Tinea pedis:
not just the curse of the athlete

Tinea pedis is a common fungal foot infection that is often associated with high rates of treatment failure or recurrence. This is often due to inadequate duration of antifungal treatment. In most cases, tinea pedis can be managed with topical antifungal treatment, however, oral antifungal treatment is sometimes required, e.g. in patients with more severe infections, including moccasin tinea pedis, those with fungal nail infections and those with repeated topical treatment failures.

Tinea pedis is a fungal infection that primarily affects the interdigital spaces and the plantar surface of the foot. It is estimated that approximately 70% of the population will be affected with tinea pedis at some point in their life.[1] The prevalence of tinea pedis is highest among people aged 31 – 60 years, and it is more common in males than in females.[1] Tinea pedis can be caused by a number of different dermatophyte fungi, including *Trichophyton rubrum*, *T. interdigitale* and *Epidermophyton floccosum*.[1]

The dermatophytes that cause tinea pedis grow best in a moist, damp environment. The fungal spores can survive for extended periods (months or even years) in bathrooms, changing rooms and around swimming pools.[2] Some practical advice that clinicians can give to patients to help reduce both the risk of contracting tinea pedis and re-infection includes:

- Wearing less occlusive shoes and changing shoes and socks on a daily basis, and if they become wet
- Thoroughly drying feet after showering or swimming
- Not sharing towels
- Wearing jandals in communal showers and changing rooms

People who are more at risk of tinea pedis include those who are immunocompromised, who sweat excessively (hyperhidrosis), and those who have poor peripheral circulation or diabetes.[2, 3]

Signs and symptoms vary according to the type of tinea pedis

Patients with tinea pedis typically present with itching, erythema and small blisters on one or both feet. Malodour is more likely to be due to bacterial infection. More specific signs and symptoms depend on the subtype of tinea pedis.

Interdigital tinea pedis (often referred to as athlete's foot) is the most common form and is predominantly caused by *T. rubrum*. It is characterised by macerated skin with fissures between the toes (usually between the fourth and fifth toes) and frequently erythema (Figures 1 and 2, over page).[1]

Moccasin (chronic hyperkeratotic) tinea pedis is also predominantly caused by *T. rubrum* and is associated with scaling plaques and mild erythema on the heels, soles and lateral aspects of one foot, or less often, both feet (Figure 3, over page). Skin markings appear exaggerated and white. The dorsal surface of the foot is usually clear.[1]

Inflammatory or vesicular tinea pedis is predominantly caused by *T. interdigitale* and is associated with clusters of vesicles and pustules on the instep or mid-anterior plantar surface.[1]

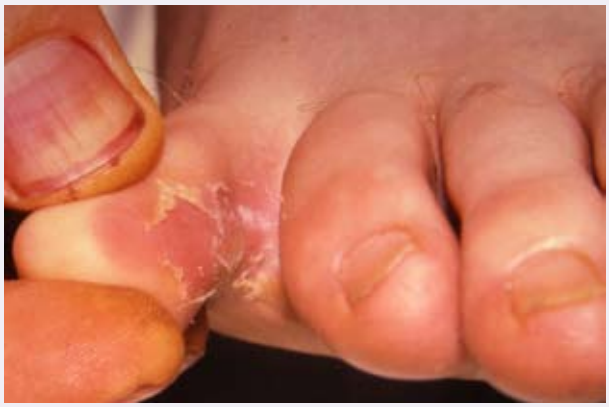

Figure 1: Interdigital tinea pedis showing macerated skin and erythema between the fourth and fifth toes (Image provided by DermNet NZ)

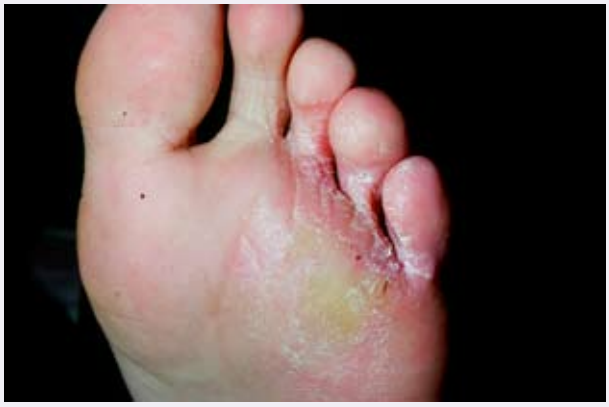

Figure 2: Interdigital tinea pedis showing scaled, peeling skin and extension on to the plantar surface of the foot (Image provided by DermNet NZ)

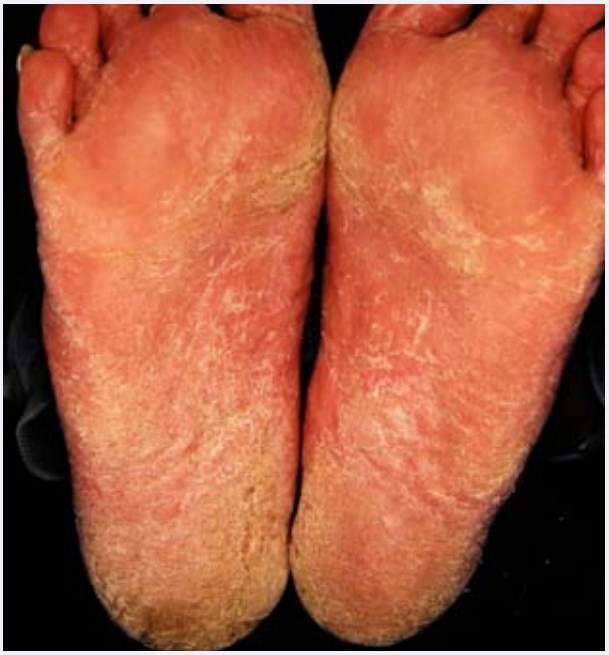

Figure 3: Moccasin tinea pedis showing dry, thickened skin covering the plantar surface with scaling and plaques (Image provided by DermNet NZ)

Ulcerative tinea pedis is predominantly caused by *T. interdigitale* and is associated with the rapid spread of vesiculopustular lesions, ulcers and erosions. The lesions are macerated with scaling borders and typically start in between the fourth and fifth toes before spreading to the lateral dorsal and plantar surfaces over a few days. The ulcerative form is often associated with secondary bacterial infection.[1]

Diagnosis and differential diagnosis – fungal cultures can be useful

The diagnosis of tinea pedis is usually based on the patient's symptoms and the clinical appearance. There are, however, a number of other conditions that should be considered when a patient presents with suspected tinea pedis, including:[1]

- Onychomycosis (fungal nail infection) – approximately one-third of patients with tinea pedis have a concomitant nail infection which can result in recurrent tinea pedis infections[1]
- Dermatophytide (ide or id) reaction – an allergic rash (secondary eczematisation) caused by an inflammatory fungal infection[4]
- Non-dermatophyte associated podopompholyx – a type of eczema which can affect the feet and may resemble a vesicular form of tinea pedis. It is more likely to be bilateral and symmetrical; mycology is negative.
- Palmoplantar pustulosis (see opposite) – typically characterised by scaly, partially or completely red, dry and thickened skin on the plantar surface of both feet, that is similar in appearance to psoriasis on other parts of the body.[5] Note that psoriatic nail dystrophy often closely resembles onychomycosis.
- Juvenile plantar dermatosis – characterised by dry, shiny, glazed skin on the sole of the foot due primarily to friction. It is most commonly seen in children who are atopic, particularly boys aged four to eight years.[6]
- Contact dermatitis – sweat, friction and home-remedies can cause irritant contact dermatitis; contact allergy may be due to accelerants (from rubber), chrome (leather tanning agent), glues and dyes in footwear
- Atopic dermatitis – usually diagnosed because of its presence on other body sites[7]
- Bacterial foot infections, e.g. pitted keratolysis (associated with very malodorous feet) and bacterial web infections secondary to tinea pedis infection

Skin scrapings for fungal microscopy should be undertaken

when initial topical treatment has been ineffective, whenever considering oral treatment, or in patients with an atypical presentation. Skin scrapings should be taken from the leading edge of the lesion using a blunt scalpel blade or curette. Nail clippings should be collected from abnormal toenails. If there is clinical evidence of a secondary bacterial infection, e.g. malodour or maceration, swabs for bacterial microscopy and culture should also be collected.

N.B. Potential bacterial infections include erythrasma which fluoresces coral pink under a Wood's lamp (this can be done in the surgery) and is not responsive to antifungal medicines.

For further information, see: "Collecting specimens for the investigation of fungal infections", Best Tests (Mar, 2011).

Treatment of tinea pedis: topical or oral

In general, patients with interdigital tinea pedis can be treated with a topical antifungal. Patients with moccasin, vesicular or ulcerative tinea pedis, or persistent tinea pedis may require oral antifungal treatment.[1]

Topical antifungals treatments – treatment duration is important

Topical miconazole, clotrimazole and terbinafine are used for the treatment of tinea pedis. Recurrence of tinea pedis after the use of a topical antifungal is common, and is often due to a patient discontinuing treatment shortly after the symptoms appear to have resolved.[1] It is therefore essential to educate the patient about the importance of applying the topical

Palmoplantar pustulosis (palmoplantar pustular psoriasis)

Palmoplantar pustolosis is a chronic, recurrent inflammatory condition that can be mistaken for a fungal foot infection. The exact cause of palmoplantar pustulosis is unknown. It is now regarded as distinct form of plaque psoriasis.[8] The disease is usually recalcitrant and affects one or both soles of the feet or palms of the hand. Patients typically have repeated eruptions of sterile pustules that are associated with scaly, thickened, red skin that often develops painful cracks (Figure 4). In patients with acute flares, the background skin is red and dotted with small yellow or darker-red blisters within the red patches. These lesions then dry and become scaly. Patients in the chronic stage of the disease often have dry, thickened skin and deep fissures.[9]

The diagnosis of palmoplantar pustulosis is usually based on symptoms and clinical appearance. A skin biopsy is sometimes used to confirm the diagnosis although this is rarely undertaken in general practice.[5] There are a number of conditions which have been reported to occur more frequently in people with palmoplantar pustulosis, including chronic plaque psoriasis (in 10 – 25%) and some autoimmune conditions, e.g. coeliac disease, type I diabetes and thyroid disorders.[5] The majority of people with palmoplantar pustulosis are current or ex-smokers (65 – 90%) and genetic factors, e.g. a family history and IL36RN gene mutation (not routinely tested for), have also been associated with the disease.[5] Palmoplantar pustulosis is more common in females than in males and is rare in children.[9]

Management of palmoplantar pustulosis can be challenging and no treatment is curative. A recent systematic review reported that intermittent ultrapotent topical corticosteroids, e.g. clobetasol propionate, topical psoralen with ultraviolet A photochemotherapy (PUVA), acitretin and ciclosporin, appear to be the most effective treatments for symptom control.[8] Referral to a dermatologist is generally recommended for patients with symptomatic palmoplantar pustolosis.

For further information, see: "The treatment of psoriasis in primary care" BPJ (Sep, 2009).

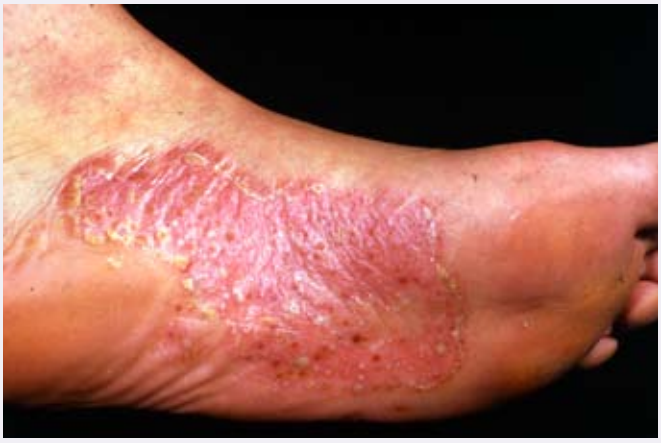

Figure 4: Palmoplantar pustulosis showing scaled, thickened skin and pustules (Image provided by DermNet NZ)

antifungal for the recommended full duration of treatment. Topical treatment should be applied to the affected area of skin, extending on to several centimetres of the surrounding normal skin.[10]

Azole antifungals

Topical azole antifungals are effective for the treatment of patients with tinea pedis infections, when used for the recommended duration, and there appears to be little difference between the individual azole medicines.[11] Therefore, the decision whether to prescribe a patient miconazole or clotrimazole is at the discretion of the clinician, as both miconazole and clotrimazole creams are fully subsidised on the Pharmaceutical schedule.[12]

Miconazole cream 2% (fully subsidised): The patient should be advised to apply a thin layer of cream, twice daily and c**ontinue treatment for ten days after symptoms have resolved**.[12] Miconazole also comes in a range of other non-subsidised formulations, including powder, solution, spray, lotion and tincture (partially subsidised).

Clotrimazole cream 1% (fully subsidised): The patient should be advised to apply a thin layer of the cream, twice or three times daily and **continue treatment for two weeks after symptoms have resolved**.[12] Clotrimazole also comes in a 1% solution which is partially subsidised.[12]

Miconazole 2% + hydrocortisone 1% (fully subsidised) combination products are also available. There is no conclusive evidence that patients with tinea will benefit from combination treatment, particularly as they will need to be switched to a miconazole-only cream,[13] but this product may be considered when inflammatory symptoms are predominant.[12] The patient should be advised to apply a thin layer of the cream, twice daily, until the inflammatory symptoms have disappeared or **for a maximum of two weeks**.[12]

When the miconazole + hydrocortisone treatment is discontinued, the patient will need to be switched to a miconazole-only cream which should be **continued for at least 10 days** after the symptoms have resolved.[12]

Topical miconazole and clotrimazole are generally well tolerated. Adverse events are relatively rare and are usually related to localised skin reactions, e.g. irritation and hypersensitivity reactions.[12]

Other topical azole treatments available in New Zealand include a econazole 1% cream and solution (partly subsidised) and a ketoconazole 2% cream (not subsidised).[12]

Topical allylamine antifungals (terbinafine)

Topical terbinafine is not subsidised on the Pharmaceutical Schedule, but is available to purchase over-the-counter as a cream, gel, solution and spray. Terbinafine should usually be applied **once daily, for one week**. It can be repeated as necessary.[12]

Allylamine antifungals such as terbinafine are reported to be generally more effective than azole antifungals, e.g. miconazole and clotrimazole, in patients with fungal infections of the foot.[11] This is because terbinafine has a fungicidal action, i.e. destroys the fungal cell, in contrast with the azole antifungals which are fungistatic, i.e. inhibit fungal growth.[14]

Topical terbinafine is generally well tolerated; adverse effects include local irritation and hypersensitivity reactions.[12]

When to consider an oral antifungal treatment

Although most people with a localised tinea pedis infection can be successfully treated with a topical antifungal medicine, some patients may require an oral antifungal medicine, including:

- Patients with a more treatment-resistant subtype of tinea pedis, e.g. moccasin, vesicular or ulcerative
- Patients with interdigital tinea pedis that is severe and involves multiple interdigital spaces or has spread to the plantar aspect of the foot
- Patients with a co-existing fungal nail infection
- If topical treatment has been unsuccessful

If oral treatment is required, the two recommended oral antifungal treatment options are terbinafine or itraconazole.[2] Both treatments are fully subsidised on the Pharmaceutical Schedule, but itraconazole requires endorsement by a specialist.[12]

Terbinafine is the first-line oral treatment for tinea pedis

Terbinafine is generally used first-line for patients with tinea pedis when oral treatment is required, as it has been reported to be more effective than itraconazole and has less potential for medicine interactions.[14]

In adults with tinea pedis, the recommended oral treatment regimen is terbinafine 250 mg, once daily, for two to six weeks.[12] If oral treatment is required for a patient with tinea pedis complicated by a fungal nail infection, it will need to be continued for at least three months.[12]

Terbinafine is associated with some potentially serious adverse effects, although these are uncommon.[15] Patients taking oral

terbinafine may experience gastrointestinal disturbance (e.g. nausea, dyspepsia and diarrhoea), allergic skin reactions (e.g. urticaria), dysgeusia (unpleasant sense of taste), headache and joint and muscle pain.[16] Serious adverse can include Stevens-Johnson syndrome, toxic epidermal necrolysis, liver dysfunction and reduced neutrophil count. The rates of terbinafine discontinuation due to adverse events are relatively low (approximately 3 – 4%).[15]

Terbinafine is not recommended in people with liver disease.[12] For all patients, liver function tests (LFTs) should ideally be performed prior to initiation of terbinafine and then performed every four to six weeks during treatment.[12] Terbinafine should be discontinued if any significant abnormalities in LFTs are observed or if the patient reports any symptoms that suggest liver damage, e.g. anorexia, nausea, vomiting, fatigue, or dark urine. Adverse hepatic effects may not arise until after the discontinuation of terbinafine treatment. Treatment discontinuation due to increases in the liver transaminase levels are reported to be <1%.[15]

Terbinafine may be used at a halved dose in patients with renal impairment (eGFR of less than 50 mL/min1.73 m^2), if there is no suitable alternative treatment.

A patient information brochure on terbinafine is available from: **www.saferx.co.nz/terbinafine-patient-guide.pdf**

Itraconazole – avoid in heart failure and be aware of potential drug interactions

Itraconazole requires specialist endorsement for subsidy, and should be considered as the second-line oral treatment in patients with tinea pedis. The recommended dosing regimen for patients aged over 12 years is either 100 mg, once daily, for 30 days or 200 mg, once daily, for seven days.[12] Absorption of itraconazole capsules is improved if it is taken with a full meal or an acidic drink such as fruit juice.[12]

Although no head-to-head randomised trials comparing the two regimens have been performed, the 100 mg/day itraconazole regimen may be preferred due to a more favourable adverse event profile. Adverse events resulting in treatment discontinuation have been reported to occur more frequently in patients receiving 200 mg/day of itraconazole (4%) compared with those receiving 100 mg/day of itraconazole (2%).[15] Treatment discontinuations due to increases in transaminase elevations are relatively low (<1%), but are also more common in patients taking 200 mg/day than in patients receiving 100 mg/day.[15]

Itraconazole is also associated with gastrointestinal adverse effects (e.g. nausea, vomiting, diarrhoea and abdominal pain), blood pressure changes, skin rashes and rarely changes in liver enzyme levels. Other less common adverse events include pancreatitis, heart failure and leucopenia.[12] Itraconazole should only be used in people with liver dysfunction if the benefits outweigh the risk of hepatotoxicity.[12] LFTs should be requested if the itraconazole treatment duration is longer than one month.[12] Treatment should be discontinued if significant abnormalities in LFTs are observed or if the patient reports any symptoms that suggest liver damage, e.g. anorexia, nausea, vomiting or fatigue.[12]

Itraconazole should not be used in people with ventricular dysfunction or in people with a history of heart failure.[12] Caution is advised in people with an increased risk of heart failure, e.g. older people, those with cardiac disorders, or those receiving negative inotropic medicines, e.g. calcium channel blockers, beta blockers or antiarrhythmics. Itraconazole is an inhibitor of the CYP3A4 enzyme and therefore should be avoided or used with caution in patients who are receiving medicines which also inhibit or are metabolised by this enzyme, e.g. simvastatin, atorvastatin, ticagrelor, felodipine and quetiapine. Itraconazole can also increase the risk of bleeding in a patient taking warfarin, so dose reduction and more frequent INR monitoring may be necessary.[17]

Complications and follow-up

Patients should be advised to return for assessment if the initial treatment is unsuccessful or if they have frequent recurrences of tinea pedis. If this occurs, take a skin scraping for a fungal culture (even if one was done at the initial consultation) to confirm that the patient has tinea pedis. Check compliance with the treatment regimen. It may also be necessary to investigate whether other members of the household have untreated tinea pedis, as this can result in re-infection from shared use of a bathroom or towels.

Complications from tinea pedis can include secondary bacterial infections; it is a common predisposing cause in cellulitis. Patients with recurrent cellulitis of the lower leg should be examined for evidence of tinea pedis. Patients undergoing CABG with vein grafts from the legs should also be assessed for tinea pedis and treated prior to surgery to help prevent postoperative infection in the leg the vein was harvested from.

Majocchi granuloma is a rare complication of tinea pedis. It is a persistent, suppurative folliculitis, usually on the lower leg, caused by a dermatophyte infection. Patients generally require treatment with an oral antifungal medicine.[18]

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