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ONYCHOMYCOSIS

Onychomycosis is the most common nail disease, affecting about 6.7% of the general Canadian population, and as much as half of the population over 70 years old.^{1,2} It can be categorized into various subtypes, and can range from mild to severe, with varying degree of hyperkeratosis, onycholysis, and discoloration (**Table 1**). Dermatophytes are the most pathogenic. Non-dermatophytes molds (NDMs) can include *Scopulariopsis brevicaulis*, *Acremonium* spp., *Aspergillus* spp. *Fusarium*, and *Neoscytalidium*, and are more common in warmer climates.³ Yeast such as *Candida* can also be a cause. Risk factors include nail trauma, diabetes, psoriasis, genetics, immunosuppression, obesity, smoking, and advanced age^{4,5}. Onychomycosis can at times cause significant pain, and psychological distress due to its often disfiguring nature. Given the older patient population, late presentation to a dermatology office, sometimes decades later, treatment can often be difficult. This can be compounded by presentations such as the dermatophytomas, which presents with abscess with white, yellow, orange or brown longitudinal streaks⁶.

	Organism	Features
Distal-lateral subungual	<i>Trichophyton mentagrophytes</i> <i>Trichophyton rubrum</i> <i>Epidermophyton floccosum</i>	Most common
Superficial	<i>T. mentagrophytes</i> <i>T. rubrum</i>	
Proximal subungual	<i>T. rubrum</i> <i>Aspergillus</i> <i>Fusarium</i>	Debris in proximal nail fold *Possible immunodeficiency

Table 1. Patterns of onychomycosis and causative organisms; courtesy of Amy Cao, MD

Differential diagnosis

Other nail diseases can often be confused for onychomycosis. It is always prudent to establish a diagnosis prior to treatment, as it is essential for treatment success, especially if multiple diseases need to be treated concomitantly.

Psoriasis can be very similar, but may also present with pitting and oil drops, which is not seen in onychomycosis. A systematic review found 18% of patients with psoriasis had concomitant onychomycosis compared to 9.1% in the general population.⁷

Lichen planus can feature dorsal pterygium, longitudinal ridging, and nail thinning.

Yellow nail syndrome which is characterized by the yellow nails of the hands and feet, with no cuticles.

Onychogryphosis – which is the thick ram horn like curve of the nail that can often be easily identified.

Retronychia is a distinct thickened opaque yellow great toenail due to ingrowth of proximal nail plate.

Nail digital dermoscopy can be used in the diagnosis of onychomycosis and when these images are evaluated the most common patterns seen include a jagged proximal border with spikes in the onycholytic area, and striae with blurred matte discoloration that resemble the Aurora Borealis.⁸

Investigations

Nail clippings and subungual debris should always be collected prior to treatment. Unfortunately, many patients have received treatment from another physician without having confirmatory testing. Approximately two-thirds of dermatologists test before treatment; conversely, half of family practitioners almost never test.⁹ This adds an element of complexity to disease management, and the clinician should try to collect a sample of nail in which no antifungal treatment has been recently initiated.^{10,11} To increase the yield, the patient can collect nail clippings at home after softening

the nail with a keratolytic cream for one month. The nail can be cleaned with 70% isopropyl alcohol, and then clipped. The patient should be reminded that the debris that was under the nail can also be collected in a sterile urine container and sent for culture. The culture can take up to 6 weeks for results and is considered the gold standard as it can confirm fungal viability unlike histopathology. An additional sample can be sent for histologic evaluation with periodic acid-Schiff staining (PAS), which in a recent study of 631 nail samples was found to be the most sensitive single test for the diagnosis of onychomycosis at 82%, followed by culture (53%) and direct microscopy (48%). Combining both methods can increase the sensitivity to 96%.¹¹

Alternatively, the specimen may be viewed on microscopy after it is placed on a slide with a potassium hydroxide 10% wet mount solution. Although microscopy will not identify the causative organism and has low sensitivity (48%), it is a quick method that can be performed in clinic.¹² Flow cytometry and polymerase chain reaction can also be used but is much more expensive.¹³

Treatments

In studies, a mycological cure (negative KOH and culture) is often compared to a clinical cure (100% visually normal nail). However, in practice the aim for most patients is a normal nail. A complete cure might not be possible in severe disease, or in patients with comorbidities that can retard the growth of the nail, especially if they are older or have infections from nondermatophyte molds (NDMs)¹⁴.

An important aspect in the management of onychomycosis is setting appropriate patient expectations. Patients should understand that nails will likely still look the same after finishing oral therapy and may take 12–18 months to normalize. Photos can also be taken at the start of therapy, and then compared at the 12-month mark to validate that the proximal nail edge is growing normally. The FDA recommends a 5-mm growth of a healthy nail at 9 months post-treatment as proper response.¹⁵

The most successful treatment approach should combine topical and oral treatments. Terbinafine was found to be moderately superior to azoles in both mycological and clinical cure for onychomycosis according to a Cochrane review in 2017.¹⁶ Itraconazole, however, offers a broad antifungal spectrum as compared to terbinafine against NDMs, and *Candida spp.*, and can be considered in these cases.¹⁷ In a recent meta-analysis looking at mycotic cure rates, azoles, such as itraconazole, were found to deliver superior efficacy when dosed continuously compared with pulse dosing (69% vs 63%).¹⁸ Baseline and follow-up bloodwork is controversial, but recommended according to the manufacturer's product monograph.¹⁹ In a double-blind study involving 151 patients, mycological and clinical relapse rates were more frequent in the itraconazole group than the terbinafine group.²⁰ A regimen including booster therapy of an additional month of terbinafine or up to nine months of pulse itraconazole has been elucidated in the literature.²¹ This management approach is typically reserved for those patients with slow growing nails, greater than 2 mm of thickness of the nail plates,

	Dosing	Side effects	Monitoring
Terbinafine	250 mg PO q.d. x 6 weeks for fingernails x 12 weeks for toenails Pulse (not approved): 250 mg PO q.d. x 4 weeks, 4 weeks break, repeat x 1	Nausea, vomiting, dizziness, headache, taste disturbance, rash	Elevated transaminase Rare neutropenia
Itraconazole	200 mg PO q.d. x 6 weeks for fingernails x 12 weeks for toenails Pulse: 200 mg PO b.i.d. x 1 week per month x 2 months for fingernails x 3 months for toenails	Nausea, vomiting, dizziness, headache, upper respiratory tract infection, rash *Congestive heart failure	Hypokalemia Elevated transaminase Elevated triglycerides
Efinaconazole	Daily to toenails for 48 weeks	Burning and itching at application site, ingrown toenails	

Table 2. Simplified common modalities of treatment and dosing for adults with onychomycosis; courtesy of Amy Cao, MD

lateral and/or matrix involvement, immunosuppressed, or with surface area involvement of more than 75% of the nail plate.^{22,23}

A Cochrane review by Foley et al. in 2020 for mild-to-moderate toenail onychomycosis found that efinaconazole 10% topical solution is superior to placebo.²⁴ It should be considered the sole modality of treatment only when the onychomycosis involves less than 50% of the nail plate and does not implicate the matrix.²⁵ An adjunctive topical antifungal can also be helpful. Complete cure vs mycological cure with topicals is highest with efinaconazole at approximately 17.8% of patients achieving a complete cure on active treatment vs 3.3% of patients who received the vehicle. Mycologic cure was achieved by 55.2% of patients on active treatment compared with 16.8% of patients who received placebo. With tavaborole, 6.5% of patients on active treatment vs 0.5% on placebo achieved complete cure and 31.1% on active treatment (vs 7.2% receiving the vehicle) achieved mycologic cure. In a study of ciclopirox, 5.5% of patients on active treatment vs 0.9% receiving the vehicle were

able to achieve a complete cure and 29% of patients on active treatment with ciclopirox were able to achieve mycologic cure compared with 11% of patients who received the vehicle.²⁶⁻²⁸ Children tend to show excellent response to topical agents as monotherapy because of their faster growing and thinner nails. In severe disease, a recent study found that efinaconazole resulted in 65% and 40% mycological vs complete cure rates, respectively, at the 52-week follow up.³¹ For adults, oral terbinafine, with topical efinaconazole, and topical antifungals should be used together for the best chance of cure. In addition, proper hygiene should be taken, and a topical keratolytic (i.e., urea) can also be added to increase the efficacy. Also, recurrence was significantly lower in patients receiving topical antifungal prophylaxis than in those not receiving prophylactic treatment following oral terbinafine ($p < .001$) once a week for prophylaxis.²⁹

Luliconazole 5% solution has very low evidence for a complete cure. Lasers such as Nd:YAG have been used to eradicate fungi by heating the affected tissue. Only three

studies compared 1064-nm Nd:YAG laser to sham or no treatment and found little or no mycological cure after one year.¹⁶ Photodynamic therapy also has a paucity of evidence to support its use.³⁰ Lasers should therefore not be the primary method of treatment but can be considered an adjunct should pain tolerance and cost not be limiting factors for the patient.

Given that onychomycosis often occurs in a warm and moist environment, any concomitant hyperhidrosis needs to be managed as well. The feet should be dried well after a shower, and some clinicians suggest using a hair dryer to be efficient. Patients should be reminded to wear 100% cotton socks, to bring an extra pair with them to the gym or on a hike, and to wash them with very hot water after use. Sandals should be used when walking to a swimming pool or at the gym, and, in general, patients should try to find less occlusive footwear. Patients should be encouraged to discard old footwear after treatment to prevent reinfection. Debridement can be ongoing during active treatment and result in higher clinical cure rate than just therapy alone.³¹ Active tinea pedis

should also be treated with topical agents. It may also be prudent to determine if family members have onychomycosis or tinea pedis as they should be treated as well.

Conclusion

Onychomycosis is a common fungal infection that may require chronic treatment for months to years. It is always recommended to perform a culture and/or PAS prior to initiating treatment. Clinicians are encouraged to use multiple treatment modalities as well as post-treatment prophylaxis as the disease may be difficult to cure.

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