ABSTRACT The diagnosis of onychomycosis is suggested by the clinical presentation as well as the family history and patient age. The definitive diagnosis of onychomycosis is based on (1) establishing the presence or absence of fungal elements using laboratory methods and/or (2) identifying the fungus using fungal culture or, in the future, by polymerase chain reaction as new developments emerge in this technology, making more widespread application of this technique possible.

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Onychomycosis is defined as a fungal infection of the nail unit (Figure 1): the nail plate, nail bed, and periungual tissue. The most common culprits in immunocompetent patients are Trichophyton rubrum (90% of cases) and Trichophyton mentagrophytes (most of the remaining 10% of cases). (1) Less commonly, yeasts and nondermatophyte molds may be causative organisms, particularly in certain patient populations, such as patients with diabetes, the elderly, and immunocompromised individuals. (For further discussion in this supplement, see Scher et al. (2) Onychomycosis caused by dermatophytes is significantly more common in toenails than in fingernails; the opposite is true of Candida infections, which are significantly more common in fingernails than in toenails. (3)

Physical Examination

The physical examination should include careful inspection of all fingernails and toenails. The extent of involvement (the number of nails and the percentage of involvement of each nail unit) should be noted.

The clinical features of onychomycosis (Table 1) include nail bed hyperkeratosis with subsequent separation of the nail plate from the nail bed (onycholysis), the presence of subungual debris, and nail plate dyschromia. Individuals with onychomycosis also may experience associated inflammation and tenderness of the nail bed or periungual tissue. Concomitant tinea pedis infection (also caused by T. rubrum) is extremely common in patients with toenail onychomycosis.

Table 1. Clinical Signs of Onychomycosis (Toenails or Fingernails)

* Onycholysis
* Debris under the nail plate
* Subungual hyperkeratosis
* Discoloration (usually nontransparent white or yellow discoloration: less frequently, brown pigmentation)
* Destruction of all or part of the nail plate

Clinical Presentations: Patterns of Nail Plate Invasion

Several patterns of nail plate invasion have been described.4 The most common of these is invasion of the nail plate from the hyponychium (distal-lateral-subungual onychomycosis) (Figure 2).
In the presentation known as proximal subungual onychomycosis (Figure 3), the organisms invade the proximal nail bed via the cuticle. This is an unusual presentation in immunocompetent individuals; the presence of proximal subungual onychomycosis should raise the index of suspicion for an underlying cause of immunosuppression. Superficial white onychomycosis is characterized by direct invasion of the nail plate surface, causing leuconychia and crumbling of the plate (Figure 4).

Chronic mucocutaneous candidiasis is a presentation that is caused by Candida catcalls, which affects the entire nail unit. Normally, Candida cannot invade the nail plate in immunocompetent patients. Candida may be a secondary invader in onycholysis and chronic paronychia (Figure 5).

**Differential Diagnosis**

Onychomycosis can mimic many other clinical conditions that affect the nail, such as trauma, other infections, and inflammatory processes including psoriasis and, occasionally, neoplastic conditions. When a solitary nail is involved, the possibility of a subungual tumor such as onychornatricoma or exostosis may be considered. The differential diagnosis of onychomycosis in adults is listed in Table 2. (5), (6)

**Table 2. Differential Diagnosis of Onychomycosis in Adults (5), (6)**

* Psoriasis  
* Nail trauma  
* Contact irritants  
* Lichen planus  
* Neoplasms  
* Bacterial infection (Pseudomonas aeruginosa, Proteus mirabilis)

Exogenous substances can cause nail dyschromia that can mimic onychomycosis. Nail polish can stain the nail yellow, and other products, such as self-tanning cream, can stain the nail plate brown. Exposure to a number of substances can cause changes in nails that resemble infectious processes. In addition, physiologic changes occur with aging that resemble fungal dyschromia and dystrophy (Figure 6).

Finally, certain systemic medications are known to induce nail changes. For example, antineoplastic drugs may cause onycholysis, and sun exposure during tetracycline therapy may cause photo-onycholysis. Retinoids may cause nail brittleness.

In children, the differential diagnosis includes several uncommon clinical conditions (Table 3). (7) However, a history of onychomycosis and/or Linea pedis in the family or other household members suggests a dermatophyte infection.

**Table 3. Differential Diagnosis of Onychomycosis in Children (7)**

* Nail psoriasis  
* Congenital malalignment of large toenail  
* Subungual exostosis  
* Subungual warts
* Subungual hematoma
* Paronychia secondary to finger sucking
* Parakeratosis pustolosa

Laboratory Confirmation of Clinical Diagnosis

The diagnosis of onychomycosis should be confirmed prior to institution of treatment. A diagnosis of onychomycosis often has been made based on clinical impressions alone, particularly in cases of mild infections limited to partial involvement of one or only a few nails and especially when topical therapy—rather than systemic therapy—is prescribed. However, this is no longer considered the ideal practice, given what is now known about the potential sequelae of onychomycosis, the importance of selecting the most appropriate treatment, and the possibility of misdiagnosis of nail disease from other causes (such as immune dysfunction (8) or psoriasis (9)).

A definitive diagnosis of the presence of a fungal infection may be readily made in the office by use of a potassium hydroxide (KOH) preparation. In patients with the distal subungual pattern, the nail should be debrided as far back as possible and a specimen of subungual debris obtained from the area as close to the cuticle as possible (Figure 7). Alternatively, scale from the involved portion of the nail plate can be used. Scrapings from the surface of the involved nail plate is preferred in patients with suspected superficial white onychomycosis. In those with a proximal subungual presentation, it is necessary to sample the deeper nail plate and bed.

To dissolve the subungual debris and make it easier to visualize the fungus, dimethyl sulfoxide can be added to the 10% to 15% KOH solution on the glass slide. Fungal stains (chlorazol black E or Parker blue-black ink) may be used to enhance microscopic visualization.

The main advantage of office-based testing is rapid confirmation that a fungus is present. The main disadvantage is that the fungus itself is not specifically identified nor is the presence of nondermatophyte organisms. Another disadvantage of direct microscopy is that an inexperienced observer may misinterpret the results.

KOH of subungual debris and periodic-acid Schiff (PAS) staining of nail plate samples provide confirmation of organisms but do not identify or ascertain the viability of organisms present. Culture is slower and less sensitive but currently is the standard method for identifying the causative organism. Polymerase chain reaction may become a useful method.

PAS showing septate hyphae is diagnostic, but PAS showing only yeast forms is not conclusive evidence of infection. Laboratory results of PAS staining of nail clippings are usually available within a few days. Nail clippings also may be obtained for histologic analysis.

The gold standard of diagnosis for onychomycosis is a fungal culture. Culturing is the only method that is widely available at this time that provides definitive identification of a specific organism, which is particularly important when yeasts or other nondermatophyte organisms are a suspected cause of onychomycosis. Such identification allows choice of a systemic agent that is most likely to be effective.

When other tests fail to provide definitive results, a nail biopsy should be considered. (10)

Conclusion

In most patients, it is likely that a clinical suspicion of dermatophytic onychomycosis can be derived based on the patient's personal and family history and on careful inspection of both fingernails and toenails. However, the diagnosis should be confirmed--using, at minimum, an office-based KOH
preparation—prior to initiating therapy. In addition, under the circumstances described in this article, a culture should be performed to obtain a definitive diagnosis and identification of the causative organism.

Caption: Figure 1. Nail Anatomy The nail plate (consisting or keratin.) forms in the matrix and is attached to the nail bed as it grows. Although the distal portion of the matrix is typically visible (as the lunula) in the thumb and forefinger, it is concealed under the proximal nail fold in the rest of the fingers and the toes. The proximal nail fold covers and adheres to the base of the nail; the distal portion of the proximal bold is the cuticle. Lateral nail folds form soft tissue boundaries at the sides of the nails.

Caption: 2. Distal-lateral-subungual onychomycosis. Note the onycholysis, along with thickening, crumbling, and discoloration of the nail plate and sublingual debris. Photo courtesy of Phoebe Rich, MD.

Caption: Figure 3. Proximal subungual onychomycosis. Proximal subungual onychomycosis. This presentation is marked by invasion of the proximal nail bed via the cuticle. It is unusual in immunocompetent patients. Photo courtesy of Antonella Tosti. Professor of Dermatology, Department of Dermatology and Cutaneous Surgery. University of Miami. Leonard M Miller School of Medicine.

Caption: Figure 4. Superficial white onychomycosis. Leuconychia and crumbling, as seen in this patient, is a result of direct invasion of the nail plate surface. Photo courtesy of Phoebe Rich, MD.

Caption: Figure 5. Candidal onychomycosis. Onycholysis and chronic paronychia may result from invasion of Candida. In immunocompetent patients, this is secondary to other causes such as trauma or chronic exposure to water. Photo courtesy of Phoebe Rich, MD.

Caption: Figure 6. Dyschromia. Yellowing and discoloration may result from both onychomycosis and aging. Even after the infection has been successfully treated, age-related dyschromia can be expected to persist. Photo courtesy of Phoebe Rich, MD.

Caption: Figure 7. Sampling scrapings for KOH preparation or culture. A scraping of the surface of the nail (A) usually does not provide sufficient material for study. The most viable hyphae are under the nail plate, clipping hollowed by paring (B) yields the most useful sample. Photo courtesy of Phoebe Rich, MD.

Boni Elewski, MD. has been an investigator for Anacor and Valeant.


Phoebe Rich, MD, has been a principal investigator and/or consultant for Valeant, Dow Pharmaceuticals, Topica, and Tolmar.

Richard K. Scher, MD, is an advisor/consultant to Valeant.
Address reprint requests to: Phoebe Rich, MD, 2565 NW Lovejoy Street, Suite 200, Portland, OR 97210, Telephone: (503) 226-3376, E-mail: phoeberich@aol.com

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* Clinical Adjunct Professor of Dermatology. Oregon Health Science University, Portland, OR
[dagger] Vice-Chair for Clinical Affairs., Professor of Dermatology University of Alabama School of Medicine, Birmingham, AL
[double dagger] Clinical Professor of Dermatology, Weill Cornell Medical College New York, NY
[section] Professor of Dermatology, Eastern Virginia Medical School Department of Dermatology, Pariser Dermatology. Norfolk, VA

Rich, Phoebe^Elewski, Boni^Scher, Richard K.^Pariser, David

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