

Common Fungal Infections of The Nail



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Although onychomycosis is the most common nail disorder, it is only one of the numerous causes of abnormal nails.¹ The prevalence of onychomycosis in the Canadian population was previously estimated to be 6.5%.² However, in a Canadian study of 15,000 patients, 16.7% of respondents had abnormal nails with 8% demonstrating mycological evidence of onychomycosis.²

The risk factors associated with an increased incidence of fungal nail infections include:

- older age,
- persons with diabetes,
- the presence of peripheral vascular disease and
- a history of previous local trauma.

Although nail disorders are not life-threatening, they may have a significant impact on a patient's quality of life, including pain, difficulty walking and social embarrassment. In the UK, nail disorder treatment failure was most common with an incorrect clinical diagnosis.²

A nail grows at a rate of 0.1 mm q.d. or 3 mm per month. Finger nails would then take six months to grow out completely and toenails require 12 to 18 months to grow; these time periods being longer with increasing age.³

This article will review the cutaneous clues for an accurate diagnosis of fungal nail

infections, but a clinical diagnosis must be confirmed by a positive microscopic exam for fungal filaments or a pathogen grown on fungal culture.

Fungal infections are usually acquired by walking on wet surfaces heavily contaminated with organisms, including communal bathing places or the home bathroom floor.

Fungal infections of the nail

Fungal infections of the nails can be divided into in four patterns:

- Distal and lateral subungual onychomycosis (Figures 1 and 2)
- Proximal subungual onychomycosis (Figure 3)
- White superficial onychomycosis
- Total dystrophic onychomycosis (Figure 4)

Distal and lateral subungual onychomycosis

Distal and lateral subungual onychomycosis is the most common pattern that is usually caused by the dermatophyte fungus *Trichophyton rubrum* (*T. rubrum*). Involvement typically starts asymmetrically from a large toenail and spreads; fingernail involvement is less common. Fungal organisms invade the nail hyponychium initially resulting in subungual hyperkeratosis and onycholysis (distal separation of the



Figure 1. Pincer nail and distal subungual onychomycosis. The secondary nail infection will disappear with treatment but the pincer change will remain.



Figure 2. Distal subungual onychomycosis and spicule formation.



Figure 3. Proximal and distal subungual onychomycosis.



Figure 4. Total plate dystrophic onychomycosis.

Onychomycosis is the most common nail disorder and only one of the numerous causes of abnormal nails.

nail). Linear streaks then spread proximally toward the nail matrix and proximal nail fold. Most patients have maceration in the fourth and fifth toe webs and powdery white dry scale in the plantar surfaces that extend around the sides of the foot (*i.e.*, moccasin-type change).

Proximal subungual onychomycosis

Involvement of the proximal portion of the nail fold, along with the adjacent distal matrix, is called proximal subungual onychomycosis; a rare pattern caused by *T. rubrum*. This pattern is often a sign of immune compromise and could be related to the presenting complaint of a previous unidentified HIV infection. The proper sampling for the culture of these nails must go through to the undersurface of the nail plate.

Superficial white onychomycosis

Superficial white onychomycosis is commonly caused by a related dermatophyte fungus: *T. mentagrophytes* or various yeast species.

With this pattern, colonies of fungus invade the surface of the nail keratin to produce chalky, white nail plate defects without deep nail plate invasion. A scraping of the infected nail surface with a scalpel blade will identify the causative fungal or yeast organism. This is the only type of fungal nail infection that can be treated topically.

Total dystrophic onychomycosis

Invasion of entire nail plate with fungus is called total plate onychomycosis. After a dermatophyte fungus has destroyed the nail plate keratin, the area may be secondarily invaded by yeast or molds, such as *Scopulariopsis brevicaulis*. Treatment of the primary invader may also correct the problem of the secondary invader.

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Diagnosing onychomycosis

Because a number of nail disorders can mimic onychomycosis, treatment with oral antifungal therapy should not be started unless a positive nail microscopic analysis or culture for fungus has been obtained. Up to 20% of fungus cultures may be falsely negative and the culturing procedure should be repeated three times before it is considered negative.⁴ Laboratory diagnosis

should also include microscopy to visualize fungal elements and, occasionally, microscopic tests are positive and the culture can come back negative so that treatment will be based on a positive microscopic exam with a negative culture. Potassium hydroxide (20%) will be added on a microscopic slide to a portion of the sample for 15 to 20 minutes to dissolve the keratin from the material prior to direct microscopy of the fungal filaments.³

The abnormal nail should be clipped and the subungual debris beneath the nail plate included in the fungal sample, as the majority of fungal organisms are often located in the subungual debris. A generous sample should be sent to the laboratory to increase the chance of detecting fungal elements in the material.

Table 1
Topical antifungal agents⁵

Class	Spectrum	Clinical effectiveness per class
Allylamines Terbinafine 1% (Rx) Naftifine Hydrochloride 1% (OTC)	<ul style="list-style-type: none"> • <i>Candida</i> • Tinea vesicolour • Dermatophytes 	90%
Imidazoles (OTC) Clotrimazole Miconazole/econazole Ketoconazole/tioconazole	<ul style="list-style-type: none"> • <i>Candida</i> • Tinea vesicolour • Dermatophytes • Limited gram-positive bacteria 	70%-80%
Pyridone Ciclopirox (Rx)	<ul style="list-style-type: none"> • <i>Candida</i> • Tinea vesicolour • Dermatophytes • Limited gram-positive <i>Pseudomonas</i> activity 	60%

Rx: By prescription

Table 2

Relative mycological cure rates from systemic antifungal agents⁶

Drug/time	Mycologic cure
Terbinafine, 250 mg q.d. (3 months)	75.7%
Terbinafine, 250 mg q.d. (4 months)	80.8%
Itraconazole, 400 mg q.d. (1 week/month x 3)	38.3%
Itraconazole, 400 mg q.d. (1 week/month x 4)	49.1%

Cultures of non-dermatophyte moulds and yeasts are usually secondary contaminants and are not the primary invading organism. They often do not need to be primarily treated.

Treating onychomycosis

Topical agents have minimal side-effects and may be indicated for white superficial onychomycosis and very limited distal subungual onychomycosis as outlined in Table 1.



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The most effective topical antifungal agents are fungicidal and some of these antifungal agents are delivered in nail lacquer to concentrate the drug on the surface of the nail plate. Ciclopirox 8% nail lacquer is a synthetic hydroxypyridone used for the treatment of mild-to-moderate onychomycosis caused by *T. rubrum*. It can be applied once a day for eight to 12 months. The abnormal nail should be clipped away and a mycological cure of 29% to 36% at three months and 59.6% at six months has been reported.² The treatment of nail infections, especially by oral antifungal agents, should not be recommended before the mycological confirmation of infection. Systemic treatment is indicated for proximal subungual onychomycosis and distal subungual onychomycosis involving several nails. Treatment with 250 mg of terbinafine

Take-home message

- Onychomycosis is one of numerous causes of nail dystrophy
- Proper specimen collection is essential for accurate diagnosis:
 - Three specimens for microscopic examination and culture should be taken before a presumptive negative diagnosis for fungus disease is made
 - Clip abnormal portions of the nail with a generous sample that also includes subungual debris
- A nail culture with either a positive microscopic or culture result is crucial prior to instituting oral therapy for onychomycosis: *Do not use oral antifungals without the confirmation of a diagnosis*
- Nail disorders may be cutaneous clues to systemic disease

Table 3

Systemic antifungal agents⁵


Class	Dose	Drug interaction	Side-effects
Allylamines			
Terbinafine	250 mg q.d. for 6-12 weeks	<ul style="list-style-type: none"> • Increased clearance with rifampicin • Decreased clearance with cimetidine 	<ul style="list-style-type: none"> • GI upset • Occasional skin rashes • Temporary loss of taste
Azoles			
Itraconazole	400 mg q.d. for 7 days per month for 2-3 cycles	<ul style="list-style-type: none"> • Drugs metabolized by CYP3A4 (cisapride, dofetilide, ergot alkaloids, lovastatin, pimozide and simvastatin, midazolam, nisoldipine, quinidine and triazolam) are contraindicated 	<ul style="list-style-type: none"> • Rare hepatotoxicity • Variable absorption • Drug resistance • Similar cure rates against <i>Candida</i>, not <i>Aspergillus</i>
Ketoconazole	200 mg q.d. for 18 months	<ul style="list-style-type: none"> • HMG-CoA reductase inhibitors (lovastatin and simvastatin) and ergot alkaloids are contraindicated 	<ul style="list-style-type: none"> • Poor penetration into central nervous system

CYP3A4: Cytochrome P450, family 3, subfamily A, polypeptide 4 HMG-CoA: 3-hydroxy-3-methylglutaryl-Coenzyme A reductase

p.o. q.d. has a mycological cure rate of 75.7% after three months of therapy and 80.8% after four months, compared to itraconazole (400 mg q.d. for one week per month) with mycological cure rates of 38.3% and 49.1% after three and four months of therapy (Table 2).

The potential drug toxicity and drug interactions of the commonly-used oral antifungal agents are listed in Table 3. It is important for clinicians to inform patients of the relative risks and benefits of these agents, along with the costs that may not be covered by their government or private drug plan.

Repeated negative mycological exams should alert the clinician to reassess the causes

of nail dystrophy. Nail changes may be a valuable diagnostic clue to other systemic disorders including psoriasis and lichen planus. 

References

1. Robert DT, Taylor WD, Boyle J: Guidelines for Treatment of Onychomycosis. *Br J Dermatol* 2003; 148(3):402-10.
2. Gupta AK, Jain HC, Lynde CW, et al: Prevalence and Epidemiology of Onychomycosis in Patients Visiting Physicians Offices: A Multicenter Canadian Survey of 15000 Patients. *JAAD* 2000; 43(2)(1):244-8.
3. Tosti A, Piraccini BM: Treatment of Common Nail Disorders. *Dermatol Clin* 2000; 18(2):339-48.
4. Sibbald RG: Nail Infections: Differential Diagnosis. *Can J CME* 1995; 7(10):93-102.
5. Alavi A, Woo K, Sibbald RG: Common Nail Disorders and Fungal Infections. *Adv Skin Wound Care*. 2007; 20(6):346-57.
6. Sigurgeirsson B, Billstein S, Rantanen T, et al: L.I.ON. Study: Efficacy and Tolerability of Continuous Terbinafine (Lamisil) Compared to Intermittent Itraconazole in the Treatment of Toenail Onychomycosis. Lamisil vs. Itraconazole in Onychomycosis. *Br J Dermatol* 1999; 141 (Suppl 56):5-14.