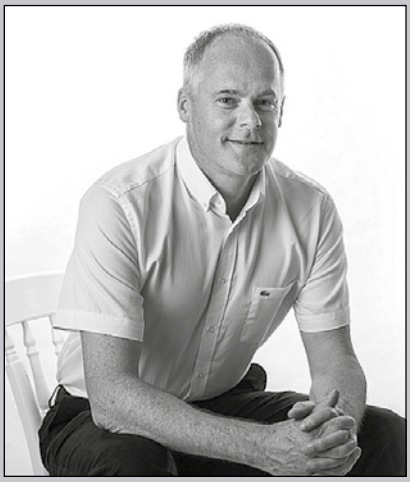
CONTINUING PROFESSIONAL UPDATE

MI PODIATRIC CPU TOOLS
Driving excellence in foot health

Psoriasis



Ivan Bristow PhD
Podiatrist, New Forest, Hampshire, United Kingdom
www.foot.expert

Summary
Psoriasis is one of the most common skin conditions seen in the dermatology clinic. Initially thought to be a disease of keratinocytes, it is now known to be one of the most common immune-mediated conditions. In recent years there has been research which has increased our understanding of the disease, how it affects the skin and other systems, but most significantly how it is managed. New targeted biological therapies have led to a significantly improved prognosis for many patients with skin and nail pathology. This article reviews the clinical features of the disease, comorbidities and modern management.

Introduction
Psoriasis is the most common of the inflammatory skin dermatoses, affecting around 2-3% of patients globally (1). A systematic review of incidence studies demonstrated a prevalence ranging from 0.1% in Eastern Asia, 1.52% in Europe to 1.58% in Australasia. Rates of psoriasis are highest in high income countries (2). Individual countries with high rates include the United States, India, China and Germany (3). Around 10% of patients with psoriasis will have associated psoriatic arthritis. Clinically, the disorder is characterized by inflammatory plaques across the body with detachable silvery scales often accompanied by pain and itching (figure 1). The most common presentation being well-delineated erythematous plaques which show a strong symmetry. Darker skin types may show darker plaques which are more purple in colour. Typical locations include the scalp (rarely showing beyond the hairline), elbows, anterior surface of knees and base of the spine. The condition also exhibits the Koebner phenomenon, where unaffected skin in a patient with active disease, may, if traumatised, develop further psoriasis. An example could be the development of psoriasis around a toe, following nail surgery using phenol. Evaluation of the age of onset reveals two peaks in its incidence. The first peak, early onset, occurs in individuals aged 16-22 years (Type 1) and a second peak, in middle age (Type 2). Type 1 is likely to be strongly linked to genetic factors, often begins in a guttate pattern (see below) and is more likely to have a course of greater severity along with associated arthritis than seen in type 2 psoriasis (5). Variants of the condition are given in table 1.

Key Point:
Psoriasis affects around 2-3% of the population.

Palmoplantar psoriasis can still be found in older textbooks, describing a form of the disease which causes yellow-brown sterile pustules to develop on the palms and soles. Current research suggests that this is likely to be a separate disease (now called palmoplantar pustulosis [PPP]) owing to features not typically associated with psoriasis. For example, different genes have been identified, it almost exclusively affects smokers, an unusually high number of females are affected but around a quarter of patients with PPP will also have psoriasis elsewhere (6).

Key Point: Recent work suggests palmoplantar pustulosis is a disease separate from psoriasis.

Sub-Type	Main features
Vulgaris	The most common type exhibiting symmetrical plaques. Usually located on the extensor surfaces, scalp and sacral skin.
Guttate	An acute form of the disease. Often observed in children and young adults as small, round scaly lesions located on the torso, arms and legs. Associated with tonsilitis and sore throats.
Pustular (Generalised)	Small pustular lesions which develop on inflamed skin across the whole body. The patient generally feels unwell.
Rupioid	A variant presenting with smaller lesions with a thick adherent scale and a darker red colour at the base of the lesion.
Small Plaque psoriasis	A sub-type most often seen as a late onset variety in the elderly.
Inverse (or flexural) psoriasis	A type that affects the body folds (groin, axillae and eyelids) which is often devoid of scale.
Acrodermatitis continua of Hallopeau	A rare form of the disease associated with pustular psoriasis which specifically affects the distal digits, nail unit and distal joints.
Erythrodermic Psoriasis	A widespread eruption of psoriasis with erythema and scaling affecting more than 90% of the skins surface. Emergency medical treatment is required to prevent hypothermia or heart failure

Table 1: Variants of Psoriasis

Genetics and Triggers

Around one-third of patients with psoriasis will have a family history of the condition. Lifetime risks for psoriasis are 4%, 28% and 65% if neither, one or both parents have the condition (7). A number of genes have been linked to the condition, but it is most probable there is an interplay between genetic and environmental factors that leads to the condition. It has been long known that psoriasis can be triggered or exacerbated by a range of external agents including stress, infections and drugs (8). A variation of the disease which affects adolescents and young adults, guttate psoriasis, is known to be triggered by streptococcal throat infections and tonsilitis. It has been postulated that cross reactivity occurs due to a toxin released by the bacteria which can misappropriate T cell activity in the skin (9). In addition, a range of drugs is known to trigger and/or worsen the condition in patients (table 2). (Those listed first are most strongly linked to aggravating or triggering the disease)

Table 2: Drugs known to trigger or exacerbate psoriasis. Modified from Fry (8).

Lithium Carbonate
Propranolol
ACE inhibitors
Chloroquine
Hydroxychloroquine
Alcohol
Digoxin
Amiodarone
Quinidine
Fluoxetine
Carbamazepine
Antibiotics : Doxycycline, Vibramycin, Penicillin / Amoxicillin / Ampicillin
α-Interferon / ß-Interferon
Imiquimod
Cimetadine

Comorbidities

Although psoriasis is a disease in its own right, many patients have additional conditions which are known to occur more frequently with the psoriasis. These are known as comorbidities. In the last decade or so, much research has been undertaken to uncover their association and effects (table 3). Psoriasis is known to co-exist with hypertension and cardiovascular disease (10-12). One UK study identified that the two were positively associated. Patients with moderate to severe psoriasis were twice as likely to have hypertension compared with patients without the skin problem. In addition, it has long been observed that obesity and psoriasis often co-exist.

More recently, a link between diabetes and psoriasis has been shown to exist (13, 14). Patients with psoriasis are around 1.36 – 1.50 times to have diabetes than those without psoriasis. The longer the patient had the skin problem, the higher the risk of having diabetes. Also, as reported in additional studies, an increasing severity of psoriasis predicts a higher correlation with diabetes. The relationship between the psoriasis and diabetes is complex. One study has identified 4 shared genes (15).

Key Point: *Many patients with psoriasis may have concomitant conditions such as hypertension & diabetes.*

Table 3: Known disorders associated with psoriasis. Adapted from Yamazaki (16).

Hypertension
Cardiovascular diseases (myocardial infarction, stroke and death)
Increased body mass index / obesity
Hyperlipidaemia
Metabolic Syndrome
Crohn's disease / Inflammatory bowel disease
Diabetes Mellitus
Non-alcoholic fatty liver disease
Psychiatric morbidities (depression)
Psoriatic arthritis

Assessment of the Patient

Assessment of the extent of psoriasis affecting the patient is an important step to quantify the disease and to understand its effect on the patient. It is well established that psoriasis can have a significant effect on the patient's health related quality of life. Patients may experience embarrassment, stigmatisation or shame. Assessment of the physical and psychological aspects can guide appropriate treatment and act as a comparator on which to assess the success of any intervention. The Psoriasis Area and Severity Index (PASI) is a widely used tool which calculates the extent of skin involvement in four segments to combine and give a score range from 0 to 72. The impact of the condition on the patient can be measured using various validated tools such as the Dermatology Life Quality Index (17) or more specifically the Psoriasis Disability Index (PDI) (18). The Dermatology Life Quality Index is a validated tool which can be used to assess the impact of any skin condition and can be used easily in a clinical setting. Full details can be found on the website including a free clinical app (https://bit.ly/3MtJJim).

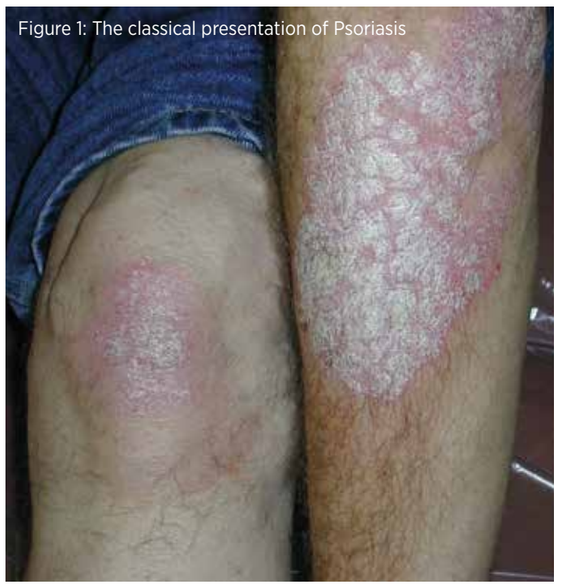


Figure 1: The classical presentation of Psoriasis

Table 4: Features of the nail associated with Psoriasis

Onycholysis
Pitting
Leukonychia (white spots)
Beau's lines (transverse grooves)
Accelerated nail growth (figure 2)
Splinter haemorrhages
Sub ungual hyperkeratosis / debris
Nail shedding
Paronychia
Oil drop discolouration

Nail involvement in psoriasis can affect anywhere between 15-79% of patients (19) with nearly 90% of patients with psoriasis developing nail involvement at some stage in their lives. A range of symptoms has been identified and are listed in table 4. Co-existing onychomycosis is a common presentation and so mycological testing is advised to rule out fungal involvement (20). Clinically, the extent of nail involvement can be measured using the Nail Psoriasis Severity Index (NAPSI) tool (21). However, in clinical practice the tool can be cumbersome and time consuming to administer and calculate so it is generally reserved for clinical trials. As a visible structure, patients with nail involvement are known to have lower quality of life scores.

Key Point: *The DLQI questionnaire is a useful clinical tool to assess the effect of skin disease on a patient's daily life.*

Pathophysiology

Psoriasis is a complex disorder which arises from both genetic and environmental factors which interplay to give rise to immunological abnormalities leading to hyperproliferation of the main cell of the epidermis, the keratinocyte. This is characterised by excessive skin which is rapidly and imperfectly formed producing visible scale. Chronic inflammation is the excessive production of cytokines from the skin and immune cells which can have comorbid effects (see above). The current theory simplified suggests that activation of dendritic (antigen presenting) cells leads to the release of cytokines IL-12, IL-23 and Tissue Necrosis Factor-alpha (TNF-α). This leads to the maturation of T helper cells Th1, Th17 and Th22. These stimulated cells promote further release of inflammatory cytokines (TNF-α, IFN-γ,

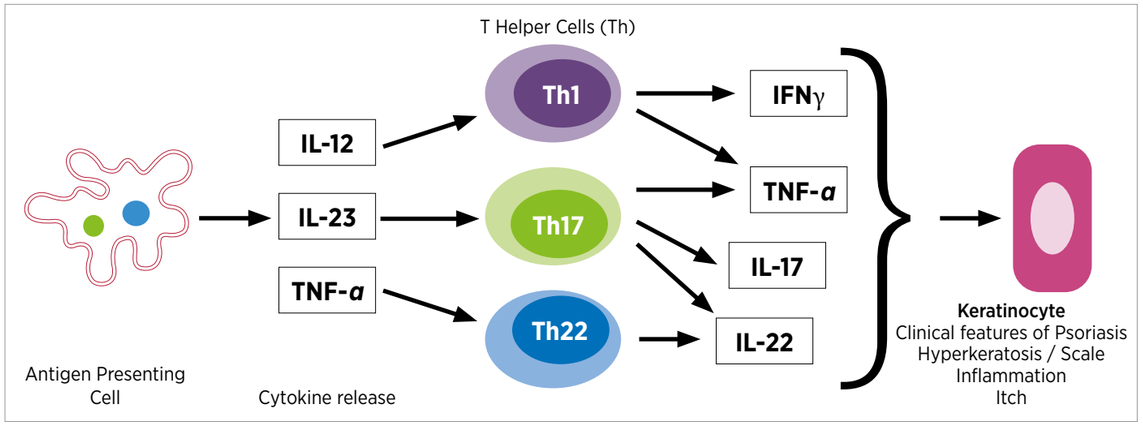


Figure 2: Simplified diagram explaining the inflammatory pathways to Psoriasis

IL-17 and IL-22). The effect of the inflammatory cascade promotes vasodilation in the affected skin and stimulates the rapid keratinocyte proliferation and turnover, along with itching and characteristic skin changes (figure 1) (22). Inflammation accelerates epidermal transit time to just a few days and an imbalance of normal epidermal keratins affects the cellular cytoskeleton. Clinically, these effects are observed as inflamed, hyperkeratotic plaques with fragile, loosely attached scale. Itching is a frequent feature provoked by the excessive release of the cytokines.

Management of Psoriasis

With a wide range of topical and systemic treatments available for patients, each patient should be assessed individually on the most suitable treatments. Treatments should be based on a range of factors including age, medical history, lifestyle, co-morbidities and disease severity using available tools such as the DLQI and PASI measurements. With increased awareness of the psychological aspects of the disease, support in this area, when required, is equally as important as pharmacological based therapies in many cases. Current

Figure 3: Rapid nail growth evident through the migration of the nail varnish edge, two weeks after the onset of an acute episode.

NIHCE guidelines (23) recommend topical therapy as the first line treatment when there is less than 10% of the skin affected. Typical treatments include the use of vitamin D3 derivatives, topical steroids and coal tar preparations with emollients. Where plaque psoriasis is failing to be controlled, the use of narrowband UVB can be effective in suppressing the disease.

Systemic drugs are generally offered for more extensive cases where topical therapy and phototherapy have failed or where there is significant psychological distress. Commonly used drugs include methotrexate and ciclosporin which have a general immune-suppressive effect and reduce the skin disease, but the former may have side effects on the liver, whilst renal impairment may occur with the latter.

Biological drugs in psoriasis

Traditional topical and systemic drug treatments for psoriasis were prescribed to reduce the effects of inflammation such as scale and redness. Moreover, older oral medications for psoriasis such as ciclosporin and methotrexate, although effective, can generate broad immunosuppression and hold additional risks. However, the discovery and understanding of the disease pathway has led to the development of novel treatments targeting specific points in the process to suppress and ameliorate the disease. These drugs are derived from living tissue (biologicals) and have a wide range of applications in inflammatory conditions like psoriasis (table 5).

Key Point: Biological drugs have made a significant impact in managing severe psoriasis.

The introduction of biological agents over the last 20 years has revolutionised the treatment of many conditions, including psoriasis, due to their effectiveness and relative safety. Most are delivered via sub-cutaneous injections, with four injections a year being most convenient for the more modern biologics. This newer class of drug simply acts by blocking particular cytokine pathways, preventing T helper (Th) cell activity and further cytokine release. Suppression of IL-1 and IL-23 has been demonstrated to be particularly effective (24). Evidence from studies has demonstrated that around 80% of patients undergoing treatment with these drugs can expect 90% or more clearance of their psoriasis (25). Safety of these newer drugs has been studied and side effects have been reported. TNF-*α* shows a slight increased risk of serious infections and IL-17 inhibitors are associated with candidiasis, neutropenia, and inflammatory bowel disease (25). The main disadvantages of biological drugs are currently their costs. Consequently, they are generally reserved for patients meeting specific NIHCE criteria (23). In addition, all these drugs may gradually lose their effectiveness over time (labelled as “drug survival” or “persistence”) requiring discontinuation of treatment or switching to alternative drugs. Generally, older agents such as infliximab and entanercept show lower survival than compared with more modern agents such as ustekinumab and adalimumab, which demonstrated longer effectiveness in follow up studies (26).

Treatment of nail disease in psoriasis

The treatment of psoriasis in the nails has been less well researched than the skin manifestations of the disease with few evidence-based guidelines available. The nail unit is a formidable barrier to many pharmacological agents, hampering effective drug delivery. The clinician should recognise where the psoriasis exists within the nail unit. This can be involvement of the nail bed, nail matrix or both. Treatment of nail bed disease can be improved by resection of any onycholytic nail to expose the affected nail bed to any applied topical treatment. Nail matrix involvement requires application of agents to the eponychial / cuticle area. Despite the lack of documented evidence topical steroid creams and ointments can be prescribed for nail involvement (usually as a once to twice a day application). Progress can be slow and anecdotally, they work best where the matrix is involved, and have a lesser effect on nail bed psoriasis (27). Steroid injections into the nail matrix to reduce symptoms offer mixed results (28). Side effects such as prolonged pain post operatively and parathaesia are well known.

TNF Inhibitors	IL-23 Inhibitors
Entanercept (Enbrel) Infliximab (Remicade) Adalimumab (Humira)	Rizankizumab (Skyrizi) Guselkumab (Tremfya)
IL-12 / IL-23 Inhibitors	**IL-17 Inhibitors**
Ustekinumab (Stelara)	Ixekizumab (Taltz) Secukinumab (Cosentyx) Tildrakizumab (Illumetri) Brodalumab (Kynthium)

Table 5: Biological Drugs used in the treatment of Psoriasis. Proprietary drug names given in brackets

In addition, oral ciclosporin and methotrexate have been used in reducing nail dystrophy with modest success, however their side effect profile precludes them for sustained use. Biological drugs used on the nail have been as successful as they have on the skin, offering hope to many patients with accompanying nail dystrophy. Studies reviewing the different types of biologicals suggest that improvement can be expected with all of them in the nail, without significant differences in their effectiveness. Generally, nail improvement can be expected typically after 12 weeks of therapy but may lag behind any observed skin improvement. However, their positive effects can be seen often up to 12 months into treatment with these drugs. The safety profile of these drugs is much better when compared with ciclosporin and methotrexate with fewer adverse events (29).

Key Point: Biological agents have been shown to significantly improve nail disease in psoriasis.

Podiatric Aspects of Psoriasis

Patients presenting with psoriasis on their feet to the podiatrist can benefit from their skills. As with all patients the key to successful management is a thorough assessment and diagnosis recognising what is required. For a few patients, the diagnosis may not have been made and careful assessment is required to make a differential diagnosis.

Differential Diagnosis

The majority of patients with psoriasis have only small areas of the skin affected and it may go unnoticed by the patient, and for some the diagnosis may have already been made or is evident. Where there is doubt, other common causes of pedal rashes with scale should be considered namely tinea pedis and eczema.

Tinea pedis can create red and scaly areas on the foot. The most typical presentation occurs interdigitally, in the lateral web spaces as scale, with or without itching. Web spaces are very uncommon locations for psoriasis (and eczema alike). Where there is doubt, treatment with an antifungal cream can clear tinea confirming the diagnosis or taking a scraping for testing can also be utilsed. Eczema, like psoriasis, typically presents on

any area of the foot but very rarely between the toes. Individual lesions in eczema tend to be less distinct than psoriatic plaques with finer scale. Psoriatic lesions are often described as "islands" within the ocean whereas the edges of eczematous lesions are less well defined. Psoriatic lesions tend to be more raised and more erythemic or inflamed with a thicker or heaped scale. Eczematous lesions may ooze and more persistent lesions may look lichenified (leathery) in appearance. Nails can be affected with all three dermatoses. Fungal nails have a typical appearance tending to affect the first, second and fifth nails. Mycological testing can confirm the diagnosis. Nail psoriasis has a broad range of presentations (see table 4, page 3) affecting around 50% of patients. Typical features on the toenails include onycholysis, sub-ungual debris, splinter haemorrhages affecting just a few or all toenails. In acute psoriasis, nail shedding is not uncommon. Nail involvement is less common in eczema (around 11% of patients (30)) with pitting being the main feature along with Beau's lines, melanonychia or koilonychia. Onycholysis does arise but is much less common.

All three diagnoses can itch. With tinea this is generally less so, unless there is an unusual animal acquired dermatophyte (zoophillic) species causing the infection. This type of tinea pedis is usually much more florid and so the diagnosis is obvious. Whilst both psoriasis and eczema can cause itching to the extent that the scratching may be so intense as to cause bleeding, it is more common with the latter. Some patients with psoriasis may say their skin stings or burns.

When taking the history, it is important to ask about other areas of affected skin. Tinea typically affects the feet, hands and groin. Psoriasis occurs most frequently on the anterior surface (extensor) surface of the knees, on the elbows, base of the spine and most often the scalp. Eczema occurs more in the flexural regions and the face. Also asking about the age of onset of their skin disease can be helpful. Psoriasis is rare before the age of 8 and most common in the age ranges of 15-35, whilst most eczema occurs in infancy. Eczema is triggered or made worse by washing and the use of soaps and detergents. Family history is also important. Around a third of patients with psoriasis will have a positive family history. Atopic eczema is also familial and may present with a history of asthma, rhinitis and food intolerances.

In addition to a diagnosis, the podiatrist may wish to undertake further questioning and examination to check if the patient is at risk of any underlying comorbidities. Diabetes mellitus and cardio-vascular disease are commonly accompanying conditions, particularly in patients with more severe psoriasis and so neuro-vascular assessment along with blood pressure and glucose testing may be advisable when suspected. The extent of the skin disease of the foot, including any nail involvement should be recorded and where appropriate, practitioners may wish to undertake a DLQI score (see above) to measure the impact of the psoriasis on their daily activities. Patients demonstrating a higher score on the measure may require a referral back to their general practitioner requesting further support for the patient as appropriate. Moreover, the score can act as a baseline and may be repeated at the conclusion of any treatment undertaken to assess its impact.

Where there is skin involvement on the foot, general advice is always beneficial. Emollients remain the mainstay of any treatment and can improve symptoms of itching, scaling and inflammation with regular use. Careful selection is required to ensure the presentation and product is suitable for use by the patient on a regular basis. Moreover, regular use of emollients can enhance the effects of any applied topical steroids and reduce the incidence of steroid-related side effects. Urea based emollients are particularly beneficial on the plantar surface where psoriasis is evident. Routine scalpel debridement of thick plantar hyperkeratosis due to psoriasis may not be beneficial for many patients as the trauma can provoke further inflammation and discomfort. In addition, unlike mechanical hyperkeratosis, removing the scale can provoke bleeding from fragile capillaries. The use of a wet wrapping with a urea-based emollient may have a more significant effect and lead to improvement in the plantar skin (see case study page 7).

Practitioners who are independent prescribers with experience in this area will have access to topical agents which can be used on the feet. Topical steroids can be prescribed and used in the short term. For plantar treatment where the skin is thicker, ointment-based preparations are more effective due to their adherence. A very potent steroid (such as clobetasol propionate 0.05% - "dermovate") is often required in this area due to the limited penetration and increased skin thickness. It is important that patients use these for around two weeks and when improvement is noted, the steroid is not abruptly halted. Sudden withdrawal of the steroid can lead to rebound phenomenon which manifests as a rebound in the psoriasis, often much worse than the original presentation. Safe steroid withdrawal should be facilitated by gradual reduction in application frequencies or reducing to a lower potency and accompanied by regular application with emollients.

Key Point: Topical steroids, particularly as a tape can be an effective safe and short-term treatment for heel fissures in psoriasis.

Case Study

Mrs Jones is a 70-year-old female patient who has been referred to the podiatry clinic by her general practitioner. At the age of 68, she developed small areas of psoriasis on her limbs which have been managed with topical vitamin D3 derivatives ("Dovonex"). She felt this was not a significant problem and whilst it has been well controlled, new areas of psoriasis have now arisen on the soles of her feet and around her heels (figure 4). She had no nail changes. She had been initially managing the hyperkeratosis on her feet with emollients but has found them to be inadequate even with regular application, two or three times a day. Of more concern, she is suffering from painful heel fissures which are limiting her mobility (figures 6 & 7).

Assessing the patient, a full history was taken. It was noted that she suffers with hypertension, which was well controlled with amlodipine and her BMI was 29. Consequently, she was advised to undertake a fasting glucose test through her general practitioner to rule out diabetes which was negative. A vascular assessment was also undertaken – assessment of her pulses and peripheral circulation was unremarkable.

The patient undertook a Dermatology Life Quality Index questionnaire to assess the effects of the psoriasis on her feet. She scored 11 which indicated that her foot problem was severely affecting her day-to-day activities. Following the assessment she was initially advised to undertake wet wrapping of her feet (31), see table 6. She was instructed to perform the wet wrapping three times a week and reviewed two weeks later.

At her follow-up appointment, she felt the plantar skin had improved but was still getting pain from her heel fissures which remained present. She was advised to continue wet wrapping and was prescribed Fluoxycortide tape [POM] (Typharm, UK) – see figure 5. This is a steroid impregnated tape (4 micrograms per cm2). The patient was instructed to apply this over her heel fissures and leave it on for 12 hours and repeat this every other day for a week. At her subsequent review two weeks later, she reported her fissures had healed and she was able to walk pain free (figure 6). In view of the improvement, the Fluoxycortide tape was stopped and she was advised to continue wet wrapping three times weekly for a further 4 weeks. Once the hyperkeratosis was under control, she could return to twice daily application of a urea-based emollient. If her plantar psoriasis deteriorated at any stage, she was advised to return to wet wrapping to bring it under control. At the conclusion of her treatment her DLQI score had reduced to 3, indicating a significant improvement in her quality of life. ■

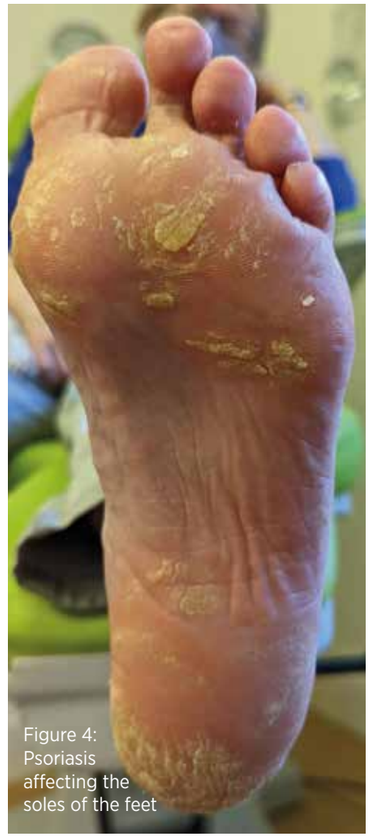


Figure 4: Psoriasis affecting the soles of the feet

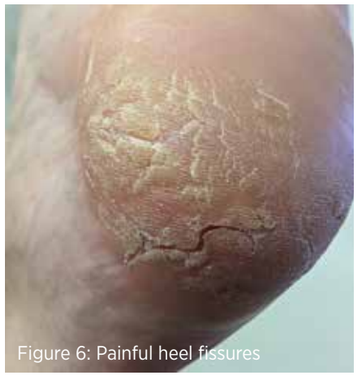


Figure 6: Painful heel fissures

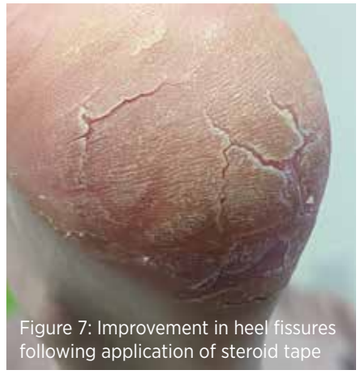


Figure 7: Improvement in heel fissures following application of steroid tape

Figure 5: Fluoxycortide tape [POM].

Wet wrapping for managing foot hyperkeratosis.	
1.	The feet are bathed in warm water and dabbed dry, just being slightly damp.
2.	Liberally apply a 20% urea preparation to the heels and plantar areas of the feet
3.	A damp sock is then applied over the foot.
4.	This is then covered with a dry sock.
5.	The patient then wears these overnight.
6.	The sock can be removed in the morning and the feet washed as normal.

Table 6: Wet wrapping procedure for plantar hyperkeratosis (31)

Conclusion

In managing patients with psoriasis affecting the feet it is important to assess their needs fully. Remembering that medications can adversely affect their psoriasis and to check for any co-existing conditions which may not have been detected. For most patients with inflammatory conditions affecting the skin of the feet, intense moisturisation, with the judicious use of topical steroids can have a significant effect in most cases. ■

The author declares he has no conflicts of interest.

References

1. Griffiths CE, Barker J, Chalmers R, Bleiker T, Creamer D, editors. Rooks's Textbook of Dermatology. 9th ed. London: Wiley; 2016.
2. Mehrmal S, Uppal P, Nedley N, Giesey RL, Delost GR. The global, regional, and national burden of psoriasis in 195 countries and territories, 1990 to 2017: A systematic analysis from the Global Burden of Disease Study 2017. J Am Acad Dermatol. 2021;84(1):46-52.
3. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:m1590.
4. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol. 1985;13(3):450-6.
5. Rocken M, Schaller M, Sattler E, Burgdorf W. Color atlas of dermatology. London: Thieme; 2021.
6. Bristow I, Cole M. Palmo-Plantar Pustulosis And Psoriasis: The Same But Different? Canadian Podiatrist. 2017(Spring):9-11.
7. Griffiths CE, Bleiker T, Creamer D, Ingram JR, Simpson RC. Rook's Dermatology Handbook. Oxford: Wiley-Blackwell; 2022. 1056 p.
8. Fry L, Baker BS. Triggering psoriasis: the role of infections and medications. Clin Dermatol. 2007;25(6):606-15.
9. Leung DY, Gately M, Trumble A, Ferguson-Darnell B, Schlievert PM, Picker LJ. Bacterial superantigens induce T cell expression of the skin-selective homing receptor, the cutaneous lymphocyte-associated antigen, via stimulation of interleukin 12 production. The Journal of experimental medicine. 1995;181(2):747-53.
10. Boehncke W, Boehncke S. Cardiovascular morbidity in psoriasis: epidemiology, pathomechanisms, and clinical consequences. G Ital Dermatol Venereol. 2008;143(5):307-13.
11. Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol. 2006;55(5):829-35.
12. Snekvik I, Nilsen TIL, Romundstad PR, Saunes M. Psoriasis and cardiovascular disease risk factors: the HUNT Study, Norway. J Eur Acad Dermatol Venereol. 2018;32(5):776-82.
13. Brauchli YB, Jick SS, Meier CR. Psoriasis and the risk of incident diabetes mellitus: a population-based study. Br J Dermatol. 2008;159(6):1331-7.
14. Lee K. JAAD Game Changers: Increased risk of diabetes mellitus in relation to the severity of psoriasis, concomitant medication, and comorbidity: A nationwide population-based cohort study. J Am Acad Dermatol. 2019:early view.
15. Patrick MT, Stuart PE, Zhang H, Zhao Q, Yin X, He K, et al. Causal Relationship and Shared Genetic Loci between Psoriasis and Type 2 Diabetes through Trans-Disease Meta-Analysis. J Invest Dermatol. 2021;141(6):1493-502.
16. Yamazaki F. Psoriasis: Comorbidities. The Journal of Dermatology. 2021;48(6):732-40.
17. Finlay A, Khan G. Dermatology Life Quality Index (DLQI) - a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19(3):210-6.
18. Fortune DG, Main CJ, O'Sullivan TM, Griffiths CE. Quality of life in patients with psoriasis: the contribution of clinical variables and psoriasis-specific stress. Br J Dermatol. 1997;137(5):755-60.
19. Ventura A, Mazzeo M, Gaziano R, Galluzzo M, Bianchi L, Campione E. New insight into the pathogenesis of nail psoriasis and overview of treatment strategies. Drug Des Devel Ther. 2017;11:2527-35.
20. Rigopoulos D, Papanagiotou V, Daniel R, 3rd, Piraccini BM. Onychomycosis in patients with nail psoriasis: a point to point discussion. Mycoses. 2017;60(1):6-10.
21. Rich P, Scher RK. Nail psoriasis severity index: a useful tool for evaluation of nail psoriasis. J Am Acad Dermatol. 2003;49(2):206-12.
22. Ogawa E, Sato Y, Minagawa A, Okuyama R. Pathogenesis of psoriasis and development of treatment. The Journal of Dermatology. 2018;45(3):264-72.
23. National Institute for Clinical Excellence. Psoriasis: assessment and management [CG153] London2011 [Available from: https://www.nice.org.uk/guidance/cg153/resources.
24. Brownstone ND, Hong J, Mosca M, Hadeler E, Liao W, Bhutani T, et al. Biologic Treatments of Psoriasis: An Update for the Clinician. Biologics. 2021;15:39-51.
25. Kamata M, Tada Y. Efficacy and Safety of Biologics for Psoriasis and Psoriatic Arthritis and Their Impact on Comorbidities: A Literature Review. Int J Mol Sci. 2020;21(5):1690.
26. Lin P-T, Wang S-H, Chi C-C. Drug survival of biologics in treating psoriasis: a meta-analysis of real-world evidence. Sci Rep. 2018;8(1):16068.
27. Thomas L, Azad J, Takwale A. Management of nail psoriasis. Clin Exp Dermatol. 2021;46(1):3-8.
28. Schons KR, Knob CF, Murussi N, Beber AA, Neumaier W, Monticielo OA. Nail psoriasis: a review of the literature. An Bras Dermatol. 2014;89(2):312-7.
29. Pasch MC. Nail Psoriasis: A Review of Treatment Options. Drugs. 2016;76:675-705.
30. Chng WQ, Yew YW. Nail manifestations in atopic dermatitis: a systematic review. Int J Dermatol. 2020;n/a(n/a).
31. Bristow IR. Urea - the gold standard for emollients? Podiatry Now. 2016;19(10):20-3.

CPU article number: 006
Editorial Team: **Mike Potter, Ivan Bristow, Anthony Maher & Morwenna Potter**
All articles are selected, commissioned, reviewed and produced independent of Canonbury Products Limited. Canonbury Products Limited kindly provide unrestricted support for the CPU series as a service to the profession.

The editorial team welcomes feedback or suggestions from readers via email: **CPUtools@canonbury.com**