

CLINICAL REVIEW

Fungal nail infection: diagnosis and management

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Onychomycosis is the term used for fungal infections of nail. A recent review of population based studies of onychomycosis in Europe and the United States found a mean prevalence of 4.3%.¹ Onychomycosis can be a source of pain and discomfort and can impact on patients' quality of life, with psychosocial and physically detrimental effects.² Disease of the fingernails can cause impaired or lost tactile function, whereas disease of the toenails can interfere with walking, exercise, and how shoes fit. Untreated patients can act as source of infection for family members and potentially contaminate communal areas. Infection may be chronic and resistant to treatment, with 16-25% of patients not achieving cure by current treatments.³ No spontaneous clearing is known to occur. This review provides an evidence based overview of the diagnosis and management of onychomycosis.

What causes onychomycosis?

Onychomycosis is commonly caused by infection with dermatophytes, a group of three types of fungi that cause skin disease in both animals and humans—namely, *Microsporum*, *Epidermophyton*, and *Trichophyton*. When nail is affected by dermatophytes, this is referred to as tinea unguium. Around 90% of cases are related to *Trichophyton rubrum*⁴ followed by a complex of *Trichophyton interdigitale/mentagrophytes*. Onychomycosis can also be caused by non-dermatophyte moulds and by yeasts, commonly *Candida albicans*. The distribution of these pathogens is determined by geography, climate, and migration.

Who is at risk?

Onychomycosis is a multifactorial disease. Fungi are ubiquitous and damaged nail increases the risk of infection. Diabetes is an independent risk factor,⁵ with one third of patients with diabetes affected. A multicentre survey showed that patients with diabetes are twice as likely as those without diabetes to have onychomycosis.⁵ In patients with diabetes, diseased nail can injure surrounding skin, which may go unnoticed because of sensory neuropathy, and this can predispose to osteomyelitis, gangrene, and diabetic ulcers.

Increasing age also poses a risk, and in elderly people (aged >70 years) damaged nail can traumatise the skin and provide an entry point for bacteria or other pathogens, causing cellulitis.

Genetics has also been implicated as a risk factor, with *T rubrum* infection showing a familial pattern of autosomal dominant inheritance.⁶ Distal lateral onychomycosis caused by *T rubrum* was noted in a familial pattern unrelated to interfamilial transmission.

In a multicentre study, the odds of patients with psoriasis having onychomycosis was 56% greater than in those of the same age and sex without psoriasis, and prevalence of pedal onychomycosis was 13%.⁷ In an epidemiological study of 500 participants, the prevalence of onychomycosis in people with HIV was 23.2% and correlated with CD4 counts of 370/mm³.⁸ In a large series of patients with onychomycosis, 83.3% smoked two or more packets of cigarettes a day compared with 14.8% who were non-smokers,⁹ and peripheral arterial disease was another confounding risk factor.

External risk factors reported are increased participation in physical activity, increased exposure to wet work, ill fitting shoes, commercial swimming pools, working with chemicals, walking barefoot, and nail biting.¹⁰ Prevalence rates are also determined by occupation (athletes), climate, living environment, and frequency of travel.

How does it present?

Onychomycosis may involve a single nail or, in exceptional circumstances, all nails. Toenails are seven times more likely to be affected than fingernails. The first and fifth toenails are the most commonly affected, often following an episode of tinea pedis. Fingernail infection is, in contrast, usually associated with tinea corporis or capitis, and is often unilateral. Table 1↓ lists the different clinical presentations and common infectious agents implicated in onychomycosis.↓

How is it diagnosed?

Many disorders of nail can mimic onychomycosis (see box for differential diagnoses). It is therefore important to establish a diagnosis microbiologically before starting treatment. The clinical hallmarks of onychomycosis are that nail becomes friable and, owing to the way the fungus invades, characteristic spikes are often visible. They appear as yellow hyperkeratotic bands that progress proximally towards the matrix.

Summary points

- Friable nail plate and nail spikes (yellow hyperkeratotic bands) suggest onychomycosis
- Histopathology of nail clippings can be done easily and quickly and is an economical way to establish a pathogenic role of fungi; specimens can be sent without fixatives or transport medium and results are available in 3-5 days
- Treatment should not be started before confirmation of infection by mycology
- False negative rates for culture are 30%; therefore a negative test result cannot exclude infection and should be repeated if clinical suspicion is high
- Consider non-dermatophyte moulds if onychomycosis is unresponsive to antifungals, and if microscopy provides a positive result but cultures give negative results

Sources and selection criteria

We searched Medline, PubMed, the National Institute for Health and Care Excellence website, and the Cochrane Library for systematic reviews, meta-analyses, randomised and non-randomised controlled clinical trials, and case series and reports using the search words "fungal nail disease/infection", "tinea unguium", and "onychomycosis". We also consulted recent guidelines submitted for publication by the British Association of Dermatologists.

Differential diagnosis of onychomycosis

Psoriasis (fig 2)

- As in onychomycosis: onycholysis, subungual hyperkeratosis, splinter haemorrhages, leuconychia, dystrophy
- Pitting
- Oil drop sign (a translucent yellow-red discoloration seen in the nail bed)
- Other cutaneous features of psoriasis, family history of psoriasis

Lichen planus

- Cutaneous disease at other sites
- Thin nail plate and ridging
- Dorsal pterygium—scarring at proximal aspect of nail

Trauma

- Nail plate can appear abnormal
- Nail bed should be normal
- Distal onycholysis with repeated trauma
- Single nail affected, shape of nail changed, homogenous alteration of nail colour

Eczema

- Irregular buckled nails with ridging
- Cutaneous signs of eczema

Yellow nail syndrome

- Nail plate is discoloured green-yellow
- Nails are hard with elevated longitudinal curvature
- Nails may be shed, painful
- Associations with bronchiectasis, lymphoedema, and chronic sinusitis

Lamellar onychoschizia (lamellar splitting) (fig 3)

- History of repeated soaking in water
- Usually distal portion of nail

Periungual squamous cell carcinoma/Bowens disease

- Single nail, warty changes of nail fold, ooze from edge of nail

Malignant melanoma

- Black discolouration of nail plate or nail bed
- Pigment can extend onto nail fold
- Can get associated bleeding

Myxoid (mucous) cyst

- Cyst at base of nail, groove in nail extending length of nail

Alopecia areata

- Pits, longitudinal ridging, brittleness
- Hair loss

A recent review suggests carrying out at least two diagnostic

investigations to determine the penetration of the nail plate,¹⁴ usually microscopy and culture. Ideally the site should be cleaned with 70% ethanol before sample collection and the sampled material divided into two portions, one for microscopy and the other for culture. For transportation the samples should be stored in commercially available packs, sterile containers, or clean sheets of white paper folded and sealed. The type of onychomycosis will determine the site from which the diagnostic specimen is taken (table 1). Nail clippers can be used to obtain nail clippings of the nail plate (fig 5). Scrapings from subungual hyperkeratosis, nail bed, or nail plate, and surrounding or affected skin, should be taken using a small curette or number 15 scalpel blade. Sampling of the distal nail plate should be avoided because contamination is common. For proximal subungual onychomycosis, the healthy nail plate should be pared away with a number 15 blade and a sharp curette used to remove infected material from the nail bed closest to the lunula.¹⁶ Alternatively, a superficial punch biopsy of the proximal nail plate can be taken from the proximal onycholytic border without anaesthesia. This is a simple procedure that can be performed by a general practitioner.

The specimen can be immediately viewed using direct microscopy by applying potassium hydroxide preparations to small pieces of affected nail on a glass slide. The slide should be warmed over a Bunsen burner flame and a coverslip applied. The specimen can then be examined with $\times 400$ magnification using a normal bright field microscope. The presence of fungal hyphae, spores, or yeast forms should be determined to establish whether fungi are implicated. Direct microscopy is unable to identify particular fungi.

Culture can identify a specific fungus but results take 2-6 weeks to obtain and false negative rates are high (30%).¹⁷ If the clinical suspicion of onychomycosis is high then culture should be repeated. Sections of the nail samples can be directly stained with periodic acid Schiff for histopathological evaluation,¹⁸ which has been shown to be more sensitive (92%) than direct microscopy (80%) and culture (59%).¹⁹

How and when do you treat topically?

Indications for topical treatment include up to 50% involvement of the distal nail plate with lack of matrix involvement, three or four nails affected, and early distal and lateral subungual onychomycosis and superficial white onychomycosis.²⁰ Other considerations include the patient's age, as children's nails are thin and grow fast, prophylaxis in those at risk of recurrence, and whether oral treatment is contraindicated.

Amorolfine

Amorolfine 5% lacquer has broad spectrum fungicidal and fungistatic activity and has been recommended, according to proposed guidelines, for onychomycosis without matrix involvement and mild cases of distal and lateral disease of up to two affected nails.^{20 21} It is applied once or twice weekly (after nail filing) for six to 12 months. A recent multicentre, randomised, open label, controlled study noted complete cure in 12.7% of patients and mycological cure in 46.5% at 48 weeks.²²

Ciclopirox

Ciclopirox (widely available, but not available in the United Kingdom), which has broad spectrum antifungal activity, is available as an 8% lacquer and is applied once daily for 24 weeks on fingernails and for 48 weeks on toenails. A review of

findings from two well designed, double blinded, vehicle controlled, parallel group, multicentre studies showed mycological cure rates of 29% and 36%, compared with complete cure rates of 5.5% and 8.4%.²³ Amorolfine has not been directly compared with ciclopirox but cure rates seem to be lower with ciclopirox. The Cochrane Collaboration²⁴ suggests that amorolfine might be more effective. A recent multicentre, randomised controlled trial has shown that chemical avulsion of the nail combined with ciclopirox cream and nail lacquer is more effective than amorolfine nail lacquer alone, with clinical cure rates of 53.5% compared with 17% reported in groups receiving amorolfine.²² Side effects from lacquers include nail fold erythema, burning, and pruritus. These are usually temporary and transient but if severe, treatment should be stopped.

Less commonly used topical treatments

Other topical treatments which may be considered in a specialist setting include tioconazole, available as a 28% solution, which has shown cure rates of up to 22% in an open ended study.²⁵ Efinaconazole solution 10%, the first triazole antifungal, is applied once daily for 48 weeks. Two identical multicentre, randomised, double blind, vehicle controlled studies conducted in patients with distal lateral subungual onychomycosis showed greater complete cure with efinaconazole (17.8% and 15.2%) compared with vehicle (3.3% and 5.5%).²⁶ This product has been approved in Canada but is still pending approval in the United States.

What systemic options are available?

Despite the availability of various systemic treatments for onychomycosis (table 2) the search for an ideal agent is ongoing. Even with optimal management, mycological cure rates are about 30% and treatment failure rates are at least 25%.¹⁰ When choosing treatment, consideration needs to be given to the patient's age and health, cost, compliance, side effects, and drug interactions, and the type and site of infection. Oral treatments are generally more effective than topical ones; however, they have more adverse effects and interactions. Oral treatment is recommended with proximal subungual onychomycosis, when at least 50% of the nail plate is affected, where the nail matrix or multiple nails are involved, and if there has been no response to topical treatment after six months.²¹ The two main systemic drugs indicated for the treatment of onychomycosis are terbinafine and itraconazole, but terbinafine should be considered as first line treatment because of lower drug interactions than itraconazole and because it is superior both in vivo and in vitro for dermatophyte onychomycosis. Other systemic therapeutic options include griseofulvin, which remains the only licensed option in children, and fluconazole, used as a third line agent; both are considered below.

Terbinafine

Terbinafine is both fungistatic and fungicidal, with lower activity against *Candida* species. It is given as 250 mg daily for six weeks for fingernails and for 12-16 weeks for toenails. Patients should be re-evaluated three to six months after the start of treatment, the period required for outgrowth of healthy nail. Further treatment should be given if disease persists as the optimal clinical effect is seen some months after mycological cure and cessation of treatment. Trials have investigated pulsed terbinafine 500 mg daily for one week every month for three consecutive months. A large randomised trial has shown mycological cure of 70.9% (continuous) compared with 58.7%

(pulsed) at 18 months.²⁹ Variable success has been shown by other trials studying pulsed or intermittent terbinafine, which would offer a viable option for reducing both the cost and the side effects of treatment. Terbinafine should not be used in patients with chronic or active liver disease. Baseline liver function testing is recommended according to the package insert and periodic monitoring (4-6 weeks) is suggested. Terbinafine should be discontinued immediately in the case of increased liver function.³⁰

Itraconazole

Itraconazole is thought to be a fungistatic agent and is active against yeast, dermatophytes, and non-dermatophyte moulds. However, it is less active against dermatophytes than terbinafine. Persistence of itraconazole in the nail plate makes intermittent dosing regimens as effective as daily dosing. In a multicentre randomised trial, intermittent treatment resulted in equal mycological and higher clinical cure compared with continuous treatment.³¹ Itraconazole can therefore be given as 200 mg a day (12 weeks for toenails, six weeks for fingernails) or as a monthly pulsed treatment of 400 mg a day for one week of each month (two pulses for fingernails, three pulses for toenails). Itraconazole is contraindicated in those with heart failure or liver abnormalities. Patients receiving continuous treatment for longer than one month should have their liver function tested; however, no monitoring is required for the pulse regimen unless there is a history of hepatic disease, other hepatotoxic drugs, or abnormal liver function at baseline, or if signs or symptoms develop at any time to suggest liver dysfunction.³²

Several studies have looked at the efficacy rates for terbinafine compared with itraconazole. A multicentre randomised trial showed cure in 55% (continuous terbinafine for 16 weeks) compared with 26% (pulsed itraconazole) at 72 weeks' follow-up.³³ A cumulative meta-analysis of systemic antifungal agents for onychomycosis confirmed these findings.³⁴ Lower recurrence rates have also been noted with terbinafine in a meta-analysis comparing terbinafine with itraconazole.³⁵ A recent review reported a synergistic action between itraconazole and terbinafine, and combination treatment may result in better eradication than monotherapy, and may also prevent recurrence of infection.³⁶

Griseofulvin

Griseofulvin has lower efficacy and higher relapse rates than either terbinafine or itraconazole but is the only agent licensed for children. It is indicated when the other drugs are unavailable or contraindicated. Griseofulvin is contraindicated in severe hepatic disease but may be used in mild impairment with regular monitoring of liver function. Doses in adults are 500-1000 mg daily for 6-9 months for fingernails and 12-18 months for toenails.¹¹

Fluconazole

Fluconazole, although not licensed for onychomycosis, remains a potential third line treatment. It is cheap, has good compliance rates owing to weekly dosing, and has few drug interactions. It is highly effective against both dermatophytes and *Candida* species. Many studies have evaluated its efficacy in onychomycosis and, based on a systematic review,³⁷ mycological cure rates between 36% and 100% are reported. A recent meta-analysis recommended a dosage of 150 mg weekly for more than six months for onychomycosis.³⁸ Fluconazole seems to be less effective (31% cure) than either itraconazole (61%) or terbinafine (75%)³⁷ but comparative trials are few.³⁹

New second generation triazoles include voriconazole, posaconazole, ravuconazole, albaconazole, and pramiconazole. They may play a useful role in immunocompromised hosts, where there is resistance to standard treatment, and in the treatment of non-dermatophyte moulds.¹¹

What is the role of nail avulsion and debridement?

Nail avulsion (complete removal) or debridement (partial removal) can be useful in severe onychomycosis, extensive nail thickening, or longitudinal streaks or spikes. These changes can cause a dermatophytoma, representing a granulated nidus of infection, which responds poorly to medical treatment. Avulsion and debridement can help reduce fungal mass and increase the penetration of antifungal treatment. Chemical avulsion involves dissolving the bond between the nail plate and the nail bed, and softens the nail plate.⁴⁰ Agents such as 40% urea or 20% urea with 10% salicylic acid, are recommended for the treatment of single nail disease and are applied with a topical antifungal (1% bifonazole⁴¹ or 1% fluconazole⁴²) under occlusion for 1-2 weeks, after which the diseased nail can be removed with a nail elevator or clipper. Surgical avulsion involves separating the nail plate from the nail bed using a nail elevator device. This is an option for disease resistant to topical and systemic antifungals. It is usually followed by a course of systemic antifungals.

Debridement involves partial removal of the nail. In a randomised controlled trial a combination of debridement and 8% ciclopirox lacquer resulted in better (77%) mycological cure than debridement alone (0%).⁴³

Is there a role for combination treatments?

Topical ciclopirox, amorolfine, and imidazoles have been used in combination with systemic antifungal agents. In toenail onychomycosis an open randomised trial showed mycological cure rates of 83% for oral itraconazole combined with amorolfine lacquer compared with 41% for itraconazole alone for 12 weeks.⁴⁴ Similar benefits were shown with terbinafine.⁴⁵ Evidence is sufficient to recommend combination treatment in cases where response to monotherapy may be poor, as is the case in proximal nail disease, treatment failure, or involvement of more than 50% of the nail plate.²⁰

What about yeasts and non-dermatophyte moulds?

Candida accounts for 5-10% of all cases of onychomycosis. Itraconazole should be considered as the first line agent for *Candida* species, and fluconazole (although unlicensed) can be used as an alternative. Terbinafine is an effective agent, with cure rates of 70-85% after 48 weeks of treatment with 250 mg daily noted in a series of 65 patients with onychomycosis caused by *C albicans*, *C parasilosis*, or *S brevicaulis*.⁴⁶ Non-dermatophyte moulds are difficult to treat. A recent review⁴⁷ concluded that the best treatment option may be systemic or topical treatment combined with periodic chemical or surgical debridement or avulsion.

What are the treatment options in children?

The prevalence of onychomycosis in children in the United Kingdom has been reported at 0.2%.⁴⁸ Toenails are usually

affected and the most common presentation is distal subungual onychomycosis. In children, concomitant tinea capitis and tinea pedis should be excluded, and parents and siblings should be examined to exclude infection. Topical treatment of onychomycosis is often advocated but not licensed in children, and no clinical trials show efficacy in this population.¹¹ Griseofulvin is licensed for children but is no longer recommended as first line treatment owing to long treatment duration and poor efficacy.¹¹ Terbinafine is licensed in some countries for use in tinea capitis and can be used in children older than 2 years and with a body weight of more than 12 kg. Children should be referred for specialist review and initiation of treatment. They can, if there are no contraindications, be treated as for adults, using terbinafine, itraconazole, or fluconazole with dose adjusting according to weight and age. None of these treatments are licensed for use in children, but efficacy and safety have been published recently in a systematic review.⁴⁹

Do patients with diabetes or immunosuppression require different treatment?

In patients with diabetes, terbinafine is the treatment of choice and is preferred over itraconazole, which is contraindicated in heart failure. Owing to drug interactions, itraconazole can also induce hypoglycaemia in patients with diabetes. Topical treatments should be considered to avoid the potential for drug interactions with antidiabetic drugs. Terbinafine and fluconazole are the agents of choice in patients with HIV as they interfere least with antiretrovirals.

How do I know if treatment is successful?

Cure of onychomycosis has been defined as the absence of clinical signs or the presence of a negative culture result, with or without negative microscopy results, after an adequate wash-out period of 3–6 months.⁵⁰ Even with optimal management 25% to 30% of patients will relapse after initial cure.⁵¹ After three months of treatment, most toenails will still look abnormal after systemic treatment. If normal nail is emerging proximal to the dystrophic nail, a scratch can be made with a scalpel blade at the base of the dystrophy. If the dystrophic nail remains distal to the scratch as it grows out no further treatment is required, but if the dystrophy moves proximal to the scratch then this indicates ongoing infection and further treatment. Serial photography is a helpful additional monitoring tool.

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When should I refer?⁵²

Patients should be referred if:

- There is coexistent nail disease (psoriasis or lichen planus)
- Onychomycosis is suspected but microscopy and culture give negative results
- Response to treatment is inadequate
- The diagnosis is uncertain
- Disease recurs or there is a relapse
- The nail plate or nail bed shows black discolouration (to exclude nail apparatus melanoma)
- They are children or young people (<18 years)
- The host is immunocompromised

Poor prognostic factors^{53 54}

These factors may influence treatment type (topical, oral, combination, surgery), length of treatment, duration of treatment, and follow-up:

- Lateral edge involvement
- Area of nail involvement >50%
- Nail thickness >2 mm
- Matrix involvement
- Onycholysis, paronychia, discolouration, dermatophytoma
- Slow nail growth
- Positive culture results at six month follow-up
- Diabetes, peripheral vascular disease, immunosuppression
- The presence of non-responsive organisms, such as *Scytalidium*

New tests and treatments on the horizon**Diagnosis**

Dermatophyte test strip: visualises mycotic antigens extracted from nail samples by immunochromatography⁵⁵

Flow cytometry generates distinct profiles for fungi invading the nail plate

Real time polymerase chain reaction assays can detect and identify dermatophytes in less than two days

Scanning electron microscopy and confocal microscopy

Treatment

Techniques to improve topical delivery of antifungals, including phonophoresis, manual and electrical nail abrasion, acid etching, microporation, ultrasonography, laser nail ablation, and iontophoresis

Technologies to improve drug uptake by fungi: transferosome vesicles (TDT 067), boosted antifungal topical treatment (BATT), and boosted oral antifungal therapy (BOAT)

Lasers approved for the management of onychomycosis include Nd:YAG short pulse and Q switch 1064 nm and the diode 870, 930, and 980 nm⁵⁶ (no randomised controlled trials as yet)

Photodynamic therapy has been shown in a single centre open trial to achieve cure rates of 44% at 12 months⁵⁷

Topical germicidal ultraviolet C light⁵⁸

Additional educational resources**Resources for healthcare professionals**

National Institute for Health and Care Excellence. Fungal nail infection. 2009 (<http://cks.nice.org.uk/fungal-nail-infection>)—Overview of onychomycosis and extensive review of evidence on treatments

Cochrane Summaries. 2009 (<http://summaries.cochrane.org/CD001434/creams-lotions-and-gels-topical-treatments-for-fungal-infections-of-the-skin-and-nails-of-the-foot>)—Discusses creams, lotions, and gels (topical treatments) of fungal infections of the skin and nails of the foot

British Journal of Dermatology. Guidelines for treatment of onychomycosis. 2003 (www.bad.org.uk/Portals/_Bad/Guidelines/Clinical%20Guidelines/Onychomycosis)—Detailed guidelines on the management of onychomycosis

Resources for patients

Dermnet NZ (www.dermnetnz.org/doctors/fungal-infections/tinea-unguim.html)—Provides a summary of causes, diagnosis, clinical appearances, and treatment of onychomycosis

British Association of Dermatologists (www.bad.org.uk/site/820/Default.aspx)—Overview of fungal nail infection: causes, clinical appearances, diagnosis, and management

WebMD (www.webmd.com/skin-problems-and-treatments/tc/fungal-nail-infections)—Treatment overview for fungal nail infection

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Tables

Table 1 | Clinical presentations of onychomycoses¹¹⁻¹³

Type of onychomycosis	Clinical appearance	Cause	Sampling site
Distal and lateral subungual onychomycosis (fig 1)	Hyperkeratosis of undersurface of distal nail plate and bed; onycholysis; dyschromias; one hand-two foot syndrome; tinea pedis often present	<i>Trichophyton rubrum</i> , <i>Trichophyton mentagrophytes</i> , <i>Trichophyton tonsurans</i> , <i>Epidermophyton floccosum</i>	Nail bed and underside of nail plate; nail clippings
Superficial white onychomycosis	Crumbling white lesions on nail surface; most common in children	<i>T mentagrophytes</i> , <i>Aspergillus</i> , <i>Acremonium</i> , <i>Aspergillus</i> , <i>Fusarium</i>	Surface scrape of white friable area
Proximal (white) subungual onychomycosis	Infection begins in proximal nail fold and distal portion normal; AIDS (gross white discoloration; leukonychia of proximal nail; nail plate surface normal early on	<i>T rubrum</i> , <i>Trichophyton megnini</i> , <i>Trichophyton schoenleinii</i> , <i>E floccosum</i>	Curette deeper nail plate and proximal nail bed (pare normal nail plate first); may need biopsy
Endonyx onychomycosis	Milky white discoloration; no subungual hyperkeratosis or onycholysis	<i>Trichophyton soudanense</i> , <i>Trichophyton violaceum</i>	Nail clipping
Candida onychomycosis:			
Paronychia	Swollen periungual skin, painful, bacterial superinfection, or nail plate disease	<i>Candida</i> species	Proximal and lateral edges; undersurface of nail
Distal nail infection	Onycholysis and subungual hyperkeratosis, fingernails, or vascular abnormality		
Total dystrophic onychomycosis	Gross thickening and hyperkeratosis		
Total dystrophic onychomycosis	Complete destruction of nail plate	Any of above; <i>Candida</i> in immunocompromised people	
Mixed	Different patterns in same individual		
Mould	Few specific clinical features; often one nail with previous disease or trauma; toenails; absence of tinea pedis	<i>Scopulariopsis brevicaulis</i> , <i>Neoscytalidium dimidiatum</i> , <i>Aspergillus</i> , <i>Acremonium</i> , <i>Fusarium</i> , <i>Neoscytalidium hyalinum</i>	

Table 2| Summary of systemic drug treatments in adults^{27 28}

Treatment and dose	Contraindications	Cautions/advice	Blood monitoring
First line treatment: itraconazole:			
200 mg/day: 6 weeks for fingernails, 12 weeks for toenails; 400 mg/day for one week a month (pulse): two pulses for fingernails, three pulses for toenails	Chronic and active liver disease; congestive heart failure or ventricular dysfunction; concomitant benzodiazepines, HMG-CoA reductase inhibitors, quinidines, pimozide; pregnancy (category C*); breast feeding	Take with food; numerous drug interactions including hypoglycaemics and antiretrovirals	Liver function test for continuous treatment only and repeat 4-6 weekly; no liver function test for pulsed treatment
First line treatment: terbinafine:			
250 mg/day: 6 weeks for fingernails, 12-16 weeks for toenails	Chronic or active liver disease; breast feeding; pregnancy (category B†)	Stop if AST/ALT increase to 2×normal; if creatinine clearance <50 mL/min or creatinine >300 µmol/L then half normal dose; caution with known autoimmune disorders	Liver function test and full blood count before treatment; monitor with liver function test and full blood count every 4-6 weeks
Fluconazole (unlicensed):			
150 mg/week: 6-9 months for fingernails, 9-18 months for toenails	Renal and hepatic impairment; benzodiazepines (increase sedation); terfenadine, cisapride, astemizole, pimozide, quinidine, or erythromycin; pregnancy (category C*); breast feeding	Many drug interactions; lactose allergen in some preparations; not approved for onychomycosis in United States, Canada, and Australia	Baseline liver function test and full blood count; liver function test if high dosages given, prolonged treatment, concomitant hepatotoxic drugs
Griseofulvin:			
500-1000 mg/day: 6-9 months for fingernails, 12-18 months for toenails	Severe liver impairment; porphyria; lupus erythematosus; pregnancy (category C*); men fathering a child for 6 months after therapy	Take with fatty food; drug interactions (oral contraceptive, anticoagulant, phenobarbital); no longer treatment of choice	Monitor with liver function test regularly if mild hepatic impairment

AST=serum aspartate aminotransferase; ALT=serum alanine aminotransferase.

*Animal reproduction studies have shown an adverse effect on the fetus but there are no adequate and well controlled studies in pregnant women.

†Animal reproduction studies have failed to show a risk to the fetus but there are no adequate and well controlled studies in pregnant women.

Figures



Fig 1 Onychomycosis of toenails showing mixed pattern in same patient—both distal and lateral subungual onychomycosis and superficial white onychomycosis

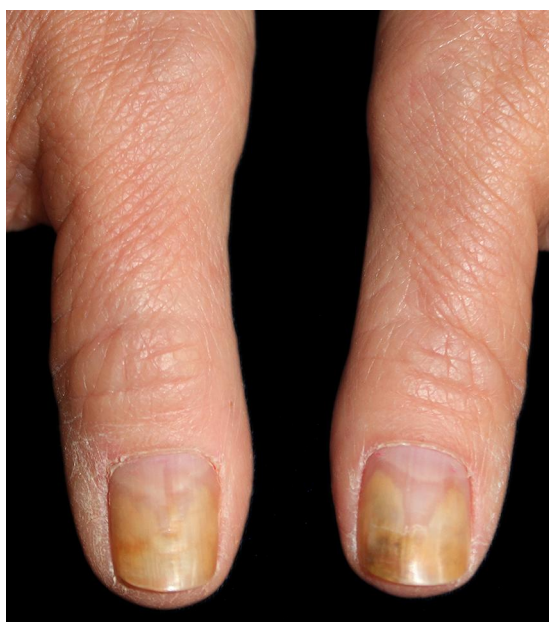


Fig 2 Psoriasis of nails, with irregular proximal border and brown onychodermal band. As with fungal infection, nail surface is not friable



Fig 3 Lamella onychoschizia in patient with history of repeated soaking of hands in water



Fig 4 Nail spike showing yellow hyperkeratotic band progressing proximally towards matrix, characteristic of fungal infection of nail, with associated tinea pedis. Cultures confirmed *Trichophyton rubrum*

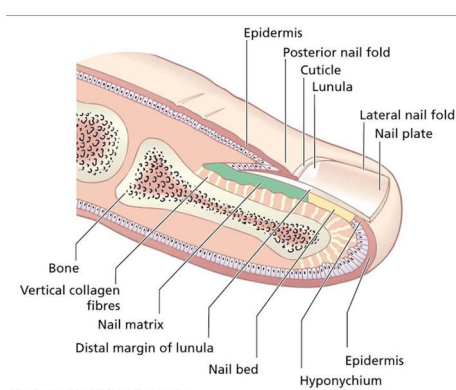


Fig 5 Longitudinal section of nail apparatus. Reproduced from Burns et al,¹⁵ with permission of Wiley-Blackwell