Complete Summary

GUIDELINE TITLE

Guidelines for treatment of onychomycosis.

BIBLIOGRAPHIC SOURCE(S)

Roberts DT, Taylor WD, Boyle J. Guidelines for treatment of onychomycosis. Br J Dermatol 2003 Mar;148(3):402-10. [39 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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SCOPE

DISEASE/CONDITION(S)

Onychomycosis, including distal and lateral subungual onychomycosis (DLSO), superficial white onychomycosis (SWO), proximal subungual onychomycosis (PSO), candidal onychomycosis, and total dystrophic onychomycosis

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Dermatology
Family Practice
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence based guidance for the management of patients with onychomycosis

TARGET POPULATION

Patients with onychomycosis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Nail bed/plate scraping
2. Punch biopsy
3. Microscopy and culture

Treatment

1. Topical therapy
    - Amorolfine (Loceryl®) nail lacquer
    - Tioconazole (Trosyd®) nail solution
    - Salicylic acid (Phytex®) paint (considered, but not recommended)
    - Undecenoates (Monphytol®) paint (considered, but not recommended)
2. Systemic therapy
    - Griseofulvin (Fulcin®; Grisovin®)
    - Terbinafine (Lamisil®)
    - Itraconazole (Sporanox®)
3. Nail avulsion

MAJOR OUTCOMES CONSIDERED

- Clinical cure rate
- Mycological cure rate
- Quality of life
- Side effects of medications
- Treatment failure rate
- Infection with secondary pathogens

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels 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 analytic 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)

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

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.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines are edited by the Therapy Guidelines and Audit Sub-committee (TGA) and subsequently returned to the task force for revision. The approved draft version is published in the quarterly British Association of Dermatologists (BAD) newsletter, and all BAD members are given the opportunity to respond, positively or negatively, but hopefully helpfully, within three months of publication. Finalised guidelines are approved by the TGA and the Executive Committee of the BAD and finally published in the *British Journal of Dermatology*.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of evidence **(I-IV)** and grading of recommendations **(A-E)** are defined at the end of the "Major Recommendations" field.

Diagnosis

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 distal and lateral subungual onychomycosis (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 superficial white onychomycosis (SWO) the surface of the infected nail plate can be scraped and material examined directly. Proximal subungual onychomycosis (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 minutes 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 degrees 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 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. 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.

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 superficial white onychomycosis (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.

Topical Agents for Onychomycosis

Agent	Strength of Recommendation and Quality of Evidence
Amorolfine (Loceryl®) nail lacquer	**B, II-ii**
Tioconazole (Trosyd®) nail solution	**C, II-iii**
Salicylic acid (Phytex®) paint	**E, IV**
Undecenoates (Monphytol®) paint	**E, IV**

Systemic Agents for Onychomycosis

Drug	Advantages	Disadvantages	Strength of Recommendation and 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	**B, I**
Terbinafine[a]	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	**A, I**
Itraconazole[a]	Active against *Candida albicans*; 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	**A, I**

[a]Terbinafine has better cure rate and lower relapse rate than itraconazole for dermatophytes **(A, I)**.

Definitions:

Levels of Evidence

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Recommendation Grades

A. There is good evidence to support the use of the procedure.
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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.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for the treatment recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Consistent quality of care for patients with onychomycosis

POTENTIAL HARMS

- Side effects of griseofulvin include nausea and rashes.
- The manufacturers caution against men fathering a child for 6 months after treatment with griseofulvin.
- Systemic agents may interact with other drugs (see Table 2 of original guideline document).
- Terbinafine may result in idiosyncratic liver and skin reactions and reversible taste disturbance.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Griseofulvin is contraindicated in pregnancy, lupus erythematosus, porphyria, and severe liver disease.
- Itraconazole is contraindicated in pregnancy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- 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 patients and special circumstances. Just as adherence to guidelines may not constitute a defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.
- It is important that these guidelines are used appropriately in that they can only assist the practitioner and cannot be used to mandate, authorise, or outlaw treatment options. Of course it is the responsibility of the practising clinician to interpret the application of guidelines, taking into account local circumstances.
- Guidelines are inherently a fluid, dynamic process and will be updated on the British Association of Dermatologists (BAD) Web site on a regular basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

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 proximal subungual onychomycosis (PSO)?

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Mar

GUIDELINE DEVELOPER(S)

British Association of Dermatologists - Medical Specialty Society

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS 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.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Griffiths CE. The British Association of Dermatologists guidelines for the management of skin disease Br J Dermatol. 1999 Sep;141(3):396-7.

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 20, 2005. The information was verified by the guideline developer on June 27, 2005.

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