



Nail disease

Is it fungal and how should it be managed?

Key points

- Onychomycosis is typically asymptomatic and subclinical, representing a cosmetic problem.
- Dermatophyte moulds are the most common cause.
- Differential diagnoses that should be considered in patients with nail abnormalities include psoriasis, lichen planus and *Pseudomonas* infection.
- Keeping the feet and toenails dry can help prevent onychomycosis.
- Systemic agents have the highest success rates in treating onychomycosis; they include terbinafine, itraconazole and fluconazole.
- Topical treatments are typically useful only for superficial white onychomycosis and very mild subungual onychomycosis; they include amorolfine, bifonazole, ciclopirox and miconazole.

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Fungal infection accounts for about half of all nail abnormalities. Differential diagnoses include psoriasis, lichen planus and *Pseudomonas* infection. Treatment usually requires long-term continuous or pulsed antifungal therapy.

Fungal infection of the fingernail or toenail plate is termed onychomycosis or tinea unguium. It accounts for about one-third of all fungal infections and half of all nail abnormalities. Onychomycosis has a prevalence of about 10%, varying geographically. The prevalence increases with age. It is mostly asymptomatic and subclinical; patients present only when affected by its clinical appearance. However, onychomycosis can be the source of dermatophytes that cause tinea on other parts of the body. Treatment typically requires a protracted course of an oral antifungal agent.

This article outlines a practical approach to the management of onychomycosis. The pharmacology of topical and oral antifungal agents used in dermatology was discussed in a previous article on dermatophyte infections, in the June 2014 issue of *Medicine Today*.¹

DERMATOPHYTE VS NONDERMATOPHYTE MOULDS

Most cases of onychomycosis are caused by dermatophyte moulds. These fungi are ubiquitous; they are found in almost any environment that can support their existence. Dermatophytes grow on keratinised tissues – the ‘dead’ component of skin and its appendages. The most common dermatophyte infecting nails and skin is *Trichophyton rubrum*. This anthropophilic organism has a worldwide distribution and is abundant in any moist, warm area frequented by humans. Other dermatophyte species can also affect the nail plate. Dermatophyte infections are typically easier to treat than nondermatophyte infections, as most respond to oral antifungal preparations.

Saprophytic nondermatophyte moulds

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Figure 1. Superficial white onychomycosis, showing a powdery white infection of the superficial part of the nail plate of the second toe.



Figure 2. Classic distal and lateral subungual onychomycosis involving multiple toe and finger nails. Note the yellow-green discoloration visible on the surface of the nail, representing tinea in the nail plate and subungual hyperkeratosis, and onycholysis of the fingernails, in contrast with the normal fingernail.

can also infect the nail plate, albeit uncommonly. Typically, these moulds do not grow on other keratinised tissues, such as the skin. *Scopulariopsis brevicaulis* is the most common nondermatophyte to infect the undamaged nail plate, whereas *Acremonium*, *Aspergillus* and *Fusarium* spp. can cause superficial white onychomycosis. Infections with nondermatophyte moulds are often more difficult to treat than dermatophyte infections, especially if deep-seated; itraconazole with or without nail plate avulsion is required.

In addition, *Candida* spp. can infect the nail plate and associated nail fold. Infection can take the form of paronychia and associated nail dystrophy or, more rarely, total nail plate involvement and destruction in the setting of chronic mucocutaneous candidiasis.

PRESENTATION

There are several types of onychomycosis, based on the mechanism of infection and clinical appearance of the nail plate.

Superficial white onychomycosis

Superficial white onychomycosis describes a very superficial infection, where the fungal elements are found on the surface of the nail plate. Powdery, white, circumscribed patches are seen (Figure 1). This is typically caused by *Trichophyton interdigitale*. *T. rubrum* and non-dermatophytes can also be causative.

Distal and lateral subungual onychomycosis

Distal and lateral subungual onychomycosis is the most common type of onychomycosis, with the infection gaining access via the distal free nail plate and extending proximally (Figure 2). Yellow, brown or white discoloration of the nail plate occurs. The nail plate may thicken and is lifted up by subungual hyperkeratosis as the infection moves upwards. Chards (streaks) of infection can be seen running up the nail plate. Eventually the nail plate can be completely involved and destroyed. Distal and lateral subungual onychomycosis may start in the nail plate of one digit and extend to the others.

Proximal subungual onychomycosis

Proximal subungual onychomycosis is unusual, where whitening of the nail starts proximally as the fungus is able to access the nail plate via the proximal nail fold. Proximal subungual onychomycosis is more common in patients who are immunosuppressed, such as in HIV infection. *T. rubrum* is the most common cause.

Endonyx onychomycosis

Endonyx onychomycosis is a highly unusual variant, where the nail plate becomes secondarily involved by an infection that begins in the finger or toe pulp. Extension of the infection to the nail plate leads to nail pits, lamellar splits, subungual hyperkeratosis and onycholysis.



Figure 3. Nail psoriasis showing subungual hyperkeratosis, which is commonly misdiagnosed as tinea. Note the absence of the yellow-green streaks expected in dermatophyte infection, and the presence of the salmon-pink 'oil drop' sign just proximal to the hyperkeratosis.



Figure 4. *Pseudomonas* infection of the nail plate showing a greenish discoloration that is not seen in tinea.

Endonyx onychomycosis is caused by fungal species responsible for endothrix infection (infection of the substance of the hair shaft), such as *Trichophyton soudanense*.

DIFFERENTIAL DIAGNOSES

Although onychomycosis is exceedingly common and in most circumstances easy to diagnose, several differential diagnoses should always be considered. It is also important to note that onychomycosis can be a secondary infection or coexist with any other nail dystrophy.

Psoriasis

Psoriasis can cause nail dystrophy and discoloration, subungual hyperkeratosis and onycholysis. It can be very difficult to differentiate clinically from onychomycosis. However, features of psoriasis that help in this differentiation include:

- a different quality of the dystrophic nail, with less yellow discoloration and no white/yellow streaks
- early involvement of multiple nails
- changes such as distinctive nail pits in a regular pattern
- the salmon pink 'oil drop' sign of subungual discoloration (Figure 3)
- psoriasis present elsewhere on the skin.

Pseudomonas infection

Pseudomonas infection should always be considered in patients who do a lot of 'wet work'. It leads to onycholysis with green discoloration of the nails (Figure 4). There is typically no subungual hyperkeratosis

or nail destruction, although an accompanying chronic paronychia may lead to nail plate distortion or dystrophy.

Lichen planus

Lichen planus is an inflammatory condition that leads to destruction of the nail complex. The characteristic feature is a pterygium. In the context of the nail apparatus, this is a scarring process in which the proximal nail fold adheres to the nail plate and is dragged along as the nail grows. The end product is a scarred nail bed with no nail plate.

Simple traumatic onycholysis

Simple traumatic onycholysis is very common. In the fingernails, this is caused by excessive wet work and hand washing, as well as fastidious nail care where the patient cleans under the nail to remove debris, inadvertently lifting the nail further. The toenails can be lifted by excessive walking and exercise in tight shoes. Scraping of the great toenail along the ceiling of the toe box of the shoe can shear the nail plate from the bed. Subungual hyperkeratosis, chards of infection and discoloration are not seen, although secondary *Pseudomonas* infection may produce a green tinge.

Onychogryphosis

Onychogryphosis can affect elderly patients and involves gross thickening of the nail plate related to age and chronic trauma. Tinea of the nail plate can often coexist with onychogryphosis.

INVESTIGATIONS FOR ONYCHOMYCOSIS

The 'gold standard' for the laboratory diagnosis of onychomycosis is a positive fungal culture of nail clippings. Although isolation of a fungus is diagnostic, culture is an insensitive test, and a negative result does not rule out onychomycosis. When a nail specimen is harvested for microscopy and culture, the greater the volume of material submitted the greater the chance of a positive culture. The soft, macerated subungual debris gives the greatest load of fungal elements. A small (2 mm) bone or skin curette is useful for scraping underneath the nail plate.

Fungal elements can also be seen on histopathology of the nail plate and are easily identified by the periodic acid-Schiff stain. This method can have a much higher positivity rate for diagnosis of onychomycosis, but the disadvantage is the lack of culture confirmation.

PREVENTION

General measures

Dermatophytes are ubiquitous organisms found in the soil and on animals and humans. Thus patients can potentially be infected from anywhere, and it is impossible to strictly avoid the fungi. The key to preventing any fungal infection is to deny the organisms favourable conditions to flourish – that is, a warm, moist, protected environment. The feet and toenails should be kept relatively dry. Open shoes are ideal, allowing the toe and webs to air dry. After a shower, the feet and web spaces can be blow dried

with a hair dryer. People who must wear closed shoes and socks for work should choose styles that are more ventilated (e.g. fabric rather than leather construction). Heavy safety boots can be ventilated with grommets and perforations by a shoe maker.

Another practical approach is to sprinkle antifungal powder into shoes. This does not treat onychomycosis but may prevent reinfection after the patient has received adequate therapy. Older shoes, which are likely to carry the fungus, should be replaced. Hot washing of socks will reduce their fungal load.

Wearing thongs or shoes in public amenities such as swimming pools and change rooms may help avoid gross contamination of the feet with detritus, but incidental contact with fungus-infested surfaces is almost unavoidable. Thorough washing and drying of the feet is important to prevent the fungus flourishing.

Predisposing factors

Predisposing factors for onychomycosis include:

- age-related changes in the toenails
- diabetes
- HIV infection
- peripheral vascular disease
- peripheral neuropathies
- sporting activities
- traumatic nail problems
- pedal anatomical abnormalities.

Good control of diabetes and peripheral vascular disease is likely to keep the skin of the feet in good condition and thus reduce the risk of infection. Patients with diabetes, peripheral vascular disease or neuropathy should inspect their feet daily for problems including onychomycosis and tinea to allow prompt treatment. However, onychomycosis is exceedingly common, and clinicians should not equate its presence with any predisposing disease.

TREATMENT

Both topical and systemic options are available for the treatment of patients with onychomycosis. In most cases,

onychomycosis is not a major clinical problem, and no treatment is also a legitimate option.

Systemic agents have higher success rates than topical agents in treating onychomycosis and are typically safe but, like all drugs, may have side effects. Patients need to be happy to use a systemic agent with its inherent risks to treat an essentially cosmetic issue.

As an alternative to systemic therapy, superficial white onychomycosis and very mild cases of distal and lateral onychomycosis can be treated with topical agents. These act slowly and have significant failure rates. Patients should be reminded of the need to be persistent and regular in applying topical therapy and also to observe for worsening onychomycosis, at which time an oral agent may be considered.

The pharmacology of therapies for cutaneous fungal infections was discussed in a previous article in the June issue of *Medicine Today*.¹

Systemic therapy

The aim of treatment is a normal-looking nail. It is important to recognise that mycological cure is not equivalent to clinical cure. After the traditional three-month course of an oral antifungal agent, mycological cure is possible but the nail may still look abnormal. Patients need to recognise that the nails grow slowly, and even if there is no active infection, the nail plate may take many more months to grow out completely. Patients should be reassured when the proximal portion of the affected nail appears normal and clear of discolouration.

However, in practice, treatment failure is common after the prescribed three-month course. I consider it advisable to continue treatment until the abnormal nail grows out completely. Cost and exposure to the drug can be minimised by a pulsed regimen. A useful technique to monitor for treatment failure is for a line to be scored into the nail plate at the most proximal portion of the visible infection. The line should move distally with the

abnormal nail if mycological cure is achieved. If the chord of fungus grows proximal to the scored line then treatment failure is likely.

Terbinafine

Terbinafine is the most effective agent for dermatophyte onychomycosis. The standard dosing regimen for dermatophyte infection is 250 mg daily for six weeks for fingernail onychomycosis and 12 weeks for toenail disease. Multiple studies have shown the efficacy of this regimen, with a short-term mycological cure rate of about 76 to 78%.²

Another recommended approach is to 'pulse' the treatment, by giving 250 mg daily for one week every two to three months until the nail grows out. My preference is to administer the drug daily for one week every month, until the nail grows out to become normal.

When to commence therapy is arbitrary. PBS subsidisation is available for terbinafine if 80% of the great toenail is affected and the infection has been mycologically confirmed. Regardless of the extent of disease, I find it more timely and efficient to write a private script for terbinafine, as the relative cost of the medication is not prohibitive, and this avoids the requisite delay for cultures to be performed. Furthermore, culture often gives false-negative results, and repeated testing simply for PBS subsidisation is undesirable.

Itraconazole

Itraconazole is a relatively expensive agent when used for the treatment of onychomycosis. It is useful when:

- terbinafine is contraindicated
- the fungus is resistant to terbinafine, as determined by treatment failure, or
- a nondermatophyte mould is cultured.

Itraconazole is given at a dose of 400 mg daily for one week each month (seven doses each month). For mycological cure of common dermatophyte tinea, two to three pulses are required for fingernails, and three to four pulses for toenails. The

short-term mycological cure rate is up to 75%.² My preference is to pulse the therapy until the nail grows out to become clinically normal.

Itraconazole is fat-soluble and is best absorbed with a low pH environment in the stomach. If patients have relative achlorhydria or cannot take the medication with a main meal then an acidic drink (such as a cola soft drink) is useful in improving absorption. A new preparation of itraconazole was recently released in Australia with twice the potency, requiring only half the dose to achieve the same efficacy as the pre-existing preparation.

Fluconazole

Fluconazole is another alternative to terbinafine, although the mycological cure rate is much lower at only about 50%.² It is given as pulse therapy, with one dose per week for six months for fingernails and nine months for toenails. Doses in the literature range from 150 to 450 mg daily. My preference is to balance cost with effectiveness, using the 200 mg tablets weekly until the nails grow out completely normally.

Griseofulvin

Griseofulvin is the oldest oral antifungal available for onychomycosis. Being fungistatic rather than fungicidal, it is much less effective than terbinafine or the azoles. A dose of 0.5 to 1.0 mg daily is required for adults; 18 months of therapy may be required before complete clinical clearance of onychomycosis. The other agents discussed are more effective for treatment of onychomycosis.

Topical therapy

There are a number of topical nail kits currently available in Australia. Although easily accessible by patients as over-the-counter preparations, the cure rates from lengthy use of these agents are typically poor, achieving a mycological cure rate of less than 50% and a clinical cure rate of less than 10%. These topical treatments typically require physical preparation of the nail to aid absorption of the active

agent, as described below.

- Amorolfine lacquer is used weekly after sanding down the nail with a nail file.
- Bifonazole cream is applied after a week of nail preparation with urea cream to break down the hyperkeratotic nail plate and allow removal by scraping.
- Ciclopirox lacquer is applied directly to the nail surface, daily until cure, with no nail preparation required.
- Miconazole tincture is applied directly to the nail surface until cure.

Topical treatments may be useful for superficial white onychomycosis and very mild subungual onychomycosis but have little role in well-established distal and lateral subungual onychomycosis.

Physical therapies

Occasionally, the thickened or dystrophic nail plate may be removed for cosmesis or pain. Both surgical and chemical means are available, and should be used in conjunction with a systemic agent for effective cure. Referral to a dermatologist with an interest in nails would be useful.

Use of vascular lasers has been in vogue for the treatment of onychomycosis. The initial enthusiasm for this treatment has waned significantly as practitioners and patients found a low and inconsistent clearance rate.³ The mechanism of action appears to be thermal destruction of the fungal elements. However, patients are typically unable to tolerate the high temperature and duration of treatment required for effective fungicidal effect.

CONCLUSION

Onychomycosis is an exceedingly common type of fungal infection that is best treated with a systemic agent. Oral terbinafine is the most effective. Clinical cure is best achieved with an intermittent/pulsed regimen until the affected nail has grown out and been replaced completely with a normal nail plate. MT

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FURTHER READING

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