

Fungal Skin & Nail Infections: Diagnosis & Laboratory Investigation



Association of
Medical Microbiologists

Quick Reference Guide for Primary Care

For consultation and local adaptation



- B**
- Many nail problems can look like a fungal infection eg psoriasis or injury. As only 45% of dermatology samples received are positive for fungal infection¹ always send samples before starting lengthy treatment.^{B-}
 - 91% of positives are detected by microscopy which provides the most rapid diagnosis.^{B-1}
 - Culture distinguishes dermatophyte from non-dermatophyte moulds, which may alter treatment.

C WHEN SHOULD I TAKE DERMATOLOGICAL SAMPLES FOR FUNGI?²⁻⁴

When are samples NOT needed?

- Uncomplicated athlete's foot
- Mild infections of the groin. *If samples are not taken treat suspected Candida or erythrasma with topical imidazole.*^{A-5}
- Mild skin ringworm.

When should I take samples for fungi?

- When oral treatment is being considered – scalp ringworm or nail disease.
- In severe or extensive skin fungal infections eg moccasin-type athlete's foot.
- Skin infections refractory to initial treatment. *Occasionally gram negative bacterial infections cause interdigital cracking that looks like tinea pedis.*⁶
- When the diagnosis is uncertain.

- Note: ensure clinical details are stated including treatment, animal contact and overseas travel**

HOW SHOULD I TAKE SAMPLES FOR FUNGAL INVESTIGATION?⁷

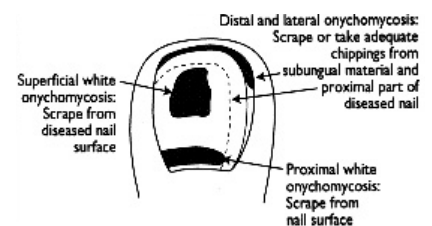
- C**
- Swabs are of little value for dermatophytes unless there is insufficient material obtained by scraping.
 - Wipe off any treatment creams before sampling.
 - Keep any samples at ROOM temperature, do NOT refrigerate⁸ as dermatophytes are inhibited at low temperatures, and humidity facilitates the growth of contaminants.
 - Samples should be collected into folded dark paper squares (secure dark paper squares with a paper clip and place in a plastic bag; or use commercially available fungal packets e.g. Mycotrans, Dermapak⁹).

Skin scrapings:

- Scrape skin from the advancing edge of lesion. Use a blunt scalpel blade or similar.
- 5mm² of skin flakes are needed for microscopy and culture.

Nail samples³: are better taken by clinicians rather than patients

- Most viable fungi are usually found in **most proximal** part of **diseased** nail.
- Sample most proximal part of **diseased** nail with chiropody scissors.
- Include full thickness clippings of the **diseased** nail.
- Sample as far back from nail tip as possible – (where fungi are usually found).
- Also sample debris from under the **diseased part** of nail.
- In **superficial** infections scrape surface of **diseased nail plate** with scalpel blade.



Denning, D W et al. BMJ 1995;311:1277-1281

Hair samples^{2,21}:

Take scalp scrapings – this often pulls out infected hair stumps which are critical for successful culture & microscopy. Hair plucking does not produce the best samples. A soft toothbrush can be used if scrapings are not possible^{21,22}

INTERPRETING THE LABORATORY REPORT

C When to treat:

- A positive microscopy (fungal elements seen) is sufficient to start antifungals.
- A positive dermatophyte culture with negative microscopy is still significant.
- A negative microscopy or culture does not rule out fungal infection, particularly with kerion and nail infections. If clinical appearance very suggestive of fungal infection, repeat sample and start treatment.

B Significant fungi isolated and reported:¹

- The most common dermatophytes from foot or trunk infections are *T. rubrum* (80%) and *T. interdigitale* (15%).¹
- *Epidermophyton floccosum* and *Microsporum* species are also encountered.
- *T. tonsurans* and *T. violaceum* cause 80% of scalp dermatophyte infections in many UK cities.¹
- *Scytalidium* spp. are the most common non-dermatophyte moulds that can cause both skin and nail infections.¹⁰
- True nail infections with the yeasts *C. albicans* and *C. parapsilosis* are rare and are more likely to affect the finger nail or finger nail folds. Other *Candida* spp may very rarely cause paronychia.^{3,4,11}

C Fungi of uncertain clinical significance:¹²

- Non-dermatophyte moulds (e.g. *Aspergillus* spp., *Fusarium* spp., *Scopulariopsis* spp., *Acremonium* spp.) are very rare causes of nail infection, usually following nail trauma, immunosuppression or underlying dermatophyte infection. Therefore discuss management with a local microbiologist or dermatologist.
- Such a diagnosis requires positive direct microscopy, isolation of the organism in pure culture and, ideally, on repeated occasions.
- A repeat sample is usually requested to confirm significance of non-dermatophyte moulds.

B Antifungal susceptibilities:^{4,13-16}

- Susceptibility testing of dermatophytes is not required, as antifungal resistance is unusual and there is no known correlation between antifungal susceptibilities and outcome

This evidence-based guidance was developed by the HPA Primary Care Unit and GP Microbiology Laboratory Use Group, in collaboration with GPs, AMM and the UK Clinical Mycology Network. It is in line with Clinical Knowledge Summaries & SIGN.

TREATING FUNGAL SKIN AND NAIL INFECTIONS⁴

For non-dermatophyte moulds other than *Candida* sp, seek the advice of a microbiologist or dermatologist

CONDITION	COMMENTS	DRUG	DOSE	LENGTH OF TREATMENT
Dermatophyte and candidal infection of the finger nail or toenail ¹⁷⁻¹⁹	Treat only if infection confirmed by lab. Only use topical treatment if superficial infection of the top surface of nail plate For infections with dermatophytes use oral terbinafine or itraconazole. For infections with candida or non-dermatophyte moulds use oral itraconazole. ^C Idiosyncratic liver and other severe reactions occur very rarely with terbinafine and itraconazole. For children seek expert advice	5% amorolfine nail lacquer ^{B-}	1–2x/weekly fingers toes	6 months 12 months
		Terbinafine ^{A-}	250 mg OD fingers toes	6–12 weeks 3–6 months
		Itraconazole	200 mg BD fingers toes	2 courses of 7 days/month 3 courses of 7 days/month
Dermatophyte infection of the skin ^{17,19,20}	Take skin scrapings for culture. Treatment: As terbinafine is fungicidal, one week is as effective as 4 weeks azole which is fungistatic. ^{A-} If intractable consider oral terbinafine. Discuss scalp infections with specialist.	Topical 1% terbinafine ^{A+}	1–2x/daily	1 week ^{A+}
		Use a 1% azole cream for groin infections Topical undecenoic acid or 1% azole ^{A+}	1–2x/daily	4–6 weeks ^{A+}
Candida infection of skin ²⁰	Confirm by laboratory. Treat with 1% azole cream. Seek advice for nail infection	1% azole cream – use lotion if treating paronychia	1–2x/daily	1 week or in case of paronychia until swelling goes ^{B+}
<i>Pityriasis versicolor</i> ²⁰	Scratching the surface of the lesion should demonstrate mild scaling	1% azole cream, 1% terbinafine or shampoo containing ketoconazole	1–2x/daily	Usually 1 week ^{A-}

Follow-up: unless there is underlying disease eg psoriasis, eradication of the fungus generally restores the nail to its pre infection state. ⁴ **Siblings of children with scalp ringworm should be screened by scalp brushing.**^{21,22}

KEY A B C D indicates grade of recommendation **good practice point**

This evidence-based guidance was developed by the HPA Primary Care Unit and GP Microbiology Laboratory Use Group, in close collaboration with the HPA Mycology Reference Unit and the UK Clinical Mycology Network. It was reviewed several times by GPs, The Association of Medical Microbiologists network, microbiologists and the Clinical Knowledge Summaries authors. It is based on expert opinion backed up by Medline literature searches in each of the relevant areas. The strength of the evidence quoted is graded as below.

Grading of guidance recommendations

Study Design	Recommendation Grade
Good recent systematic review of studies	A+
One or more rigorous studies, not combined	A-
One or more prospective studies	B+
One or more retrospective studies	B-
Formal combination of expert opinion	C
Information opinion, other information	D
Good practice point	<input checked="" type="checkbox"/>

References

- Borman AM, Campbell CK, Fraser M, Johnson EM. Analysis of the dermatophyte species isolated in the British Isles between 1980 and 2005 and review of worldwide dermatophyte trends over the last three decades. *Med Microbiol* 2006;**44**:1-11.
- Fuller LC, Child FJ, Midgley G, Higgins EM. Clinical Review: Diagnosis and management of scalp ringworm *BMJ* 2003;**326**:539-41
- Denning D, Evans EGV, Kibbler CC, Richardson MD, Roberts MM, Rogers TR, Warnock DW, Warren RE. Fortnightly Review: Fungal nail disease: a guide to good practice (report of a working group of the British Society for Medical Mycology) *BMJ* 1995;**311**:1277-81
- Roberts DT, Taylor WD, Boyle J. Guidelines for treatment of onychomycosis. *Brit J Dermatol* 2003;**148**:402–410. *Excellent well referenced comprehensive review of the management of fungal nail and skin infections.*

This evidence-based guidance was developed by the HPA Primary Care Unit and GP Microbiology Laboratory Use Group, in collaboration with GPs, AMM and the UK Clinical Mycology Network. It is in line with Clinical Knowledge Summaries & SIGN.

5. Clayton YM, Knight AG. A clinical double blind trial of topical miconazole and clotrimazole against superficial fungal infection and erythrasma. *Clin Exp Dermatol* 1976; **1**: 225–9. *Erythrasma is due to a Gram-positive bacterium Corynebacterium minutissimum that produces porphyrins and therefore fluoresces a characteristic coral-pink colour under a Wood's light. Azoles are effective for the treatment of erythrasma as they are active against Gram-positive bacteria.*
6. Leyden JJ, Kligman AM. Interdigital athlete's foot: the interaction of dermatophytes and residual bacteria. *Arch Dermatol* 1978; **114**: 1466–72
7. G Davey, C K Campbell, and D W Warnock Mycological techniques *J Clin Pathol*. 1996;**49**: 95–99
8. E. floccosum in Rebell G and Taplin D Eds. Dermatophytes. Their recognition and identification. University of Miami press, Florida, 1970 page 115. *There are three reasons for not refrigerating specimens: firstly it is important to keep skin / hair / nail dry as this reduces bacterial growth, and refrigeration and warming to room temperature might increase the humidity. Secondly storage at room temperature is simpler, and indeed most specimens are sent in the ordinary post which is all at room temperature. Finally, low temperatures do affect the growth of some dermatophytes, malassezia species and a very few candidas.*
9. Dermapak: Dermaco Limited PO Box 470, Toddington, Bedfordshire, LU5 6BF, <http://www.dermapak.com> . MycoTrans Specimen Transport System, Mycotrans Limited, PO Box 1172, Biggar, Lanarkshire ML12 6NN, Tel/Fax: 01899 830555, mail@mycotrans.com
10. Campbell CK, Mulder JL Skin and nail infection by *Scytalidium hyalinum* sp. nov. *Sabouraudia*. 1977;**15**:161-6
11. Hay RJ, Baran R, Moore MK *et al*. *Candida* onychomycosis: an evaluation of the role of *Candida* species in nail disease. *Br J Dermatol* 1988; **118**: 47–58.
12. Summerbell RC, Cooper E, Bunn U, Jamieson F, Gupta AK. Onychomycosis: a critical study of techniques and criteria for confirming the etiologic significance of nondermatophytes. *Med Mycol*. 2005;**43**:39-59
13. Santos DA, Hamdan JS In vitro antifungal oral drug and drug-combination activity against onychomycosis causative dermatophytes *Med Mycol*. 2006;**44**:357-62
14. Sheehan DJ, Hitchcock CA, and Sibley CM. Current and Emerging Azole Antifungal Agents *Clin Microbiol Rev*. 1999;**12**:40–79
15. Sarifakioglu E, Seckin D, Demirbilek M, Can F. *In vitro* antifungal susceptibility patterns of dermatophyte strains causing tinea unguium. *Clin Exp Dermatol*. 2007;**32**:675-9
16. Kikuchi I, Tanuma H, Morimoto K, Kawana S. Usefulness and pharmacokinetic study of oral terbinafine for hyperkeratotic type tinea pedis. *Mycoses* 2008;**51**:7-13
17. Crawford F. Athlete's foot. *BMJ Clinical Evidence* 2006 ;**11**:1712. <http://clinicalevidence.bmj.com/ceweb/conditions/skd/1712/1712.jsp#Q1>
18. Hunt D. [Fungal toenail infections](http://clinicalevidence.bmj.com/ceweb/conditions/skd/1715/1715_12.jsp) (updated). *BMJ Clinical Evidence* 2008;12:1715 http://clinicalevidence.bmj.com/ceweb/conditions/skd/1715/1715_12.jsp
19. Crawford F, Hart R, Bell-Syer S, *et al*. Topical treatments for fungal infections of the skin and nails of the foot. In: The Cochrane Library, Issue 3, 2007. Chichester, UK: John Wiley & Sons, Ltd. Search date 2005; *primary sources Medline, Embase, Cinahl, Cochrane Controlled Trials Register, the Science Citation Index BIOSIS, CAB – Health, Healthstar and Economic databases, and hand searches of reference lists and podiatry journals, and contact with the pharmaceutical industry.*
20. Spiekermann, P.H. and Young, M.D. (1976) Clinical evaluation of clotrimazole. A broad-spectrum antifungal agent. *Archives of Dermatology* **112**(3), 350-352. *This large study including 1,361 patients, includes the treatment of patients with Dermatophytes, Candida albicans, and Malassezia furfur (Pityrosporum orbiculare) the causative agent of Pityriasis versicolor.*
21. White JML, Higgins EM, Fuller LC. Screening for asymptomatic carriage of *Trichophyton tonsurans* in household contacts of patients with tinea capitis: results of 209 patients in South London. *JEADV* 2007; **21**: 1061-1064.
22. Brushes are available from: Brushaway Products, Croft House, Croft Road, Bromley, Kent BR1 4DR. *Some GP stores will supply them to a local area. They are small, easy to use and are robust enough to be posted without damage. They are very useful for screening family contacts or when insufficient material can be obtained by scraping. They are not a direct alternative to scraping as you have to wait for the culture result (~2-3 weeks) whereas the microscopy result from a scrape should be available within 1-2 days.*

Other reading:

Clinical Knowledge Summaries accessed April 2009:

Fungal nail infections: http://cks.library.nhs.uk/fungal_candidal_nail_infection/leaflets_for_patients/fungal_nail_infection

Fungal (dermatophyte) skin infections: http://cks.library.nhs.uk/fungal_skin_infections/background_information/prevalence

Candida http://cks.library.nhs.uk/candida_skin/evidence#-367703

The following individuals were closely involved in the development of this guidance:

Health Protection Agency: Clodna McNulty; Michael Palmer; Elizabeth Johnson

Sowerby Centre for Health Informatics at Newcastle (SCHIN): Michael Power

UK Clinical Mycology Network: Roderick Hay; Susan Howell; Christopher Kibbler