well as reinforcement to response of therapy with review of photos, are

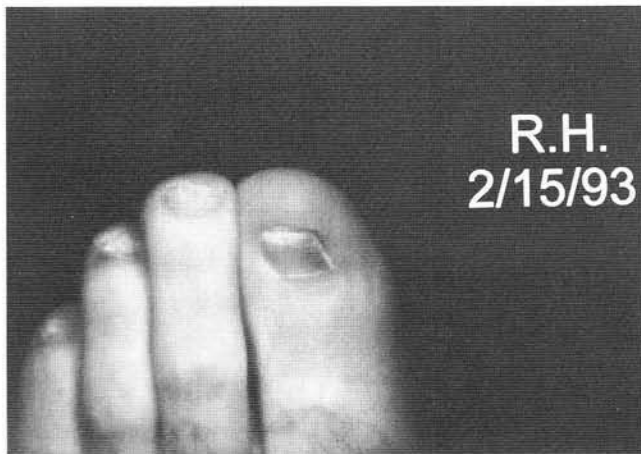


Figure 1. Significant involvement of distal subungual onychomycosis digits 1, 4, and 5. Pretreatment appearance, prior to oral and topical medications, as well as environmental modifications.

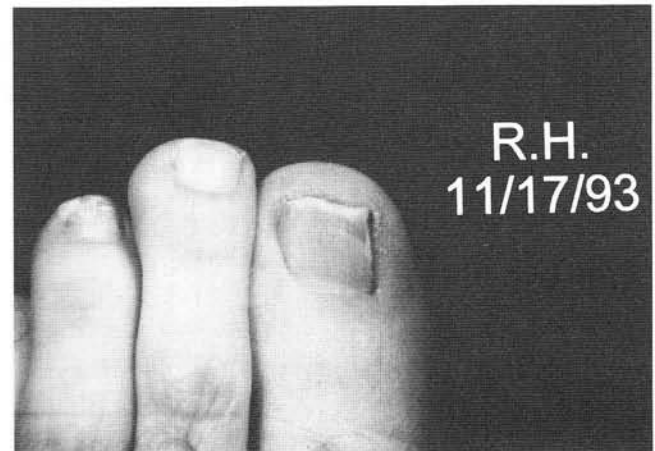


Figure 2. Follow-up evaluation of distal subungual onychomycosis, 9 months into management program, with satisfactory clearing of all sites.

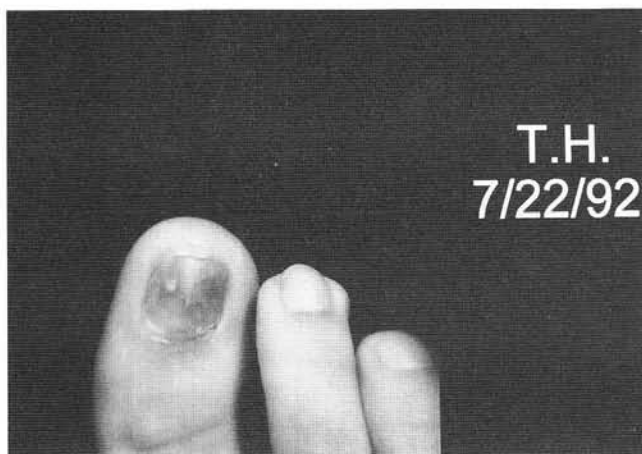


Figure 3. Lesser involvement of distal subungual onychomycosis of the hallux. Pretreatment appearance prior to topical treatment only as well as environmental modifications, in a penicillin allergic patient.

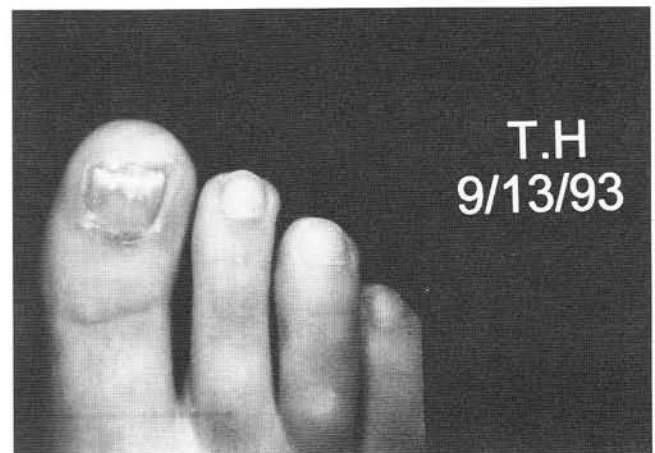


Figure 4. Follow-up evaluation lesser involvement of distal subungual onychomycosis, 12 months into management program with good but slower response to treatment.



Figure 5. White superficial onychomycosis, pretreatment appearance with topical medication and environmental modifications only.

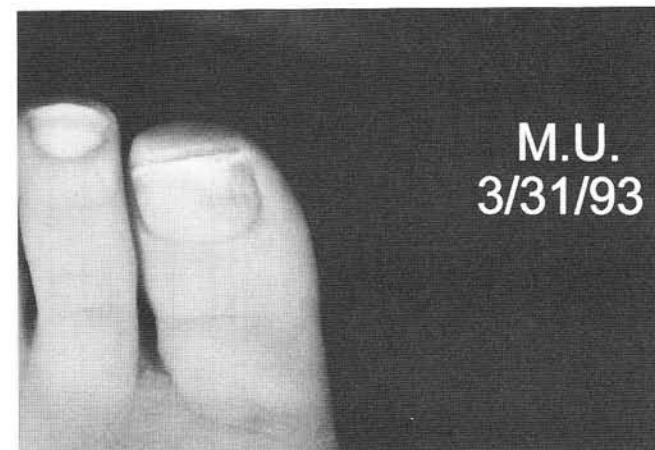


Figure 6. Follow-up evaluation white superficial onychomycosis with satisfactory clearing at 7 months.

## CONCLUSION

It is hoped that through this back to basics review, as well as application of a practical management protocol, the podiatric physician and patient can be fully informed as to onychomycosis and its long-term care. Basic understanding of fungus or dermatophytic infections is necessary. Appreciating the environment for fungal growth is important. Management is a multifaceted approach to include not only oral but topical medications. Important as well are alterations in the local nail environment that can enhance fungus destruction. With the physician and patient fully understanding these concerns, long-term cure and maintenance can be effected. With the newer medications approaching the market, use of long-term current oral medications may be obviated. The podiatric physician is encouraged to maintain a current knowledge of dermatophytic infections, so that as the new medications arrive on the scene, a more knowledgeable approach can be taken for our patients.

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