Identifying and treating psoriasis

Psoriasis is a common skin condition that can present in many ways. Treating the condition can be simple or a major challenge for GPs. A patient's response to treatment can be unpredictable and a step-wise approach is usually adopted.

BRUCE TATE
PhD, FACD

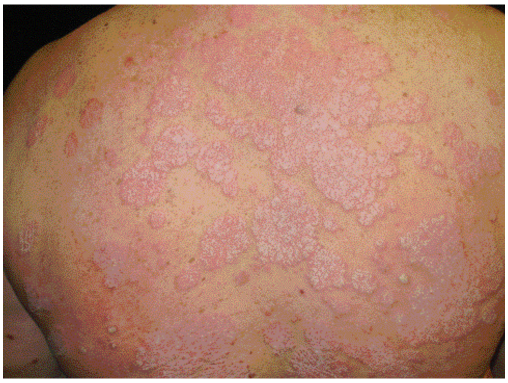
Dr Tate is a dermatologist in St Albans, Vic, and with the Skin and Cancer Foundation of Victoria.

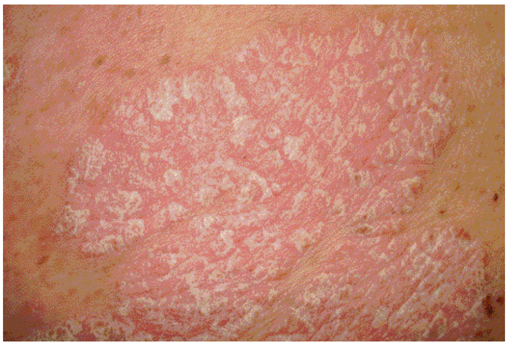
Psoriasis is one of the most common skin conditions worldwide and it can have a significant impact on a patient's quality of life. It is a chronic condition with a severity that varies markedly – both between patients and in an individual patient over time – from a few small plaques to erythroderma with up to total skin involvement. Triggers for onset or flares can only sometimes be identified.

The English physician Robert Willan, in his treatise *On Cutaneous Diseases* in 1808, described the condition and coined the term psoriasis – using the Greek word *psora* (meaning itch).[1] Some years later, the Austrian dermatologist, Ferdinand Ritter von Hebra, in *Lehrbuch der Hautkrankheiten (Textbook of Skin Diseases)* more accurately distinguished psoriasis from leprosy.[2]

Usually psoriasis is easy to distinguish from other skin conditions. But it can present in many ways and can be difficult to distinguish from tinea, dermatitis, pityriasis rosea and Bowen's disease, or rarer dermatoses such as pityriasis rubra pilaris, cutaneous T cell lymphoma, keratodermas and secondary syphilis.

The prevalence of psoriasis is about 2% worldwide, affecting men and women equally; however, figures vary widely. A population survey in Victoria





Figures 1a and b. a (top). Chronic plaque psoriasis in an obese man. b (bottom). In close up.

IN SUMMARY

- **The prevalence of psoriasis is about 2%, affecting men and women equally.**
- **The severity of psoriasis varies markedly between patients and in an individual patient over time.**
- **The chronic plaque form of psoriasis is seen in 80 to 90% of cases.**
- **Treatment of psoriasis is tailored to the patient depending on the extent of the disease, patient preference and response to previous treatment.**

found an overall prevalence of 6.6%, with 81.1% of patients being mildly affected, 16.1% moderately affected and 2.8% of patients severely affected.[3] Rates vary significantly in different populations – it is rare in Aboriginal Australians and American Indians, less common in African blacks and Asians and more common in Northern Europeans.[4]

In 75% of patients, the onset is before the age of 46 years but there are two peaks of onset, at ages 16 to 22 years and 57 to 60 years.[5] It is less common in children and they more often experience the guttate form. Studies have shown reductions in quality of life scores similar to those seen in conditions such as endogenous depression, diabetes and ischaemic heart disease.[6] These scores do not necessarily closely relate to the severity of psoriasis.

Clinical features

The chronic plaque form is seen in 80 to 90% of cases of psoriasis (Figures 1a and b), and is characterised by usually symmetrical, well-demarcated small to very large, 'salmon pink' to 'ham red' plaques with a silvery scale of variable thickness. About 30% of patients with chronic plaque psoriasis complain of itch, which can be severe. Sites most commonly affected are elbows, knees, scalp and lower back/buttocks but it can occur anywhere, including on the palms of the hands and soles of the feet, face (an uncommon site), genitals, umbilicus, external auditory meati and nails.

Although most people with the chronic plaque form have a small number of plaques, 16 to 35% have moderately widespread psoriasis (surface area of three to 10 palms) and 2 to 8% have extensive psoriasis. It usually persists for many years but it may clear or be relatively mild for prolonged periods of time. Exacerbations often occur slowly but can happen suddenly, particularly for guttate, pustular or erythrodermic forms of the disease. The severity is gauged by the Psoriasis Area Severity Index (PASI)[7] – based on the surface area, thickness, scaliness and redness of the plaques.

In people with more active psoriasis, the severity of the disease fluctuates more rapidly. Pustules are seen in more active psoriasis and more rapidly expanding plaques may be annular (Figure 2). The Köebner response occurs at sites of trauma or pressure-like scratches, cuts or friction sites. The severity of the disease is often worse in the winter as sunlight often suppresses psoriasis. Spontaneous remissions may occur in up to one-third of patients.[8]

Identifying and treating psoriasis

This image is unavailable due to copyright restrictions

In 80 to 90% of patients with psoriasis, the chronic plaque form is seen. It is characterised by usually symmetrical, well-demarcated small to very large, 'salmon pink' to 'ham red' plaques with a silvery scale of variable thickness.

© CHRISTY KRAMES

Different forms of psoriasis

Guttate psoriasis (Latin gutta, meaning drop)

Guttate psoriasis is most often seen in children, teenagers and young adults and is characterised by many small (less than 1 cm in diameter) plaques on the trunk, limbs and scalp (Figure 3). It often appears about two weeks after a β-haemolytic streptococcal infection, usually a sore throat but occasionally a genital streptococcal infection or cellulitis. It is usually self-limiting, settling in three to four months.

Figure 2. Annular pattern of chronic plaque psoriasis.

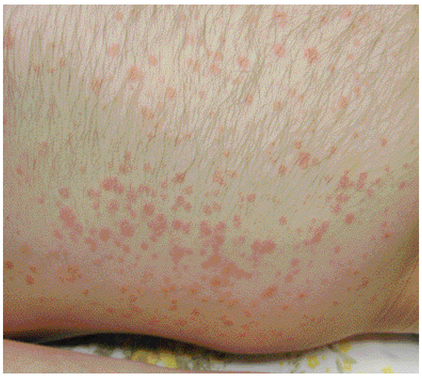


Figure 3. Guttate psoriasis in a 31-year-old man. This appeared about two weeks after a bad sore throat.

Figure 4. Flexural psoriasis. Note the lack of scale and the well-demarcated smooth red thin plaque.

Flexural (inverse) psoriasis

Flexural psoriasis is seen in the skin folds of sites such as the groin, axillae and submammary areas (Figure 4). Few or no scales form because of maceration, and a well-demarcated smooth red thin plaque is seen. There is often chronic plaque psoriasis elsewhere on the body. It may be confused with tinea, candidiasis, erythrasma or flexural seborrhoeic dermatitis.

Napkin psoriasis

Napkin psoriasis is uncommon, and presents as a well-demarcated, minimally scaly confluent form of psoriasis in the nappy area of babies. Scalp involvement is more common in this form of psoriasis.

Sebopsoriasis

Sebopsoriasis is usually seen on the scalp (Figure 5) and also the face (glabella, eyebrows and nasolabial folds), postauricular and pre-auricular areas and sometimes on the central chest. It overlaps with seborrhoeic dermatitis but is distinguished by having more well-demarcated plaques.

Palmoplantar psoriasis

Palmoplantar psoriasis may only affect the palms and/or soles (Figure 6), but about 25% of patients have chronic plaque psoriasis elsewhere. There are well-demarcated or confluent plaques on the palms of the hands or soles of the feet, which may extend further around the hands or feet and/or on to the digits. More hyperkeratotic types of psoriasis tend to form painful fissures. Sterile pustules are more common in palmoplantar psoriasis than in other types of psoriasis. Nail changes of psoriasis are also more common but can occur independently of palmoplantar psoriasis. The same holds true for psoriatic arthritis.

It can be difficult to distinguish palmoplantar psoriasis from:

- tinea (scrapings for fungal culture should be routinely ordered)
- dermatitis of various types including:
  - pompholyx, which may alternate between vesicular and hyperkeratotic forms
  - chronic irritant dermatitis
  - allergic contact dermatitis.

Identifying the causes of these forms can be challenging and, because all are common, multiple aetiologies may be an issue in an individual patient.

Figure 5. Sebopsoriasis on the scalp. This is distinguished from seborrhoeic dermatitis by it having a well-demarcated edge.

Figure 6. Palmar psoriasis. This was on both of the patient's hands and plantar psoriasis was present on the soles of the feet. The well-demarcated edge is a helpful clue to distinguish psoriasis from dermatitis.

Generalised pustular psoriasis

Generalised pustular psoriasis is a rare severe form of the condition with a rapid onset of widespread pustular psoriasis. The patient with this form is often unwell, achy and febrile. It may be precipitated by concurrent infection or rapid withdrawal of systemic and occasionally ultrapotent topical corticosteroids.

Erythroderma

Erythroderma is present when 90% or

Figure 7 (left). Erythrodermic psoriasis.

Figure 8 (above). Nail psoriasis. Different nails demonstrate general dystrophy or pits (from psoriasis affecting the nail matrix) and mild onycholysis (from psoriasis affecting the nail bed).

more of the skin is inflamed, and is an uncommon condition. The second most common cause of erythroderma is psoriasis, being responsible for 25% of all cases (eczema is the most common cause at 40%). The development of erythroderma may be a slow worsening of chronic plaque psoriasis or an explosive form of unstable psoriasis (Figure 7).

Hospitalisation for close monitoring is required because the patient will be unwell, have poor regulation of body temperature and be prone to high output cardiac failure, secondary infection, capillary leak syndrome, hypoalbuminaemia from negative nitrogen balance (from the rapid loss of skin) and electrolyte disturbances. Erythroderma can be precipitated by rapid withdrawal of systemic or occasionally ultrapotent topical corticosteroids, use of coal tar preparations in unstable or pustular psoriasis, antimalarial therapy, hypocalcaemia and concurrent infections.

Nail changes

Nail changes in patients with psoriasis may be subtle to severe and affect few to all nails (Figure 8). It has been found that, on careful observation, 25 to 50% of patients have nail changes. Mild involvement of the nail matrix causes pits in the nail plate. More severe involvement causes thickened or crumbly (dystrophic) nail plates, which can sometimes be severe. This can be difficult to distinguish from tinea, so nail clippings should routinely be taken for fungal culture.

Severe involvement may cause complete loss of the nail plate. Nail bed involvement causes the oil spot sign (yellowing of the nail bed) and/or lifting of the nail plate from the bed, usually distally (onycholysis). Most of these changes can be caused by other conditions such as alopecia areata (pitting), tinea, nail matrix trauma (dystrophy) or both tinea and nail bed trauma (onycholysis). Nail changes can precede the development of psoriasis elsewhere by years.

Psoriatic arthritis

Estimates of the prevalence of psoriatic arthritis worldwide vary from 5 to 30% of patients with psoriasis, and 10% of patients get the arthritis before any skin changes occur. Patients with psoriatic arthritis are usually seronegative. The classic type of psoriatic arthritis is oligoarthritis with distal interphalangeal joint involvement, dactylitis and enthesitis of various sites, particularly the heels. Moll and Wright proposed five types of psoriatic arthritis in 1973:[9]

- distal interphalangeal joint involvement only
- asymmetrical oligoarthritis
- polyarthritis
- spondylitis
- arthritis mutilans.

As with other inflammatory arthropathies, morning stiffness can be a helpful clue to the diagnosis.

Comorbidities

Psoriasis is linked to some autoimmune diseases and other diseases. Patients with the condition have an increased frequency of Crohn's disease, type 2 diabetes, the metabolic syndrome and some cancers. Recent work pointed to a threefold relative risk of myocardial infarction in younger patients and a smaller increased risk for older patients with more severe but not mild psoriasis.[10] This was partly explained by the fact that patients with psoriasis have a higher rate of other known cardiovascular risk factors.

Histopathology

The three key histopathological features of psoriasis are epidermal hyperplasia, increased dermal vasculature and an inflammatory infiltrate of lymphocytes and neutrophils. It usually spares hair follicles and mucosal epithelium. Clinically uninvolved skin is histologically normal.

Aetiology

There is strong evidence that psoriasis has a polygenic basis with the effect of increased epidermal turnover and vascular change both being driven by a T-cell-mediated immune attack on the skin, which also involves an influx of neutrophils. Both the innate and acquired immune pathways are involved. The antigen target of the T-cells is not known. Although the immune system plays a key role in the aetiology of psoriasis, it is not clear whether it is the fundamental driver or a result of some other event. Streptococcal infection is usually the stimulant of guttate psoriasis but often an initiating event cannot be identified.

Flare factors

Apart from streptococcal infections, the following are sometimes implicated in the flare of psoriasis:

- drugs – especially lithium, occasionally terbinafine, hydroxychloroquine or chloroquine, and withdrawal of systemic corticosteroids, and rarely β-blockers, ACE inhibitors and NSAIDs[11]
- stress – patients are often aware of the link
- smoking – this seems linked to an increased risk of chronic plaque and palmoplantar pustulosis[12]
- high alcohol intake – this is more common in men with more severe psoriasis, but it is more likely to be effect rather than cause
- HIV infection – exacerbations of psoriasis may be more common in those with more advanced HIV infection
- sun exposure – a small proportion of psoriasis cases worsen with sun exposure[13]
- diet – there is a possible role of (often silent) gluten enteropathy in both chronic plaque psoriasis and palmoplantar pustulosis. In those patients with anti-endomyseal antibodies, a gluten-free diet can substantially improve the severity of psoriasis.[14-16]

Treatment

The treatment of psoriasis[17,18] varies from being simple to a major challenge, and a patient's response to therapy is unpredictable. Treatments are tailored to the patient depending on the extent of the disease, patient preference and practical issues, response to previous treatment and relative or absolute contraindications. A try it and see approach is usually adopted. Broadly, treatments can be thought of as a ladder of options:

- topical agents, which are unreliable but have less side effects, are low down
- one rung up are intralesional corticosteroid injections, which are effective but only suitable for small areas of skin
- UV therapies are in the the middle of the treatment ladder
- at the top are systemic options, which have the advantage of being convenient and having a higher efficacy but more side effects.

A step-wise approach to treatment is usually adopted. Rotation of treatments is often required as the effect of one approach wanes. Treatments that were not effective in the past may work well in the future. The evidence base for psoriasis therapies is often lacking, particularly for the older topical agents.

The impact of psychological and lifestyle factors on psoriasis are paramount: patients are often fearful that direct contact will pass it on to others, which is reinforced by other peoples' responses. The desire to hide it, for example with clothing or hairstyles, makes many patients reluctant to play sports or socialise, and sexual inhibition can be significant. The condition can also impact on patients' work, from the time needed to treat psoriasis or issues such as painful fissuring on hands or feet, itching, discomfort, nail problems or arthritis. A patient should be asked about joint problems and referred to a rheumatologist when necessary.

Topical therapy

Topical medications are appropriate for all levels of severity of psoriasis but are the main therapy of choice for mild psoriasis. Most commonly used are potent topical corticosteroids, calcipotriol (Daivonex Cream, Daivonex Ointment, Daivonex Scalp Solution), coal tar derivatives and salicylic acid. Also used are dithranol (DithraSal, Micanol), tazarotene (Zorac Cream) and, occasionally, calcineurin inhibitors such as pimecrolimus (Elidel) and tacrolimus. Combinations of treatments are often required.

The base of the agent is also important. Ointments are preferred for broad skin areas because they are occlusive, which makes them more effective, but they are messy, stain fabrics and can induce occlusive folliculitis or acne. Lotions or creams are used for hairy areas and creams for flexural areas. The amount applied is important: for topical corticosteroids I recommend a thin but visible smear (although pharmacists often emphasise sparing use). A slightly more generous application of coal tar, salicylic acid and calcipotriol preparations is needed. Often PBS authority prescriptions are required to get sufficient quantities – the amount that fits on the tip of the finger is a useful guide for what is needed.[19] Note, the compliance rates of topical therapy tend to be lower and the long-term cost is often significant, adding to the complexity of choosing treatments. The costs of various therapies is outlined in the table.

Topical corticosteroids

Topical corticosteroids are popular as they are easy to apply, relatively cheap and can be very effective. They are usually used in combination with other agents and applied once, sometimes twice, daily. Potent agents such as mometasone furoate (Elocon, Novasone), betamethasone valerate (Antroquoril, Betnovate Preparations, Celestone M Cream and Ointment, Cortival) and betamethasone dipropionate (Diprosone, Eleuphrat) are generally required, but this must be tailored to the site treated. On the face or flexures, hydrocortisone 1% ointment (DermAid Cream, DermAid Soft Cream, Egocort Cream 1%) or desonide lotion (Desowen) may be effective. If not, methylprednisolone aceponate ointment (Advantan) should be tried.

Topical corticosteroids work slowly and psoriasis is often slower to settle than dermatitis. Atrophy is helpful given that

Table. Some prescription medications for psoriasis and their cost, including on the PBS*

Generic name	Brand name	PBS quantity	PBS cost	Private script cost
Acitretin†	Neotigason 10 mg Capsules	100	$205.34	$205.00 to $230.00
	Neotigason 25 mg Capsules	100	$392.78	$395.00 to $420.00
Betamethasone	Celestone Chronodose	5	$25.74	
Betamethasone dipropionate§	Diprosone Cream/Ointment	15 g	$13.12	
	Diprosone Lotion	30 mL	n/a	
	Diprosone OV Cream/Ointment	30 g	n/a	$26.00 to $31.00
	Eleuphrat Cream/Ointment	15 g	$13.12	
	Eleuphrat Lotion	30 mL	n/a	$22.15
Betamethasone dipropionate plus calcipotriol	Daivobet 50/500 Ointment	30 g	n/a	$49.00 to $60.00
Betamethasone valerate§	Antroquoril Cream/Ointment	2 x 100 g	$24.89	
	Betnovate Cream/Ointment	30 g	$22.00	
	Betnovate 1/5 Cream‡	2 x 100 g	$31.07	
	Betnovate 1/2 Cream‡	15 g	$10.03	
	Betnovate 1/2 Ointment‡	15 g	$10.03	
	Celestone M Cream/Ointment	2 x 100 g	$24.89	
	Cortival 1/5 Cream	2 x 100 g	$24.89	
	Cortival 1/2 Cream	15 g	$8.12	
	Cortival 1/2 Ointment	15 g	$8.12	
Calcipotriol§	Daivonex Cream/Ointment	30 g	$27.63	
	Daivonex Scalp Solution	30 mL	$27.63	
Calcitriol†	Citrihexal 0.25 μg Capsules	100	$42.82	
	Kosteo 0.25 μg Capsules	100	$42.82	
	Rocaltrol 0.25 μg Capsules	100	$42.82	
	Sical 0.25 μg Capsules	100	$42.82	
Cyclosporin†	Cicloral 25 mg Capsules	60	$102.49	
	Cicloral 50 mg Capsules	60	$206.51	
	Cicloral 100 mg Capsules	60	$395.87	
	Neoral 25 mg Capsules‡	60	$104.77	$110.00 to $125.00
	Neoral 50 mg Capsules‡	60	$208.75	$215.00 to $240.00
	Neoral 100 mg Capsules‡	60	$398.13	$426.00 to $450.00
	Neoral 10 mg Capsules	120	$93.99	
	Sandimmun 25 mg Capsules	50	n/a	$187.61
	Sandimmun 50 mg Capsules	50	n/a	$728.46
Desonide	Desowen Lotion	60 mL	n/a	$25.78

Continued on page 23

Table cont. Some prescription medications for psoriasis and their cost, including on the PBS*

Generic name	Brand name	PBS quantity	PBS cost	Private script cost
Dithranol 0.5% liquor picis carbonis 8% salicylic acid 5% in aqueous cream/in white soft paraffin	Extemporaneous product	200 g	$31.30	$41.00
Efalizumab†	Raptiva 4 x 125 mg vials	1	$1029.14	$1050.00
Etanercept†	Enbrel 4 x 25 mg vials Enbrel 4 x 50 mg vials	2 1	$1828.57 $1773.94	
Hydrocortisone 1%§	Egocort Cream 1%	50 g	$8.27	
Hydroxyurea	Hydrea Capsules	100	$76.03	
Infliximab†	Remicade 100 mg vials	1	$846.55	$800.00
Liquor picis carbonis 8% salicylic acid 5% in aqueous cream/ in white soft paraffin	Extemporaneous product	200 g	$17.00	
Methotrexate	Methoblastin 2.5 mg Tablets Methoblastin 10 mg Tablets	30 15/50†	$13.11 $22.37/$47	
Methylprednisolone aceponate§	Advantan Ointment/Fatty Ointment Advantan Cream	15 g 15 g	$14.02 $14.02	 $26.48
Mometasone furoate§	Elocon Cream Elocon Ointment Elocon Lotion Novasone Cream/Ointment Novasone Lotion	15 g/45 g 15 g/45 g 30 mL 15 g 30 mL	$13.96/$26.38 $13.96/$26.38 $18.54 $13.96 $18.54	
Mycophenolate mofetil†	CellCept 500 mg Tablets CellCept 250 mg Capsules	150 300	$627.38 $627.38	$620.00
Pimecrolimus†	Elidel Cream	15 g	$33.36	
Propylthiouracil	Propylthiouracil 50 mg Tablets	200	$47.21	
Sulfasalazine	Pyralin EN Tablets Salazopyrin Tablets Salazopyrin-EN Tablets‡	200 200 200	$56.61 $52.31 $58.19	
Tazarotene	Zorac Cream 0.05% Zorac Cream 0.1%	30 g 30 g	n/a n/a	$40.90 $40.90
Thioguanine	Lanvis Tablets	25	$198.23	
Triamcinolone acetonide§	Aristocort Cream/Ointment 0.02%‡ Tricortone Cream/Ointment	2 x 100 g 2 x 100 g	$17.75 $14.45	

* Prices are provided as a guide only and are correct, to the best of our knowledge, at February 2009. Please refer to product information, PBS or MIMS for up-to-date information. Refer to PBS for details of cost of products on authority. Only those drugs that require a prescription and are not available over the counter are included.
† = authority required, ‡ = brand premium applies, § = restricted benefit.

the plaques are thick but is more of an issue if used in the flexures, on other thin skin sites or in people with skin prone to sun damage. Tachyphylaxis (reduced effectiveness as treatment continues) occurs but is not a major problem. Systemic absorption is an issue with the potent agents, especially for children and those with extensive disease, but serious suppression of the hypothalamic adrenal axis is uncommon. Ideally moderate or potent agents would be used for a shorter time (days to weeks) and less than 100 g would be used each month, although often these limits are exceeded.

Calcipotriol

Calcipotriol is a vitamin D_3 analogue available as Daivonex ointment, cream or scalp solution, or in combination with betamethasone dipropionate as Daivobet 50/500 ointment.[20] Only Daivonex is available on the PBS. It should be applied twice daily, does not smell and can be very effective. Success rates for calcipotriol alone show a mean reduction in PASI from 48 to 72% compared with about a 60% reduction with potent topical corticosteroids. Most of the improvement occurs within two months of starting treatment and tachyphylaxis is not an issue. The amount applied should not exceed 100 g per week to minimise the risk of hypercalcaemia.

Skin irritation is noted by 25% of patients and 5% stop using calcipotriol for this reason, so it is less often used on the face or flexures. Daivonex is best used with a topical corticosteroid to improve efficacy. Daivobet is more expensive so it is usually used for limited disease. Calcipotriol and salicylic acid should not be used together because calcipotriol is degraded by salicylic acid .

Coal tar preparations

The most often used coal tar preparations are liquor picis carbonis (LPC) – a detergent derivative of crude coal tar available as an extemporaneous product on the PBS – and similar products such as Exorex and coal tar shampoos (Neutrogena T/Gel Plus Dual Action Shampoo, Neutrogena T/Gel Therapeutic Shampoo). Crude coal tar is not often used because it is more smelly and messy. It is a complex mixture of compounds and the active ingredients are poorly characterised. It has anti-inflammatory and antiproliferative effects and can be very effective. Pine tar is not effective for psoriasis.

LPC is used in concentrations from 2 to 12% (often 6 to 8%) and is often formulated with salicylic acid in a cream or ointment base. It is relatively slow to work. The issues with its use are the asphalt-like smell, staining of fabrics and white hair (to a light mustard yellow), occasionally irritation, folliculitis and rarely photosensitivity. It should not be used for unstable or pustular psoriasis. There is a possible very low risk of skin and systemic carcinogenicity of coal tar preparations from polycyclic aromatic hydrocarbons. Mutagenicity concerns make it wise to avoid its use in pregnancy.

Salicylic acid

Salicylic acid 2 to 6% is used in a cream or ointment base and is available as an extemporaneous product on the PBS. It is a keratolytic agent often used in combination with some of the other topical therapies to help remove scale. Alone it may be used in liquid or soft white paraffinat a higher concentration (10 to 15%) to soften and remove thick scale, for example on the scalp nightly for a week, before other topical therapies are started. Absorption can cause potentially serious systemic salicylism, particularly in children or those with significant renal impairment.

Dithranol

Dithranol is 1,8-dihydroxy-9-anthrone, a synthetic form of a tree bark extract. Commercially, it is available as DithraSal and Micanol but, like LPC and salicylic acid, it is available as an extemporaneous product on the PBS. Salicylic acid is included in this product to prevent oxidative degradation. Its shelf life is less than three months if it is stored in the dark, which are thought to be optimal storage conditions. It has an effect on mitochondria, inhibits DNA synthesis and epidermal turnover. It can be very effective with mean PASI reductions of about 60%.

The preparation may cause delayed (by days) irritation and stains skin, hair and fabrics brown. These effects are minimised by Short Contact Anthralin Therapy (SCAT), where the time of dithranol application is gradually increased from about 10 minutes to 40 minutes each night before being washed off. A topical corticosteroid is then applied immediately after the dithranol has been washed off or the next morning. For SCAT, once the application time has been increased to a tolerable level a higher concentration of dithranol can be used – starting at 0.5 to 1.0% and slowly increasing to a maximum of 2% if needed and tolerated. If used overnight, the starting concentration is 0.1%, which can be slowly increased to a maximum of 2% but it will stain the skin.

Tazarotene

Tazarotene 0.05% or 0.1% cream is a retinoid that helps to normalise keratinocyte proliferation and differentiation. It has similar efficacy to topical corticosteroids with at least 75% improvement in PASI in 45 to 62% of patients treated for six to eight weeks.[21] It works slowly but its effect lasts longer. Irritation with dryness is common so the lower strength cream should be used at the start and applied for 10 minutes. The application time should then gradually be increased until it is left on all night. The higher strength form can then be used if needed. Topical corticosteroids applied in the morning will increase the rate of response and reduce irritation. It can also be used with calcipotriol. Tazarotene should not be used on more than 20% of the skin's surface area. Retinoids are teratogenic, so the use of tazarotene is contraindicated in pregnancy.

Intralesional corticosteroids

Intralesional corticosteroids can be very effective and induce prolonged remission in the treated area. A dose of 10 mg/mL triamcinolone acetonide (Aristocort, Tricortone) or 5.7 mg/mL betamethasone (Celestone Chronodose) is diluted in 5 mL of normal saline and repeatedly injected into the upper dermis to cover the area of the plaques. Disadvantages are pain, sometimes skin atrophy and that it is only suitable for use on a limited area.

Phototherapy

Phototherapy is very useful for the treatment of psoriasis and is mainly used for more extensive areas, although not for inaccessible sites such as the scalp. Three types of ultraviolet light can be used but most dermatologists use 'narrow band' ultraviolet (UV) B (with a wavelength in a narrow peak of about 312 nm), which maximises efficacy and minimises the risk of burning. It is usually performed three times a week, starting with a short treatment time of about 30 seconds, which is gradually increased to 10 minutes or longer. Clearance time varies a lot but is typically 20 to 40 treatments, with about 55% of patients achieving total clearance.

Phototherapy possibly works by a combination of antiproliferative effects and local immunosuppression. It is particularly effective in guttate psoriasis but can be used for all forms of psoriasis. It is used in combination with many of the topical treatments or some of the oral treatments. The main side effects are sunburn (including of the cornea), photoageing and hyperpigmentation, and occasionally photosensitive drug eruptions and skin cancers. PUVA using UVA light and oral or topical psoralen is less commonly used. Solarium-type sun beds have a small beneficial effect on psoriasis but nowhere near that of medical phototherapy.[22]

Oral therapies

Acitretin

Acitretin (Neotigason) is a retinoid that works by altering the differentiation cycle of epidermal keratinocytes and via anti-inflammatory and immunological effects. Typical doses are 10 to 30 mg daily. It is particularly useful in pustular and erythrodermic psoriasis and is quite helpful in palmoplantar psoriasis. Using 50 mg daily in chronic plaque psoriasis, 23% of patients achieved a 75% reduction and 54% achieved a 50% reduction in PASI over eight weeks of treatment.[23] Maximal response occurs after three months of therapy.

Acitretin use increases the efficacy of topical treatments and phototherapy, and it may reduce the risk of skin cancer associated with phototherapy. It is suitable for long-term use, but is usually not used in women of childbearing age because severe teratogenicity is a major issue, with no dose being considered safe and the risk persisting for up to three years after ceasing therapy. Men can safely father a child while taking acitretin.

The most common side effect is dry lips (a dose-dependent effect, managed by greasy emollients). The skin may generally become dry and the palms and soles tend to peel, which is managed with emollients. The skin may feel sticky and skin fragility with more susceptibility to cuts and slower healing is common. At higher doses, after months of treatment, hair shedding is not uncommon. Nails may become slightly brittle and occasionally paronychia or periungual granulation tissue develops. Reduced Meibomian gland secretion causes conjunctival and corneal dryness requiring appropriate eye drops and eyelid care, particularly if the patient wears contact lens.

The main systemic side effects of acitretin are:

- raised serum lipids – particularly triglycerides but also cholesterol
- idiosyncratic hepatotoxicity – severe reactions are rare; liver function tests (LFTs) and lipids should be checked before, one month after starting acitretin and then every three months.

Uncommon or rare side effects include headaches, pseudotumour cerebri (more common if the patient is also taking tetracyclines), aching muscles, neuropsychiatric effects including lack of energy, osteoporosis, ligament calcifications and diffuse idiopathic skeletal hyperostosis.

Methotrexate

Methotrexate (Methoblastin) is a folic acid antagonist used for both psoriasis and psoriatic arthritis ata dose of about 10 to 25 mg once a week. It inhibits synthesis of DNA and some amino acids, with effects on lymphocyte and neutrophil function and keratinocyte proliferation. A maximal effect is seen after about two to three months. One study showed clearance or near clearance of psoriasis in 76% of patients, a poor response in 6% and discontinuation of use because of side effects in 20% of patients.[24] Once controlled, a lower maintenance dose will often suffice and the patient may take methotrexate for years.

Although most patients tolerate methotrexate well, side effects are significant. It is renally excreted and has many drug interactions.[25] Contraindications include hypersensitivity, pregnancy (it is a category X drug – teratogenic and can induce miscarriage), alcohol intake (alcohol use is prohibited with methotrexate), infectious diseases such as tuberculosis, bone marrow dyscrasias, liver disease and significant renal impairment. Women need to be on adequate contraception and it can temporarily reduce male fertility – men and women should stop taking methotrexate three months before trying to conceive.

Full blood count (FBC), LFTs, urea and electrolytes, and creatinine should be checked before methotrexate is commenced. A test dose of 5 mg methotrexate is initially given and then LFTs and FBC are rechecked one week later to rule out an idiosyncratic reaction. The dose is gradually built up as needed or tolerated clinically. FBC and LFTs are checked at two weeks after the test dose is given, monthly for three months then every two to three months. The most common side effects from methotrexate are fatigue and nausea, which may be helped by adding 1 to 5 mg folic acid daily.[26] Death from taking methotrexate is rare but the most common cause is myelosuppression, particularly if there are drug interactions or renal function is poor. Liver cirrhosis is also rare, but more common if the patient drinks alcohol or is elderly or obese. The best way to monitor liver problems is contentious. Routine liver biopsies at specific cumulative doses are recommended in some countries but Australian hepatologists often do not agree with this approach. Methotrexate-induced pulmonary fibrosis is rare.

Cyclosporin

Cyclosporin (Cicloral, Neoral, Sandimmun) inhibits T cell activation and affects neutrophil and keratinocyte differentiation. At the beginning, cyclosporin is given twice a day up to a total dose of 3 mg/kg per day; this can be built up to 5 mg/kg per day if needed. Maximal effect is usually achieved within one month but the psoriasis can break through quickly once the dose goes below the minimum needed for control (often 2 to 3 mg/kg per day). Efficacy is similar to methotrexate.

Cyclosporin is heavily metabolised in the liver and there are many drug interactions.[27] The most common reason to stop it are dose-dependent hypertension and (sometimes permanent) renal impairment, so these need to be carefully monitored. Hypertension can be treated while the patients are on cyclosporin but they should be monitored for drug interactions. Other common side effects of cyclosporin include hypertrichosis, gum hypertrophy (good dental hygiene is recommended), temporary gastrointestinal upsets, paraesthesia, headaches and some neuropsychiatric effects. Cyclosporin may raise triglyceride, potassium and uric acid levels and lower magnesium levels. It can cause osteoporosis. The malignancy risk (particularly lymphoma and skin cancer) is uncertain. It should not be used during pregnancy.

Other oral therapies

There are many other oral agents that are occasionally used for widespread psoriasis. These include:

- immunosuppressive and antimitotic agents such as mycophenolate mofetil (CellCept),[28] hydroxyurea (Hydrea),[29] azathioprine[30] and thioguanine (Lanvis)[31]
- oral calcitriol (Citrihexal, Kosteo, Rocaltrol, Sical)[32]
- propylthiouracil[33]
- sulfasalazine (Pyralin EN, Salazopyrin)[34]
- leflunomide (Arabloc, Arava).[35]

Biological agents

There has been a lot of recent publicity about the use of biological agents for psoriasis but their place in psoriasis management is still being established. They are by no means always effective, with clearance rates for some agents below those seen with methotrexate and cyclosporin.

There are currently three agents licensed for use in Australia – efalizumab (Raptiva; a humanised monoclonal antibody that inhibits T cell functions) and the tumour necrosis factor (TNF) inhibitors, etanercept (Enbrel) and infliximab (Remicade). Another TNF inhibitor, adalimumab (Humira) is likely to be PBS-listed for cutaneous psoriasis in 2009. These drugs are extremely expensive and there are substantial PBS limits on their prescription.[36,37]

Patients need to have very widespread psoriasis, and have failed or contraindicated treatment with three systemic therapies (methotrexate, acitretin or cyclosporin) or phototherapy to receive PBS benefits. There are special criteria for psoriasis on the face, palms of the hands and soles of the feet. In addition, once therapy is initiated the PASI must improve by at least 75% in three months for any of the agents tried and if all the biological agents fail to meet these criteria, they are not eligible for re-trial within five years. Experience in the use of some of these agents is being shared with their use in treating inflammatory bowel disease or inflammatory arthropathies.

Summary

Psoriasis is a common, often distressing disease with a plethora of presentations from almost nonexistent to devastating in severity. The arthritis can also be debilitating. The many treatment options and their various limitations lead to a complex set of decisions, particularly for more severely affected patients with various relative or absolute contraindications to therapy. Fortunately, there is considerable ongoing research into many aspects of the disease and this is leading to an intriguing array of current and future management options. MT

References

A list of references is available on request to the editorial office.

COMPETING INTERESTS: None.

Medicine Today 2009; 10(2):14-28

Identifying and treating Psoriasis

BRUCE TATE PhD, FACD

References

1. Willan R. On cutaneous diseases. London; 1808.
2. Hebra FR von. Lehrbuch der hautkrankheiten. Vienna; 1841.
3. Marks R, Plunkett A, Merlin K, Jenner N. Atlas of common skin diseases in Australia. 1999. Available online at http://www.dermatology.svhm.org.au/Resources/4548-Atlas.pdf (accessed February 2009).
4. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet 2007; 370: 263-271.
5. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol 1985; 13: 450-456.
6. Rapp SR, Feldman SR, Exum ML, Fleischer AB, Jr, Reboussin DM. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol 1999; 41: 401-407.
7. Medicare Australia. PASI calculation and body diagram. http://www.medicareaustralia.gov.au/provider/pbs/drugs1/files/ma_4178_PASI_calculation_and_whole_body_diagram.pdfhttp://www.medicareaustralia.gov.au/provider/pbs/drugs1/files/ma_4178_PASI_calculation_and_whole_body_diagram.pdf (accessed February 2009).
8. Farber EM, Nall ML. The natural history of psoriasis in 5600 patients. Dermatologica 1974, 148: 1-18.
9. Moll JM, Wright V. Psoriatic arthritis. Semin Arthritis Rheum 1973; 3: 55-78.
10. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. J Am Med Assoc 2006; 296: 1735-1741.
11. Cohen AD, Bonneh DY, Reuveni H, et al. Drug exposure and psoriasis vulgaris: case-control and case-crossover studies. Acta Derm Venereol 2005; 85: 299-303.
12. Williams HC. Smoking and psoriasis (Editorial). BMJ 1994; 308: 428-429.
13. Ros AM, Eklund G. Photosensitive psoriasis. An epidemiologic study. J Am Acad Dermatol 1987; 5: 752-758.
14. Michaelsson G, Gerden B, Hagforsen E, et al. Psoriasis patients with antibodies to gliadin can be improved by a gluten-free diet. Br J Dermatol 2000; 142: 44-51.
15. Michaëlsson G, Kristjánsson G, Pihl Lundin I, Hagforsen E. Palmoplantar pustulosis and gluten sensitivity: a study of serum antibodies against gliadin and tissue transglutaminase, the duodenal mucosa and effects of gluten-free diet. Br J Dermatol 2007; 156: 659-666.
16. Wolters M. Diet and psoriasis: experimental data and clinical evidence. Br J Dermatol 2005; 153: 706-714.
17. The British Association of Dermatologists. Psoriasis – general management. http://www.bad.org.uk/site/769/Default.aspx (accessed February 2009).
18. Menter A, Griffiths CE. Current and future management of psoriasis. Lancet 2007; 370: 272-284.
19. DermNet NZ. Fingertip unit. http://dermnetnz.org/treatments/pdf/fingertipunit-dermnetnz.pdf (accessed February 2009).
20. Scott LJ, Dunn ChJ, Goa KL. Calcipotriol ointment. A review of its use in the management of psoriasis. Am J Clin Dermatol 2001; 2: 95-120.
21. Roeder A, Schaller M, Schäfer-Korting M, Korting HC. Tazarotene: therapeutic strategies in the treatment of psoriasis, acne and photoaging. Skin Pharmacol Physiol 2004; 17: 111-118.
22. Turner RJ, Walshaw D, Diffey BL, Farr PM. A controlled study of ultraviolet A sunbed treatment of psoriasis. Br J Dermatol 2000; 143: 957-963.
23. Gollnick H, Bauer R, Brindley C, et al. Acitretin versus etretinate in psoriasis. Clinical and pharmacokinetic results of a German multicenter study. J Am Acad Dermatol 1988; 19: 458-469.
24. Haustein UF, Rytter M. Methotrexate in psoriasis: 26 years' experience with low-dose long-term treatment. J Eur Acad Dermatol Venereol 2000; 14: 382-388.
25. Methotrexate injection and tablets. http://www.medsafe.govt.nz/profs/Datasheet/m/Methotrexateinjmayne.htm (accessed February 2009).
26. Salim A, Tan E, Ilchyshyn A, Berth-Jones J. Folic acid supplementation during treatment of psoriasis with methotrexate: a randomized, double-blind, placebo-controlled trial. Br J Dermatol. 2006; 157: 1169-1174.
27 Neoral. http://www.medsafe.govt.nz/profs/datasheet/n/Neoralsolcap.htm (accessed February 2009).

28. Zhou Y, Rosenthal D, Dutz J, Ho V. Mycophenolate mofetil (CellCept) for psoriasis: a two-center, prospective, open-label clinical trial. J Cutan Med Surg 2003; 7: 193-197.
29. Kumar B, Saraswat A, Kaur I. Rediscovering hydroxyurea: its role in recalcitrant psoriasis. Int J Dermatol 2001; 40: 530-534.
30. Hacker SM, Ramos-Caro FA, Ford MJ, et al. Azathioprine: a forgotten alternative for treatment of severe psoriasis. Int J Dermatol 1992; 12: 873-874.
31. Sherer DW, Lebwohl MG. 6-thioguanine in the treatment of psoriasis: a case report and literature review. J Cutan Med Surg 2002; 6: 546-550.
32. Perez A, Raab R, Chen TC, Turner A, Holick MF. Safety and efficacy of oral calcitriol (1,25-dihydroxyvitamin D3) for the treatment of psoriasis. Br J Dermatol 1996; 134: 1070-1078.
33. Chowdhury MM, Marks R. Oral propylthiouracil for the treatment of resistant plaque psoriasis. J Dermatolog Treat 2001; 12: 81-85.
34. Gupta AK, Ellis CN, Siegel MT, et al. Sulfasalazine improves psoriasis. A double-blind analysis. Arch Dermatol 1990; 126: 487-493.
35. Nash P, Thaçi D, Behrens F, Falk F, Kaltwasser JP. Leflunomide improves psoriasis in patients with psoriatic arthritis: an in-depth analysis of data from the TOPAS study. Dermatology 2006; 212: 238-249.
36. Medicare Australia. Severe chronic plaque psoriasis. http://www.medicareaustralia.gov.au/provider/pbs/drugs2/psoriasis.jsp (accessed February 2009).
37. Infliximab. http://www.health.vic.gov.au/hsdp/infliximab_psoriatic_plaque.pdf (accessed February 2009).