

## GUIDELINES

# Guidelines for treatment of onychomycosis

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### Summary

These guidelines for management of onychomycosis have been prepared for dermatologists on behalf of the British Association of Dermatologists. They present evidence-based guidance for treatment, with identification of the strength of evidence available at the time of preparation of the guidelines, and a brief overview of epidemiological aspects, diagnosis and investigation.

### Disclaimer

These guidelines have been prepared for dermatologists on behalf of the British Association of Dermatologists and reflect the best data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

### Introduction

Onychomycosis is one of the commonest dermatological conditions. A large questionnaire survey of 10 000 people suggested a prevalence of 2.71% in the U.K.<sup>1,2</sup> More recent mycologically controlled surveys in Finland<sup>3</sup> and in the U.S.A.<sup>4</sup> indicate a prevalence of between 7 and 10%. Increasing publicity about disease prevalence, and the advent of new and more effective antifungal drugs, has led to a greater enthusiasm

among sufferers to seek treatment and among medical practitioners to institute therapy. However, treatment is often prescribed without mycological confirmation of infection, there may be confusion as to whether fungi isolated on culture are primary or secondary pathogens, the relative efficacy of different antifungal agents against different fungi is not completely understood and drugs are often prescribed for inappropriate treatment durations.

### Definition

Onychomycosis is an infection of the nail apparatus by fungi that include dermatophytes, nondermatophyte moulds and yeasts (mainly *Candida* species). The toenails are affected in 80% of all cases of onychomycosis; dermatophyte infection, mostly due to *Trichophyton rubrum*, is the cause in over 90% of cases.<sup>5</sup>

Onychomycosis is classified clinically as distal and lateral subungual onychomycosis (DLSO), superficial white onychomycosis (SWO), proximal subungual onychomycosis (PSO), candidal onychomycosis and total dystrophic onychomycosis.

### Distal and lateral subungual onychomycosis

DLSO accounts for the majority of cases and is almost always due to dermatophyte infection. It affects the hyponychium, often at the lateral edges initially, and spreads proximally along the nail bed resulting in subungual hyperkeratosis and onycholysis although the nail plate is not initially affected. DLSO may be

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confined to one side of the nail or spread sideways to involve the whole of the nail bed, and progresses relentlessly until it reaches the posterior nail fold. Eventually the nail plate becomes friable and may break up, often due to trauma, although nail destruction may be related to invasion of the plate by dermatophytes that have keratolytic properties. Examination of the surrounding skin will nearly always reveal evidence of tinea pedis. Toenail infection is an almost inevitable precursor of fingernail dermatophytosis, which has a similar clinical appearance although nail thickening is not as common.

### Superficial white onychomycosis

SWO is also nearly always due to a dermatophyte infection, most commonly *T. mentagrophytes*. It is much less common than DLSO and affects the surface of the nail plate rather than the nail bed. Discoloration is white rather than cream and the surface of the nail plate is noticeably flaky. Onycholysis is not a common feature of SWO and intercurrent foot infection is not as frequent as in DLSO.

### Proximal subungual onychomycosis

PSO, without evidence of paronychia, is an uncommon variety of dermatophyte infection often related to intercurrent disease. Immunosuppressed patients, notably those who are human immunodeficiency virus-positive, may present with this variety of dermatophyte infection; conditions such as peripheral vascular disease and diabetes also may present in this way. Evidence of intercurrent disease should therefore be considered in a patient with PSO.

### Candidal onychomycosis

Infection of the nail apparatus with *Candida* yeasts may present in one of four ways: (i) chronic paronychia with secondary nail dystrophy; (ii) distal nail infection; (iii) chronic mucocutaneous candidiasis; and (iv) secondary candidiasis.

Chronic paronychia of the fingernails generally only occurs in patients with wet occupations. Swelling of the posterior nail fold occurs secondary to chronic immersion in water or possibly due to allergic reactions to some foods, and the cuticle becomes detached from the nail plate thus losing its water-tight properties. Microorganisms, both yeasts and bacteria, enter the subcuticular space causing further swelling of the posterior nail fold

and further cuticular detachment, i.e. a vicious circle. Infection and inflammation in the area of the nail matrix eventually lead to a proximal nail dystrophy.

Distal nail infection with *Candida* yeasts is uncommon and virtually all patients have Raynaud's phenomenon or some other form of vascular insufficiency. It is unclear whether the underlying vascular problem gives rise to onycholysis as the initial event or whether yeast infection causes the onycholysis. Although candidal onychomycosis cannot be clinically differentiated from DLSO with certainty, the absence of toenail involvement and typically a lesser degree of subungual hyperkeratosis are helpful diagnostic features.

Chronic mucocutaneous candidiasis has multifactorial aetiology leading to diminished cell-mediated immunity. Clinical signs vary with the severity of immunosuppression, but in more severe cases gross thickening of the nails occurs, amounting to a *Candida* granuloma. The mucous membranes are almost always involved in such cases.

Secondary candidal onychomycosis occurs in other diseases of the nail apparatus, most notably psoriasis.

### Total dystrophic onychomycosis

Any of the above varieties of onychomycosis may eventually progress to total nail dystrophy where the nail plate is almost completely destroyed.

### Diagnosis

This section follows the criteria set out by Evans and Gentes.<sup>6</sup> Treatment should not be instituted on clinical grounds alone. Although 50% of all cases of nail dystrophy are fungal in origin it is not always possible to identify such cases accurately. Treatment needs to be administered long-term and enough time must elapse for the nail to grow out completely before such treatment can be designated as successful. Toenails take around 12 months to grow out and fingernails about 6 months. This is far too long to await the results of therapeutic trial and, in any case, treatment is not always successful. If the diagnosis is not confirmed, and improvement does not occur, it is impossible to tell whether this represents treatment failure or an initial incorrect diagnosis. Although the cost of diagnostic tests may be deemed high at times of budgetary constraint, the cost is always small relative to inappropriate and unnecessary treatment.

Laboratory diagnosis consists of microscopy to visualize fungal elements in the nail sample and

culture to identify the species concerned. The success or otherwise of such tests depends upon the quality of the sample, the experience of the microscopist and the ability of the laboratory to discriminate between organisms that are likely pathogens, organisms growing in the nail as saprophytes, and contamination of the culture plate.

Given that dermatophyte onychomycosis is primarily a disease of the nail bed rather than of the nail plate, subungual debris taken from the most proximal part of the infection is likely to yield the best results. In DLSO material can be obtained from beneath the nail: a small dental scraper is most useful for this purpose. If the nail is onycholytic then this can be cut back and material can be scraped off the underside of the nail as well as from the nail bed. As much material as possible should be submitted to the laboratory because of the relative paucity of fungal elements within the specimen. In SWO the surface of the infected nail plate can be scraped and material examined directly. PSO is rare and again should be scraped with a scalpel blade. However, punch biopsy to obtain a sample of the full thickness of nail together with the nail bed may be necessary. Some of the material obtained is placed on a glass slide and 20% potassium hydroxide added. Fifteen to 20 min should be allowed to elapse before examining the sample by direct microscopy. The addition of Parker's blue/black ink may enhance visualization of the hyphae. An inexperienced observer may very well misdiagnose cell walls as hyphae and care should be taken to examine all of the specimen as fungal elements within the material may be very scanty.

The remaining material should be cultured on Sabouraud's glucose agar, usually with the addition of an antibiotic. The culture plate is incubated at 28 °C for at least 3 weeks before it is declared negative, as dermatophytes tend to grow slowly.

Direct microscopy can be carried out by the clinician, and higher specialist training includes teaching of this technique. However, nail microscopy is difficult and should only be carried out by those who do it on a regular basis. Fungal culture should always be carried out in a laboratory experienced in handling mycology specimens, because of potential pitfalls in interpretation of cultures. It must be remembered that the most common cause of treatment failure in the U.K. is incorrect diagnosis, which is usually made on clinical grounds alone. This should not be further compounded by incorrect laboratory interpretation of results.

Histology is almost never required and its use is usually confined to other causes of nail dystrophy.

Such dystrophies, notably psoriasis, regularly yield *Candida* yeasts on culture but they are rarely causal in aetiology of fungal nail infection.

## Reasons for treatment

Although dermatophyte onychomycosis is relentlessly progressive there remains a view among some practitioners that it is a trivial cosmetic problem that does not merit treatment. In the elderly the disease can give rise to complications such as cellulitis and therefore further compromise the limb in those with diabetes or peripheral vascular disease. While these complications may not be common they are certainly serious. The high prevalence of the disease is the result of heavy contamination of communal bathing places<sup>7</sup> by infected users; disinfecting the floors of such facilities is very difficult because fungal elements are protected in small pieces of keratin. It is therefore logical to try to reduce the number of infected users by effective treatment and thus reduce disease prevalence. Finally, onychomycosis is a surprisingly significant cause of medical consultation and of absence from work.<sup>8</sup>

Onychomycosis should not therefore be considered a trivial disease, and there is a sound case for treatment on the grounds of complications, public health considerations and effect on quality of life.

## Treatment

### Introduction

Both topical and oral agents are available for the treatment of fungal nail infection. The primary aim of treatment is to eradicate the organism as demonstrated by microscopy and culture. This is defined as the primary end-point in almost all properly conducted studies. Clinical improvement and clinical cure are secondary end-points based on a strict scoring system of clinical abnormalities in the nail apparatus. It must be recognized that successful eradication of the fungus does not always render the nails normal as they may have been dystrophic prior to infection. Such dystrophy may be due to trauma or nonfungal nail disease; this is particularly likely in cases where yeasts or nondermatophyte moulds (secondary pathogens and saprophytes, respectively) are isolated.<sup>9</sup>

Invariably mycological cure rates are about 30% better than clinical cure rates in the majority of studies, the clinical cure rates often being below 50%. Publications of clinical trials in onychomycosis are often

criticized for quoting mycological cure rates and thus overemphasizing the efficacy of treatment. While it is understood that the patient is more concerned with improvement in the clinical appearance of the nail rather than eradication of the organism, questions regarding patients' satisfaction at the end of a study usually mirror very closely the mycological cure rate. This suggests that eradication of the organism does restore the nail to its previous state prior to infection even though that state may not be completely 'normal' as defined by a scoring system.

Systemic therapy is almost always more successful than topical treatment, which should only be used in SWO, possibly very early DLSO or when systemic therapy is contraindicated.

#### *Topical therapy*

There are several topical antifungal preparations available both as prescription-only medicines and on an over-the-counter basis. The active antifungal agent in these preparations is either an imidazole, an allylamine or a polyene, or a preparation that contains a chemical with antifungal, antiseptic and sometimes keratolytic properties such as benzoic acid, benzyl peroxide, salicylic acid or an undecenoate. Products that are specifically indicated for nail infection are available as a paint or lacquer that is applied topically. There are four such preparations (Table 1).

There are no published studies on the efficacy of salicylic acid (Phytex<sup>®</sup>; Pharmax, Bexley, U.K.) and methyl undecenoate (Monphytol<sup>®</sup>; LAB, London, U.K.) in fungal nail infection and their use cannot be recommended.

Amorolfine (Loceryl<sup>®</sup>; Galderma, Amersham, U.K.) nail lacquer has been shown to be effective in around 50% of cases of both fingernail and toenail infection in a large study where only cases with infections of the distal portion of the nail were treated.<sup>10</sup> There are several published studies examining the efficacy of tioconazole (Trosyl<sup>®</sup>; Pfizer, Sandwich, U.K.) nail solution, with very variable results ranging from cure rates of around 20% up to 70%.<sup>11</sup> While it is clearly possible

to achieve clinical and mycological cure with topical nail preparations, these cure rates do not compare favourably with those obtained with systemic drugs. Currently, topical therapy can only be recommended for the treatment of SWO and in very early cases of DLSO where the infection is confined to the distal edge of the nail.

A combination of topical and systemic therapy may improve cure rates still further or possibly shorten the duration of therapy with the systemic agent. Thus far the results of such studies are inconclusive. A study comparing terbinafine and amorolfine with terbinafine alone produced somewhat idiosyncratic results<sup>12</sup> and was not properly blinded, so further evidence from well-controlled double-blind studies is required before combination therapy can be advocated.

Although there are no studies comparing one topical preparation with another in a properly controlled fashion, it is likely that amorolfine nail lacquer (Loceryl<sup>®</sup>) is the most effective preparation of those available.

#### *Systemic therapy*

The three drugs currently licensed for general use in onychomycosis are listed in Table 2. The two other systemic agents available for oral use, ketoconazole and fluconazole, are not licensed for nail infection. Ketoconazole may be used in some recalcitrant cases of yeast infection affecting the nails but cannot be prescribed for dermatophyte onychomycosis because of problems with hepatotoxicity. The use of fluconazole thus far has concentrated on vaginal candidiasis and systemic yeast infections although it is active against dermatophytes. There are some published studies of its use in nail infection but the dose and duration of treatment are not yet clear and it is not licensed for this indication in the U.K., nor does it appear likely to be so in the near future.

*Griseofulvin.* Griseofulvin (Fulcin<sup>®</sup>; Grisovin<sup>®</sup>; Glaxo-SmithKline, Uxbridge, U.K.) is weakly fungistatic, and acts by inhibiting nucleic acid synthesis, arresting cell

**Table 1.** Topical agents for onychomycosis, with strength of recommendation and quality of evidence grading

Agent	Strength of recommendation and quality of evidence
Amorolfine (Loceryl <sup>®</sup> ; Galderma, Amersham, U.K.) nail lacquer	Strength of recommendation B, Quality of evidence II-ii
Tioconazole (Trosyl <sup>®</sup> ; Pfizer, Sandwich, U.K.) nail solution	Strength of recommendation C, Quality of evidence II-iii
Salicylic acid (Phytex <sup>®</sup> ; Pharmax, Bexley, U.K.) paint	Strength of recommendation E, Quality of evidence IV
Undecenoates (Monphytol <sup>®</sup> ; LAB, London, U.K.) paint	Strength of recommendation E, Quality of evidence IV

**Table 2.** Systemic agents for onychomycosis, with major advantages and disadvantages, and strength of recommendation and quality of evidence grading

Drug	Advantages	Disadvantages	Main drug interactions	Strength of recommendation, quality of evidence
Griseofulvin	Licensed in both adults and children, inexpensive, extensive experience	Lengthy treatment necessary in both fingernail and toenail infection; poor cure rates; high relapse rates; no paediatric formulation currently available; contraindicated in lupus erythematosus, porphyria and severe liver disease	Warfarin, ciclosporin, oral contraceptive pill	B-I
Terbinafine <sup>a</sup>	Fungicidal; high cure rates (compared with griseofulvin); short duration of therapy; good compliance	No U.K. licence for children; no suspension formulation; idiosyncratic liver and skin reactions; reversible taste disturbance in 1 : 400 patients	Plasma concentrations reduced by rifampicin, increased by cimetidine	A-I
Itraconazole <sup>a</sup>	Active against <i>Candida albicans</i> ; pulsed treatment regimens are possible	Less effective in dermatophyte onychomycosis than terbinafine; monitoring of liver function required for treatment durations of longer than 1 month; not licensed for use in children and contraindicated in pregnancy	Enhanced toxicity of anticoagulants (warfarin), antihistamines (terfenadine and astemizole), antipsychotics (sertindole), anxiolytics (midazolam), digoxin, cisapride, ciclosporin and simvastatin (increased risk of myopathy); reduced efficacy of itraconazole with concomitant use of H2 blockers, phenytoin and rifampicin	A-I

<sup>a</sup>Terbinafine has better cure rate and lower relapse rate than itraconazole for dermatophytes (A-I).

division and inhibiting fungal cell wall synthesis.<sup>13–15</sup> It is available in tablet form and is the only antifungal agent licensed for use in children with onychomycosis, with a recommended dose for age groups of 1 month and above of 10 mg kg<sup>-1</sup> daily. It requires to be taken with fatty food to increase absorption and aid bioavailability. In adults the recommended dose is 500 mg daily given for 6–9 months in fingernail infection and 12–18 months in toenail infection. Mycological cure rates in fingernail infection are reasonably satisfactory at around 70% but griseofulvin is a disappointing drug in toenail disease where cure rates of only 30–40% can be expected.<sup>16</sup>

It is generally recognized that 500 mg daily is too small a dose for nail infection and 1 g daily is most often prescribed, but there is no certain evidence that this improves cure rates in toenail infection. Although the cost of griseofulvin is very low, its poor cure rate, often necessitating further treatment, suggests that its cost/efficacy ratio is relatively high. Both direct and historical comparison with studies of the newer antifungal agents terbinafine<sup>17–19</sup> and itraconazole<sup>20–22</sup> suggest that griseofulvin is no longer the treatment of choice for dermatophyte onychomycosis.

Side-effects include nausea and rashes in 8–15% of patients. In adults, it is contraindicated in pregnancy and the manufacturers caution against men fathering a child for 6 months after therapy.

**Terbinafine.** Terbinafine (Lamisil®; Novartis, Camberley, U.K.), an allylamine, inhibits the enzyme squalene epoxidase thus blocking the conversion of squalene to squalene epoxide in the biosynthetic pathway of ergosterol, an integral component of the fungal cell wall.<sup>23</sup> Its action results in both a depletion of ergosterol, which has a fungistatic effect, together with an accumulation of squalene, which appears to be directly fungicidal. The minimum inhibitory concentration (MIC) of terbinafine is very low, approximately 0.004 µg mL<sup>-1</sup>. This is equivalent to the minimal fungicidal concentration (MFC), demonstrating that this drug is truly fungicidal *in vitro*. It is the most active currently available antidermatophyte agent *in vitro* and clinical studies strongly suggest that this is also the case *in vivo*.<sup>24</sup>

**Itraconazole.** Itraconazole (Sporonox®; Janssen-Cilag, High Wycombe, U.K.) is active against a range of fungi including yeasts, dermatophytes and some nondermatophyte moulds. It is not as active *in vitro* against dermatophytes as terbinafine, its MIC being 10 times

greater. Although it is generally felt to be a fungistatic agent it can achieve fungicidal concentrations, although its MFC is about 10 times higher than its MIC.<sup>25</sup>

Both terbinafine and itraconazole persist in the nail for a considerable period after elimination from the plasma.<sup>26</sup> This property has given rise to a novel intermittent ('pulsed') treatment regimen using itraconazole in nail infection.

*Terbinafine vs. itraconazole in dermatophyte onychomycosis.* Both of these drugs have been shown to be more effective than griseofulvin in dermatophyte onychomycosis and therefore the optimum choice of treatment lies between terbinafine and itraconazole.

Terbinafine is licensed at a dose of 250 mg daily for 6 weeks and 12 weeks in fingernail and toenail infection, respectively. Itraconazole is licensed at a dose of 200 mg daily for 12 weeks continuously, or alternatively at a dose of 400 mg daily for 1 week per month. It is recommended that two of these weekly courses, 21 days apart, are given for fingernail infections and three courses for toenail disease.

There have been numerous open and placebo-controlled studies of both drugs in dermatophyte nail infection. However, historical comparisons of such studies do not provide evidence of equivalent quality as that achieved by directly comparative double-blind trials, as even in properly conducted studies the results can be influenced by variation in the criteria for mycological or clinical cure, or by the period of follow-up. It is generally accepted that patients entered into such studies should be both microscopy- and culture-positive for fungus and that mycological cure should be defined as microscopy and culture negativity at completion. Clinical criteria for cure are difficult to interpret as the appearance of the nail prior to infection is generally unknown and, especially in the case of toenails, because trauma can affect their appearance. Short follow-up periods after cessation of therapy are unlikely to allow interpretation of which is the superior drug; a follow-up period of at least 48 weeks (preferably 72 weeks) from the start of treatment should be allowed both in order to allow the most effective preparation to become apparent and to identify relapse as far as possible.

There are various published studies comparing terbinafine with continuous itraconazole therapy,<sup>27-29</sup> most of which demonstrate terbinafine to be the more effective agent. Thus far there are only two studies comparing terbinafine with intermittent itraconazole

therapy. The first compared terbinafine 250 mg daily for 16 weeks with four 'pulses' of itraconazole 400 mg daily for 1 week in every 4 weeks for 16 weeks and also with terbinafine 500 mg daily for 1 week in every 4 weeks for 16 weeks.<sup>30</sup> As only approximately 20 patients were recruited in each study group, this was a very small study; the regimens used were not those of the U.K. product licences, and the results comparing the groups were not significantly different. A more recent and much larger study has been completed comparing terbinafine 250 mg daily for both 3 and 4 months with itraconazole 400 mg daily for 1 week  $\times$  3 and 1 week  $\times$  4. One hundred and twenty patients were recruited to each group and the follow-up period was 72 weeks.<sup>31</sup> The study was carried out in double-blind, double-placebo fashion and demonstrated terbinafine 250 mg daily for both 3 and 4 months to be very significantly superior to both three and four 'pulses' of itraconazole (*Strength of recommendation A, Quality of evidence I*; see Appendix 1).

The 151 patients in the Icelandic arm of this study were further studied for long-term effectiveness of treatment during a 5-year blinded prospective follow-up study.<sup>32</sup> At the end of the study mycological cure without a second therapeutic intervention was found in 46% of the 74 terbinafine-treated subjects but in only 13% of the 77 itraconazole-treated subjects. Mycological and clinical relapse was significantly higher in the itraconazole group (53% and 48%) than the terbinafine group (23% and 21%) (*Strength of recommendation A, Quality of evidence I*).

The superiority of terbinafine has recently been supported by a systematic review of oral treatments for toenail onychomycosis;<sup>33</sup> this reference documents many additional studies and also the varied and often incompletely presented criteria that have been used to describe a 'clinical cure'.

### Treatment of yeast infections

Most yeast infections can be treated topically, particularly those associated with paronychia. Antiseptics can be applied to the proximal part of the nail and allowed to wash beneath the cuticle, thus sterilizing the subcuticular space. Ideally, such antiseptics should be broad spectrum, colourless and nonsensitizing. They require to be applied until the integrity of the cuticle has been restored, which may be several months. An imidazole lotion alternating with an antibacterial lotion is usually effective.

Itraconazole (Sporonox<sup>®</sup>) is the most effective agent for the treatment of candidal onychomycosis where the nail plate is invaded by the organism.<sup>34</sup> It is used in the same dosage regimen as for dermatophytes, i.e. 400 mg daily for 1 week per month repeated for 2 months in fingernail infection. *Candida* infection of toenails is much less common but can be treated as above using three or four pulses.

### Treatment of nondermatophyte moulds

Many varieties of saprophytic moulds can invade diseased nail. *Scopulariopsis brevicaulis* is the commonest of these and may be a secondary pathogen. Its response to systemic antifungal agents is variable, although terbinafine is probably the drug of choice in that the primary nail disease is quite likely to be a dermatophyte infection that is masked by the *Scopulariopsis*. There is little categorical evidence to support the choice of one drug.<sup>35</sup> In the U.S.A. and Europe cyclopirox nail lacquer has its advocates but it is not available in the U.K. Nail avulsion followed by an oral agent during the period of regrowth is probably the best method of restoring the nail to normal.

### Treatment failure

Although terbinafine is demonstrably the most effective agent in dermatophyte onychomycosis a consistent failure rate of 20–30% is found in all studies. If the most obvious causes of treatment failure, notably poor compliance, poor absorption, immunosuppression, dermatophyte resistance and zero nail growth are excluded, the commonest cause of failure is likely to be kinetic.<sup>36</sup> Subungual dermatophytoma has been described<sup>37</sup> and it is likely that this tightly packed mass of fungus prevents penetration of the drug in adequate concentrations. In such cases partial nail removal is indicated. It is been demonstrated that cure rates of close to 100% can always be achieved if all affected nails are avulsed under ring block prior to commencement of treatment. However, this is neither feasible nor necessary in most cases and the best approach is to try to identify those individual nails that are likely to fail and to remove the offending area.

Reports of long-term follow-up of treated patients have recently been presented, suggesting that positive mycology at 12 and 24 weeks after commencement of therapy are poor prognostic signs and may indicate a need for retreatment or for a change of drug. However, this work remains to be confirmed.

Cure rates, both short- and long-term, may be influenced by correction of associated orthopaedic and podiatric factors to avoid, as much as possible, trauma that particularly affects the great toenails.

### Summary of conclusions

- 1 Treatment should not be commenced before mycological confirmation of infection.
- 2 Dermatophytes are by far the commonest causal organisms.
- 3 Culture of yeasts and nondermatophyte moulds should be interpreted carefully in each individual case. In the majority, yeasts are likely to be a secondary infection and nondermatophyte moulds to be saprophytic in previously damaged nails.
- 4 Topical treatment is inferior to systemic therapy in all but a small number of cases of very distal infection or in SWO.
- 5 Terbinafine is superior to itraconazole both *in vitro* and *in vivo* for dermatophyte onychomycosis, and should be considered first-line treatment, with itraconazole as the next best alternative.
- 6 Cure rates of 80–90% for fingernail infection and 70–80% for toenail infection can be expected. In cases of treatment failure the reasons for such failure should be carefully considered. In such cases either an alternative drug or nail removal in combination with a further course of therapy to cover the period of regrowth should be considered.

### Audit points

- 1 Has a positive culture been obtained before commencing systemic therapy for onychomycosis?
- 2 Has an appropriate agent been chosen, based on the type of organism cultured?
- 3 Are arrangements in place for adequate duration of treatment to be supplied from hospital or general practitioner?
- 4 Has immunosuppression been considered in cases of PSO?

### Declaration of interest

David T.Roberts is a member of the Dermatology Advisory Board of Novartis Pharmaceuticals Ltd. He has given advice to almost all other manufacturers of antifungal agents and has spoken at symposia organized by a number of these companies. The other authors have no conflict of interest.

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## Appendix 1

The consultation process and background details for the British Association of Dermatologists guidelines have been published elsewhere.<sup>38,39</sup>



*Strength of recommendations*

- A There is good evidence to support the use of the procedure.
- B There is fair evidence to support the use of the procedure.
- C There is poor evidence to support the use of the procedure.
- D There is fair evidence to support the rejection of the use of the procedure.
- E There is good evidence to support the rejection of the use of the procedure.

*Quality of evidence*

- I Evidence obtained from at least one properly designed, randomized controlled trial.

- II-i Evidence obtained from well-designed controlled trials without randomization.
- II-ii Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group.
- II-iii Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
- III Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.
- IV Evidence inadequate owing to problems of methodology (e.g. sample size, or length or comprehensiveness of follow-up or conflicts of evidence).