

Managing athlete's foot

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Abstract

This article is aimed at providing a succinct overview of the condition *tinea pedis*, commonly referred to as athlete's foot. *Tinea pedis* is a very common fungal infection that affects a significantly large number of people globally. The presentation of *tinea pedis* can vary based on the different clinical forms of the condition. The symptoms of *tinea pedis* may range from asymptomatic, to mild-to-severe forms of pain, itchiness, difficulty walking and other debilitating symptoms. There is a range of precautionary measures available to prevent infection, and both oral and topical drugs can be used for treating *tinea pedis*. This article briefly highlights what athlete's foot is, the different causes and how they present, the prevalence of the condition, the variety of diagnostic methods available, and the pharmacological and non-pharmacological management of the condition.

Keywords: athlete's foot, tinea pedis, dermatophyte, fungal infection, allylamines, azole antifungals, griseofulvin, terbinafine

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Introduction

Athlete's foot, also called *tinea pedis*, is the single most common dermatophyte infection¹ Dermatophytes are a scientific label that refers to a group of three genera (Microsporum, Epidermophyton and Trichophyton) of fungus that cause skin diseases in humans and animals.² *Tinea pedis* may lead to onychomycosis (a fungal nail infection that commonly affects toe nails more than fingernails), and is associated with onychomycosis in 30–59% of cases.³ The prevalence of *tinea pedis* generally rises with increasing age and it is more common in males than in females.⁴ It is most often prevalent in men that are aged between 31 and 60 years.⁵ It is characterised by white, macerated skin, fissuring and scaling, usually in the interdigital spaces of the feet (i.e. between the toes). In most cases, it occurs between the third, fourth and the fifth toes. The condition may also present itself in the form of scaling plaques and slight erythema on the soles, heels and lateral aspect of one foot, or both feet. Markings on the skin may look exaggerated and white. The dorsal surface of the foot is generally clear of any signs.^{1,5}

Clinical forms of *tinea pedis*

Athlete's foot is a skin infection caused by a type of fungus called a dermatophyte.⁶ There are four presentations of *tinea pedis*, namely interdigital *tinea pedis*, frequently referred to as athlete's foot, moccasin (chronic hyperkeratotic) *tinea*

pedis, inflammatory or vesicular *tinea pedis*, and ulcerative *tinea pedis*.^{1,7} Patients who have *tinea pedis* usually present with itching and small blisters on one or on both feet.⁷ The various forms of this condition are described and compared in Table 1.

Fungal infections grow well in humid and warm conditions, and hence tend to be more predominant in countries that generally have a warm climate.⁹ It is even more contagious in environments that are warm and moist, such as hot tubs or locker rooms and showers.⁶ The fungal spores are able to survive for very long periods (months or even years), anywhere from bathrooms, changing rooms and even around swimming pools.¹⁰

Aetiology of athlete's foot

Athlete's foot is a clinical condition that manifests as a superficial fungal infection of the skin.¹¹ The risk in attaining the infection is increased in people who have contact with swimming pools, communal showers, athletic shoes, sports equipment and locker rooms. The presence of diseases such as psoriasis or atopic dermatitis have a tendency of increasing the incidence of contracting *tinea pedis*.¹² *Tinea pedis* is the most common fungal infection of the skin that is transmitted via dermatophytes.¹³ Examinations of 600 keratinised tissues, conducted by the mycology laboratory of the National Institute of Health in Portugal during 2006, reported that dermatophytes caused 48.0% of *tinea pedis*

Table 1: A comparison between the various clinical forms of *tinea pedis* in terms of symptoms, complications, localization of the infection, characteristics that may be observed, as well as the causative agent of the infection^{5,8}

Clinical form of <i>tinea pedis</i>	Causative agent(s)	Characteristics of clinical form	Location of anomalies	Complications	Symptoms
Interdigital <i>tinea pedis</i>	<i>T. rubrum</i> is the most common agent followed by anthropophilic <i>T. interdigitale</i> (anthrophilic organisms are parasitic organisms that need host human beings to survive. They spread from one human host to another)	This type of <i>tinea pedis</i> usually presents with interdigital erythema, scaling, maceration and fissuring	The lesions can be found between the fourth and fifth toes. The dorsal surface of the foot is generally unaffected, but adjacent plantar areas may be involved	Hyperkeratosis, leukokeratosis or erosions	Itching, burning and malodour
Inflammatory or vesicular <i>tinea pedis</i>	Anthropophilic <i>T. interdigitale</i> is the primary causative agent	The observed characteristics of vesicular <i>tinea pedis</i> include hard, tense vesicles, bullae and pustules on the in-step or mid-anterior plantar surface of the foot	The bullae appear in round, polycyclic, herpes-like or gradually spreading clusters with an erythematous base and are localised to the arches of the feet, sides of the feet, toes and sub-digital creases. New vesicles develop on the periphery, with fissures often appearing in the cleft and sub-digital creases	Cellulitis, adenopathy and lymphangitis	Severe itching accompanied by burning and pain. The intensity of inflammation varies amongst individuals and may make walking difficult
Ulcerative <i>tinea pedis</i>	Most commonly caused by Anthropophilic <i>T. interdigitale</i>	This clinical form of <i>tinea pedis</i> usually presents with rapidly spreading vesiculo-pustular lesions, ulcers and erosions. Bacterial infections are usually present as a secondary infection	This clinical form usually begins in the third and fourth interdigital spaces. It then spreads to the lateral dorsum and the plantar surface. In severe cases, it may even extend to large areas whereby the entire sole can even be sloughed	Cellulitis, lymphangitis, fever and malaise	Ulcers, pain of varying degrees and itching
Chronic hyperkeratotic (moccasin) <i>tinea pedis</i>	Primarily caused by <i>T. rubrum</i>	The infection typically presents with chronic plantar erythema ranging from slight scaling to diffuse hyperkeratosis	The infection pattern typically presents with dry hyperkeratotic scaling, which primarily affects the entire plantar surface. It then extends to the lateral foot. On the dorsal foot surface, the foot is usually clear	Due to the constant scratching of the feet, <i>Tinea manuum</i> (fungal infection of the hands) may develop as a result	The condition may be asymptomatic but may also present with mild erythema, thick hyperkeratotic scales with fissures, moderate-to-severe pruritus, and painful fissures while walking

and the remaining 52.0% were caused by yeasts and non-dermatophyte moulds.¹² The most commonly detected dermatophyte in patients with *tinea pedis* is *T. rubrum*; it is the most commonly isolated organism in adult populations, whilst *T. tonsurans* is the most common causative organism in children with *tinea pedis*.¹¹⁻¹³ In addition to these dermatophytes, non-dermatophyte moulds, such as *Neoscytalidium dimidiatum*, which is endemic in Africa, Asia, the Caribbean, Central and South America, and several states in the United States, can result in treatment-resistant *tinea* infections of the feet.¹²

Diagnosis of *tinea pedis*

Tinea pedis can be diagnosed through different clinical methods.¹² One method is through physical examination,

which usually refers to the presentation of the scaling and maceration of the most lateral interdigital spaces, extending medially. The infection presents with a dry-type pattern, which is seen and inclusive of hyperkeratosis of the plantar and lateral part of the foot.¹⁴ These are the most common physical presentation patterns of a *tinea pedis* infection. The less common patterns are observed as minute vesicles and blisters that are present on an erythematous base on the plantar surface of the feet.¹⁴ The other methods of diagnosis include examination with a Wood's light, direct microscopic examination, and fungal culture.⁵ Even though a Wood's light may be used, it is not necessarily sensitive in detecting dermatophytes, because they do not fluoresce. The primary reason for using this test may be to distinguish the *tinea* from erythrasma (a superficial skin infection that causes

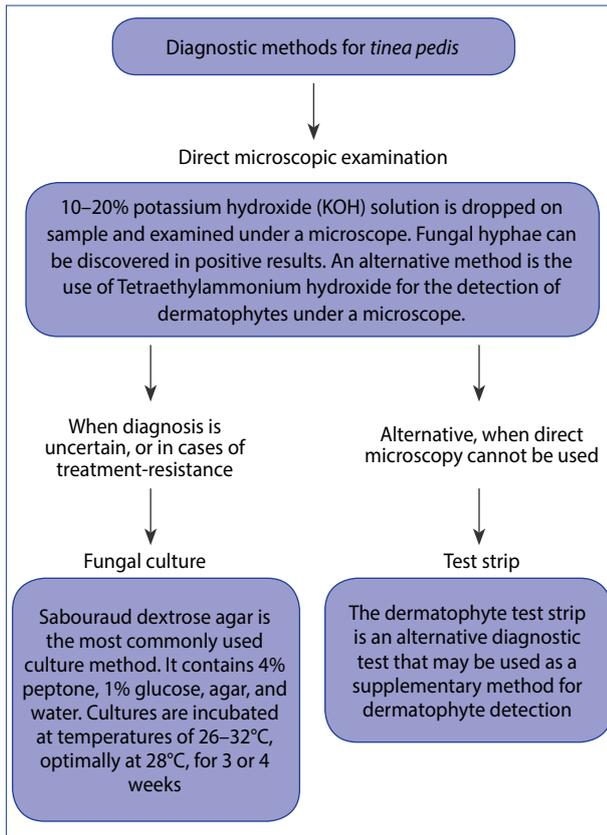


Figure 1: In direct microscopic examinations, scraped-off samples are tinted with 10–20% potassium hydroxide or alternatively tetraethylammonium hydroxide. The samples are then viewed under a microscope for detection of fungal hyphae. In cases of treatment resistance or uncertain diagnosis, a fungal culture is a viable alternative. In cases where direct microscopy is not feasible for use, dermatophyte test strips can provide a diagnosis for dermatophyte detection.¹²

brown, scaly skin patches) caused by *Corynebacterium minutissimum*.¹² The other method may be collection of keratinised tissue for mycological examination. The samples are cultured on agar and results can be expected after two weeks. Even if the results from the microscopic examination may be negative, the clinician can still prescribe treatment for *tinea pedis*, if the physical presentation of the disease is obvious or convincing¹⁴

Identifying of *tinea pedis*, using techniques other than clinical diagnosis, requires a scraped-off sample from an active area

where the lesion is suspected of being *tinea pedis*. Skin scrapings should ideally be collected from the peripheral raised border. Direct microscopic examination is one of the techniques that can be performed. The test is easy and quick, and is highly specific and sensitive for dermatophyte identification. Alternative methods of identification include the use of dermatophyte test strips and performing a fungal culture.^{8,12,14} Refer to Figure 1.

Non-pharmacological management

Tinea pedis can infect by contact with tainted scales on shower or pool floors; therefore, wearing protective footwear in communal facilities (public areas) may help diminish the probability of contamination. Since contaminated scales can be present on attire, regular washing of laundry would be a beneficial preventative measure to take.¹⁵ Occlusive footwear advances disease by creating warm, muggy, macerating situations where dermatophytes flourish. Accordingly, patients should endeavour to limit foot dampness by restricting the utilization of occlusive footwear, and dry their feet thoroughly and in between the toes after showering, bathing, or swimming. Do not put on socks when feet or socks are wet.^{6,15} Other measures to help prevent infection include wearing shoes that are roomy or ventilated and that would allow some air to circulate; try to avoid the sharing of nail tools, like clippers and scissors, and avoid sharing shoes and towels. Also use hot water and bleach to increase the chance of killing fungi when washing some clothing.⁶

Box 1 summarises a few general healthcare tips that may benefit patients suffering from *tinea pedis*.

Box 1: Healthcare tips for managing athlete's foot

- Wear clean socks daily.
- Use suitable foot powder, or a medicated foot spray, both on the feet and inside the shoes.
- Air the feet as frequently as possible and dry shoes in the sun when not on the feet.
- Practice good foot hygiene, washing feet daily with soap and water, washing between the toes, and then also drying feet properly before putting on socks and shoes.
- Try to alternate between different pairs of shoes on a daily basis.
- Use topical and/or systemic treatment, as recommended or prescribed by a healthcare professional.

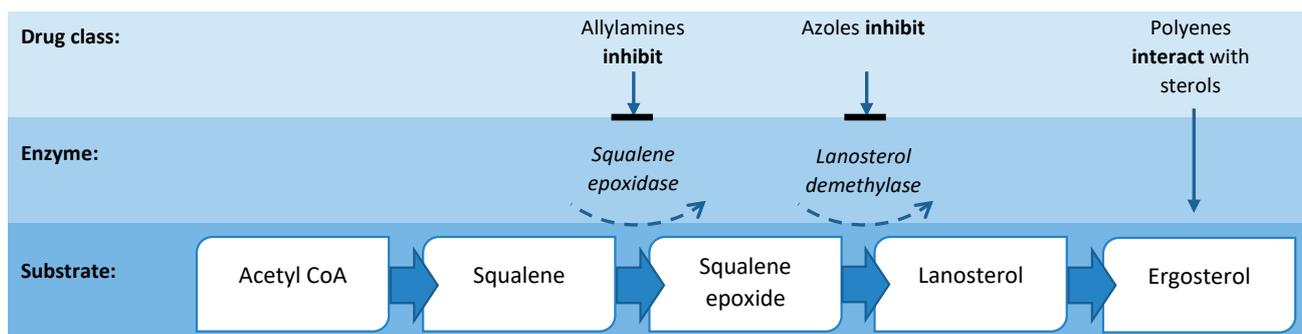


Figure 2: The ergosterol synthesis pathway, showing where the different classes of antifungal drugs exert their effects.

Table 2: An overview of the medication most often used to treat *tinea pedis*^{3,16-20,22-24}**The azole antifungal agents:**

The azoles are a class of five-membered, heterocyclic compounds containing a nitrogen atom and at least one other non-carbon atom (i.e. nitrogen, sulfur or oxygen) as part of the ring structure. Azoles that are available for clinical use are classified as either imidazoles or triazoles, according to the number of nitrogen atoms they contain in their chemical structure^{3,17}:

- Imidazoles (*ketoconazole, miconazole, econazole and clotrimazole*)
- Triazoles (*fluconazole, itraconazole and voriconazole*).

Although these medications share a similar mechanism of action and spectrum of activity, their pharmacokinetics and therapeutic uses vary significantly. Imidazoles, in general, are fungistatic.

Mechanism of action: They inhibit C-14 alpha demethylase, thereby blocking the demethylation of lanosterol to ergosterol. Ergosterol is the primary sterol of fungal membranes. Inhibition of ergosterol synthesis disrupts fungal membrane structure and function, which in turn, prevents fungal growth.¹⁶

The selective toxicity of the imidazoles results from their greater affinity for fungal, rather than for human cytochrome P450-enzymes.

Resistance is seen with prolonged therapy in advanced HIV-infection, or following bone marrow transplant procedures. Mutations in the C-14 alpha demethylase gene that leads to decreased azole binding can also occur. Some strains of fungi have developed efflux pumps that actively pump out azole molecules from their cell contents.

Spectrum of activity: The azoles are broad-spectrum antifungal agents, with their spectrum of activity including the following:

- Many species of *Candida* and *Cryptococcus neoformans*
- Dermatophyte-mycoses.

Drug interactions: All azoles inhibit the hepatic CYP450 isoenzymes (especially CYP450 3A4) to varying degrees; decreasing the metabolism of other drugs, and leading to numerous drug interactions. Potent CYP450-inducers, e.g. rifampicin, can lead to decreased effect of azoles. On the other hand, potent CYP450-inhibitors, e.g. ritonavir, can lead to increased adverse effects of the azoles.

Terbinafine:

Terbinafine^{17,19,23} is a synthetic allylamine (squalene epoxidase inhibitor) that is available in both oral and topical formulations.

Mechanism of action: Allylamines act by inhibiting the squalene epoxidase enzyme (see Figure 2), thereby blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. Accumulation of toxic amounts of squalene results in increased membrane permeability and death of fungal cells.¹⁹

Terbinafine is the drug of choice for treating onychomycosis.

Applicable pharmacokinetics: More than 70% of the drug is absorbed and it is highly bound to plasma proteins. However, due to the first-pass effect only 40% of the ingested drug is available to the systemic circulation. It is metabolised in the liver by several CYP 450 isoenzymes and mainly excreted in the urine.¹⁷

It accumulates in breast milk and should not be given to nursing mothers.

Side-effects: These include headaches, gastrointestinal disturbances and skin rashes. Terbinafine should be used with caution in the presence of renal and hepatic impairment.²³

Griseofulvin:

Griseofulvin¹⁹ was first discovered in 1939 from *Penicillium griseofulvum*, and was the first available oral agent for the treatment of dermatophytosis. Now it has been largely replaced by oral terbinafine for the treatment of onychomycosis, although it may still be used for the treatment of dermatophytoses.

Mechanism of action: Following oral administration, griseofulvin is deposited in the keratin precursor cells and has a greater affinity for diseased tissue. It tightly binds to newly synthesised keratin, forming a keratin-griseofulvin complex, which becomes highly resistant to fungal invasion. Once the complexes reach the site of action in the skin, they bind to fungal microtubules (tubulin), thus altering fungal mitosis.

Applicable pharmacokinetics: This agent is available in oral tablet form only; it is ineffective topically. In terms of its distribution, it tends to become concentrated in the skin, hair, nails and adipose tissue. Griseofulvin is metabolised by the liver to 6-desmethyl-griseofulvin and its glucuronide conjugate, and is ultimately excreted in urine, faeces and perspiration.

Side-effects: These include skin rashes, headache, urticaria, gastrointestinal disturbances and oral thrush. This agent is contraindicated in patients with porphyria.

Topical agents:

Several antifungal agents may be employed to effectively manage dermatophytoses (*tinea* infections) of the skin. These include undecenoic acid (and zinc undecenoate) and tolnaftate. The azoles (refer to the afore-mentioned text) and terbinafine (an allylamine; as is naftifine) can also be used, and are effective against candidiasis as well. Topical nystatin may be used for mucocutaneous candidiasis, such as oropharyngeal and vulvovaginal thrush, but is not effective against *tinea* infections (including *tinea pedis*). Fungal infections of the nails (onychomycoses) may be treated topically with amorolfine. Ciclopirox is another topical treatment option in the management of dermatophytosis, and is also available as a shampoo, as well as a nail lacquer solution for the treatment of mild onychomycosis.^{17,18,24}

Pharmacologic treatment

Medical therapy is the main treatment for *tinea pedis*; surgical care is usually not indicated in these patients. *Tinea pedis* is treated with topical antifungal agents; however, depending on patient's response to topical agents and the severity of the infection, both topical and oral (i.e. systemic) agents may be used. Medications used to treat *tinea pedis* work by disrupting the synthesis of ergosterol, which is a crucial component of fungal cell membrane (see Figure 2).^{19,20,22}

Commonly-used medications in the management of athlete's foot are summarised in Table 2.

Conclusion

Fungal foot infections, particularly athlete's foot, are very common. They are more prevalent with increasing age and most often occur in men. Athlete's foot is a very contagious condition and spreads quite easily; the infection can often spread from one site on the body to other sites. The spores

live in the moist warm areas of the body, or the environment, and the risk of infection increases when in contact with such an environment. *Tinea pedis* is usually diagnosed via clinical observation, but there are variety of other methods used to diagnose it. Prevention can effectively be done non-pharmacologically. There is also a variety of pharmaceutical products available for the management and treatment of this condition.

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