DERMATOLOGY ACADEMY 2016

FEATURE ARTICLE

Could it be fungal?

Fungal infections present frequently in pharmacy, but their diagnosis is not always straightforward.

THE most common fungal infections appearing in the community are tinea, candida and pityriasis versicolor caused by Malassezia yeast species, said Professor Rodney Sinclair, director of Epworth Dermatology, Melbourne.

Managing skin mycoses

Initial management of fungal skin infections involves the identification of any possible causes or triggers. Pharmacists need to consider:

- Why is the infection where it is?
- Why has the infection occurred now?
- What has the patient been doing differently and/or what might have changed to increase the patient's susceptibility to infection?
- What patient-related or environmental factors might need to be addressed or modified to help treat the infection and minimise the risk of a recurrence?

It is also important to look for any other co-existing infection that might need to be treated at the same time, such as secondary bacterial infection of a fungal rash or a fungal infection occurring elsewhere on the body.

Most fungal skin infections can be successfully treated with an appropriate topical antifungal such as, for example, an azole or allylamine.

Oral antifungal medication is generally only required if the infection is particularly extensive or severe, if it is resistant to topical antifungal therapy, or sometimes if it affects certain hair-bearing areas such as the scalp.

The choice of topical azole depends on both the characteristics of the rash and the likely pathogen, as well as the relative antibacterial and anti-inflammatory effects of the medication.

Clotrimazole and bifonazole are both broad-spectrum antifungals that are fungicidal against both dermatophytes and yeasts

(unlike allylamines), have activity against Gram-positive bacteria and also have anti-inflammatory activity (table 1).

The anti-inflammatory action of bifonazole is equivalent to that of 1% hydrocortisone and it is also retained in the skin for 36-48 hours, enabling once-daily application.

Clotrimazole combined with hydrocortisone (1%) has superior anti-inflammatory activity to bifonazole on its own.

Other azoles, such as ketoconazole and econazole, are also broad-spectrum antifungals, but they have weaker antibacterial activity than clotrimazole and bifonazole, and they also exert weaker anti-inflammatory effects.

More severe fungal skin infections are better treated with a combination of broad-spectrum antifungal activity, antibacterial activity and anti-inflammatory activity.

The anti-inflammatory action of an azole can be augmented by the addition of hydrocortisone. Azole/corticosteroid products such as clotrimazole/hydrocortisone (Canesten-Plus) are now available OTC.

There is no known resistance to azole antifungals. If symptoms do not improve with azole therapy, resistance of the fungal infection to that particular azole won't be the cause, said Professor Sinclair. Reasons for response failure are more likely to be continuing triggering or exacerbating factors, poor or inadequate adherence to treatment, insufficient treatment duration or misdiagnosis.

There is a range of topical allylamines that may be used in the treatment of fungal skin infections. (table 1).

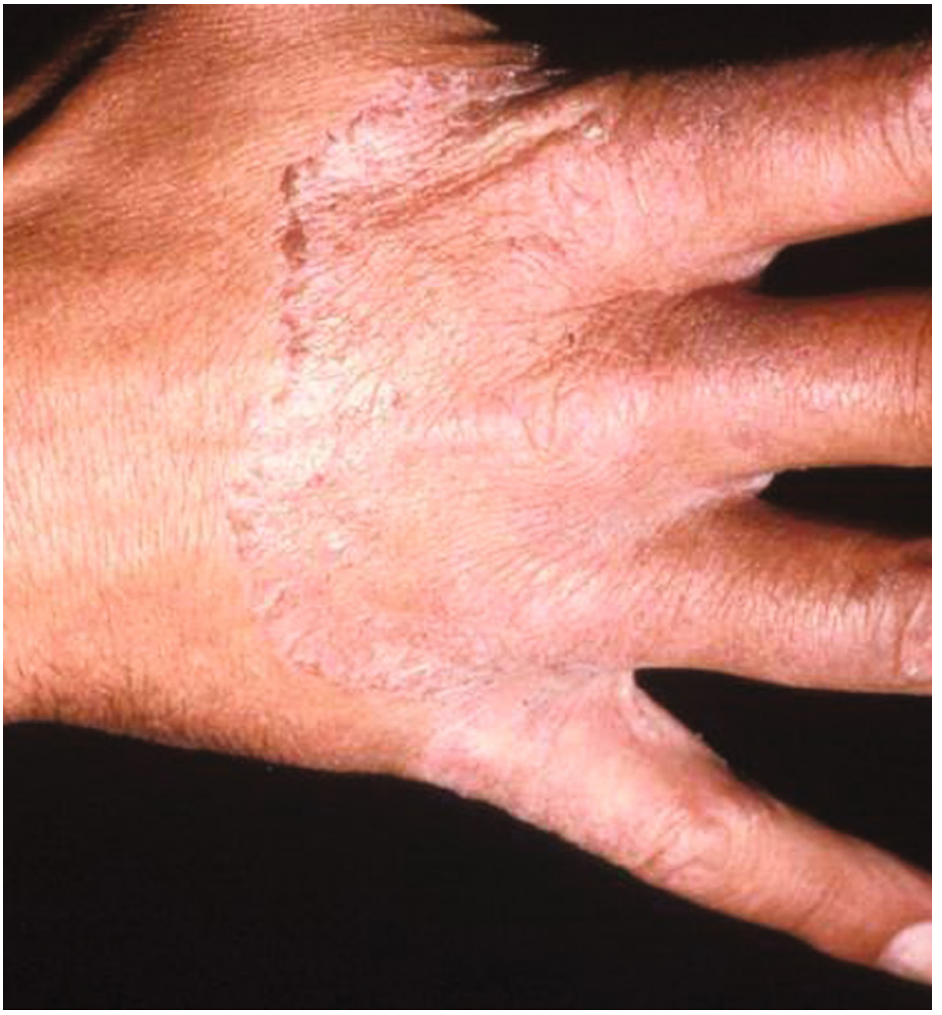
Terbinafine and naftifine are both fungicidal against dermatophytes, but are only fungistatic against yeasts, such as Candida albicans.

In addition, terbinafine is effective for mild cases of tinea pedis, but less so for moderate–to severe cases that usually involve a secondary bacterial infection.

Initially the aim should be to induce a remission of the patient's symptoms, usually with the use of an azole antifungal, in combination with 1% hydrocortisone. This should then be followed with ongoing maintenance therapy, such as azole therapy alone, perhaps applied twice a week to help prevent re-infection.

A closer look at tinea

Tinea is a common fungal infection that can present in multiple ways, affecting different parts of the body. The fungi most commonly implicated include Trichophyton, Microsporum and Epidermophyton species; these are all dermatophyte species, filamentous fungi that metabolise and subsist upon keratin in the skin, hair and nails.



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Tinea pedis is a highly contagious form of tinea that affects "three out of four adults over their lifetime," according to Professor Sinclair.

It can be spread directly, by skin-to-skin contact, or indirectly, by contact with (contaminated) surfaces.

It can also be transferred from one site on the body to another.

In the feet, tinea can often be misdiagnosed as pompholyx eczema. An important differentiating feature is that eczema usually starts at the big toe and spreads laterally, while tinea pedis most often starts at the little toe.

Tinea pedis is more common in men than women, and is uncommon in children.

Its incidence is generally higher in warmer, more humid climates. Other predisposing factors include the presence of diabetes, obesity, immunosuppression, trauma and/or the use of occlusive footwear.

Symptoms typically include itching and sometimes a burning sensation. The progression of tinea pedis is commonly a worsening of the itch, increasing maceration

and the development of malodour, a sign of secondary bacterial superinfection.

Co-infection is "particularly common" in tinea pedis, says Professor Sinclair.

"[The patient] commonly gets superinfected, first of all with candida and secondarily with Gram-positive cocci."

As a patient's tinea pedis worsens, and the population of any co-infecting pathogens increases, the burden of dermatophytes may actually decrease, even becoming absent in severe cases.

For this reason, more advanced cases of tinea pedis — involving mixed infections — can often respond poorly to antifungal therapy alone.

Treating tinea pedis

The "vast majority" of tinea pedis cases, particularly the milder cases, can be successfully treated with over-the-counter antifungals, which may be available in the form of a cream, spray, gel or powder.

The main types of topical antifungals used to treat tinea pedis are azoles (for example, miconazole, bifonazole, ketoconazole), allylamines (for example, terbinafine, naftifine), Whitfield ointment (benzoic acid and salicylic acid) and amorolfine.

Milder cases of tinea pedis can usually be managed with any of the above alone. Nystatin is only active against yeasts and therefore of no use when treating a pure tinea pedis infection.

Combining an antifungal agent with hydrocortisone (1%) is often very useful if the tinea has an acute inflammatory component.

"If you combine your antifungal with some hydrocortisone, it doesn't diminish the effectiveness of the antifungal ... but it reduces the inflammation and it leads to much faster resolution," says Professor Sinclair.

If a patient's tinea hasn't resolved after seven days of combined antifungal/hydrocortisone therapy, then it is worthwhile rechecking the diagnosis and considering whether a secondary infection may be involved.

For more severe tinea, a more broad-spectrum antifungal is recommended that will be active against both the dermatophyte and the yeast, as it's very common for a secondary candida infection to be present, says Professor Sinclair.

"Ideally, you might want something that's also got some antibacterial action, for the more severe cases."

If malodour is present, then an antifungal with some antibacterial activity is necessary. Malodour is a good sign that there's a bacterial infection present, Professor Sinclair says.

Tinea incognito

If tinea is mistakenly treated with a topical corticosteroid alone, the body's inflammatory response to the fungal infection will be suppressed. The tinea may then have a chance to infiltrate the deeper layers of skin.

In this situation, the clinical appearance of the tinea may change — it can lose its annulus or central clearing, it often loses its surface scale and pustules may appear. The resulting lesion is called a tinea incognito or 'tinea in disguise'.

If treating a solitary patch of skin, or a couple of patches, with topical steroids and the rash appears to be getting worse, consider tinea incognito, Professor Sinclair advises.

Table 1: Topical treatment options for tinea pedis

Antifungal	Spectrum of activity	Grading	Anti-inflammatory	Dosing
Azoles				
Bifonazole	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ +++ +++	++	Once daily for 3 weeks
Clotrimazole	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ +++ +++	+	2–3 times daily Should be continued for ↗ 1 month to prevent re-infection
Clotrimazole plus 1% hydrocortisone	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ +++ +++	+++	Twice daily Should not be used for > 7 days
Allylamines				
Terbinafine	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ + –	+++	Once daily for 1 week
Naftifine	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ + +	+++	Once daily for 1 month
Butenafine	• Dermatophytes • Yeasts • Gram-positive bacteria	+++ +++ +	+	Once daily for 1 month or twice daily for 1 week

+++ Strong activity; ++ Moderate activity; + Mild activity; – No activity.

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This article features highlights from Professor Rodney Sinclair's presentation on fungal infections at Dermatology Academy, May 2016.

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