JUNE 2025 VOL 9 NO 1

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A teenage boy with patchy hair loss after a haircut

A widespread erythematous targetoid eruption

DERMATOLOGY COLLECTION
REPRINTS IN DERMATOLOGY
JUNE 2025 VOL 9 NO 1

ISSN 1443-430X

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A MEDICINE TODAY PUBLICATION

Dermatology Collection

PEER REVIEWED UPDATES FOR MEDICAL PRACTITIONERS

FOREWORD FROM THE EDITOR-IN-CHIEF, DERMATOLOGY COLLECTION

Our June 2025 *Dermatology Collection* covers several important and frequently encountered dermatological conditions, with a focus on both chronic disease management and cosmetic concerns.

Acne scarring can occur even in patients with mild acne and causes lasting psychological and social effects. Read about how acne scarring occurs, who is at risk and the wide range of management options now available – from topical therapies and laser treatments, to subcision and dermal fillers – many of which may be best managed with specialist input.

Keratinocyte cancers are the most common skin malignancies seen in general practice. An update on their diagnosis and management reviews the latest treatment advances, including lesion- and field-directed treatments for actinic keratoses, systemic therapies for advanced disease and the evolving role of brachytherapy.

Psoriasis is increasingly understood as a systemic inflammatory condition. Review the current systemic treatment options for moderate-to-severe disease in adults, including nonbiologic and biologic therapies now available on the PBS.

Atopic dermatitis continues to be a challenge for patients and practitioners alike. A review of new and emerging treatments provides practical insights into the evolving therapeutic options for this common and often distressing condition.

Finally, test your knowledge with two dermatology quizzes. One explores patchy hair loss in a teenage boy post-haircut, and the other presents a widespread erythematous targetoid eruption in a 16-year-old girl. How would you investigate and manage these diagnostic dilemmas in clinical practice?

Gayle Fischer OAM, MB BS, FACD, MD
Clinical Professor of Dermatology at Sydney Medical School – Northern, The University of Sydney, Royal North Shore Hospital, Sydney, NSW.

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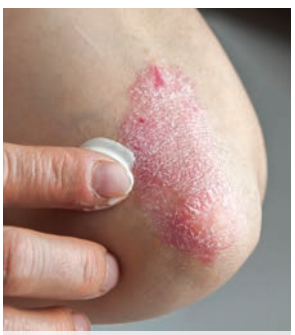

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Acne scarring

Why it occurs and what can be done

JO-ANN SEE MB BS, FACD(Hons)
AAKRITI GUPTA MB BS, FACD, IFAAD

Acne scarring is associated with significant psychosocial morbidity. Early and effective treatment is essential for all patients with acne, regardless of the severity, to minimise the inflammation that drives scarring. There are a variety of treatment options for acne scarring and these may be best facilitated by referral to a dermatologist.

KEY POINTS

- Acne scarring affects about half of all patients with acne.
- Inflammatory acne lesions can stimulate an abnormal healing response, leading to atrophic or thickened scars, regardless of the acne severity.
- Early and effective treatment of acne is necessary to reduce the risk of acne scarring.
- All patients with acne should be informed about the risk of acne scarring.
- High-risk patients include those with severe acne, those with a family history of acne, males and individuals with skin of colour.
- There are a variety of treatment options for acne scarring; a referral to a dermatologist for the development of a comprehensive and multimodal approach should be considered.
- Active acne should be under control before initiating scar treatment.
- Patients should be provided with realistic expectations and a timeframe for treatment.

Acne vulgaris is a common skin disorder, affecting about 85% of individuals.[1] Nearly half of these patients may go on to develop acne scarring, which can have significant psychological consequences, including reduced quality of life, depressed mood and, in severe cases, an increased risk of suicide.[2] It is important for doctors to recognise that even mild acne can lead to scarring and that we should prioritise early and effective treatment, especially in patients at higher risk of scarring. Once acne scarring occurs, a range of treatment options are available, often requiring a multimodal approach. Many patients present with a combination of different scar types, as well as post-inflammatory hyperpigmentation and erythema, all of which should be addressed for optimal outcomes. This article discusses the assessment of and preventive measures for patients with acne, and the available treatment options once scarring is present.

Why does acne scarring occur?

The rupture of the follicular wall in acne lesions triggers an inflammatory response, initiating a wound-healing response that can lead to atrophic or hypertrophic scarring (Figure 1). The location and severity of this wound-healing response determines the types of acne scars that develop. In the early stages, inflammation induces vasodilatation and melanogenesis, leading to postinflammatory erythema (PIE) or postinflammatory hyperpigmentation (PIH). This is followed by fibroblast-mediated matrix remodelling. The release of matrix metalloproteinases (MMPs) degrades the extracellular matrix and can result in atrophic scarring. In contrast, tissue inhibitors of MMPs promote excessive matrix deposition, leading to hypertrophic scarring.[3]

Atrophic scars are thought to form because the inflammation in an acne lesion is mostly localised to the infundibulum, which is located below the skin surface. Surface contracture creates an atrophic appearance.[4] There is an association between this type of scarring and the severity and duration of the inflammatory response. Destruction of sebaceous structures may also contribute to the atrophic appearance.[3]

Hypertrophic scars are thought to arise from increased fibroblast activity, leading to excessive extracellular matrix formation and collagen overproduction.[3]

What do acne scars look like?

Acne scars are classified based on their appearance and are further defined within each category by structure and depth (Figure 2).

- Atrophic scars are the most common type, occurring three

MedicineToday Dermatology Collection 2025; 9(1): 3-6
First published 2025; 26(4): 25-29

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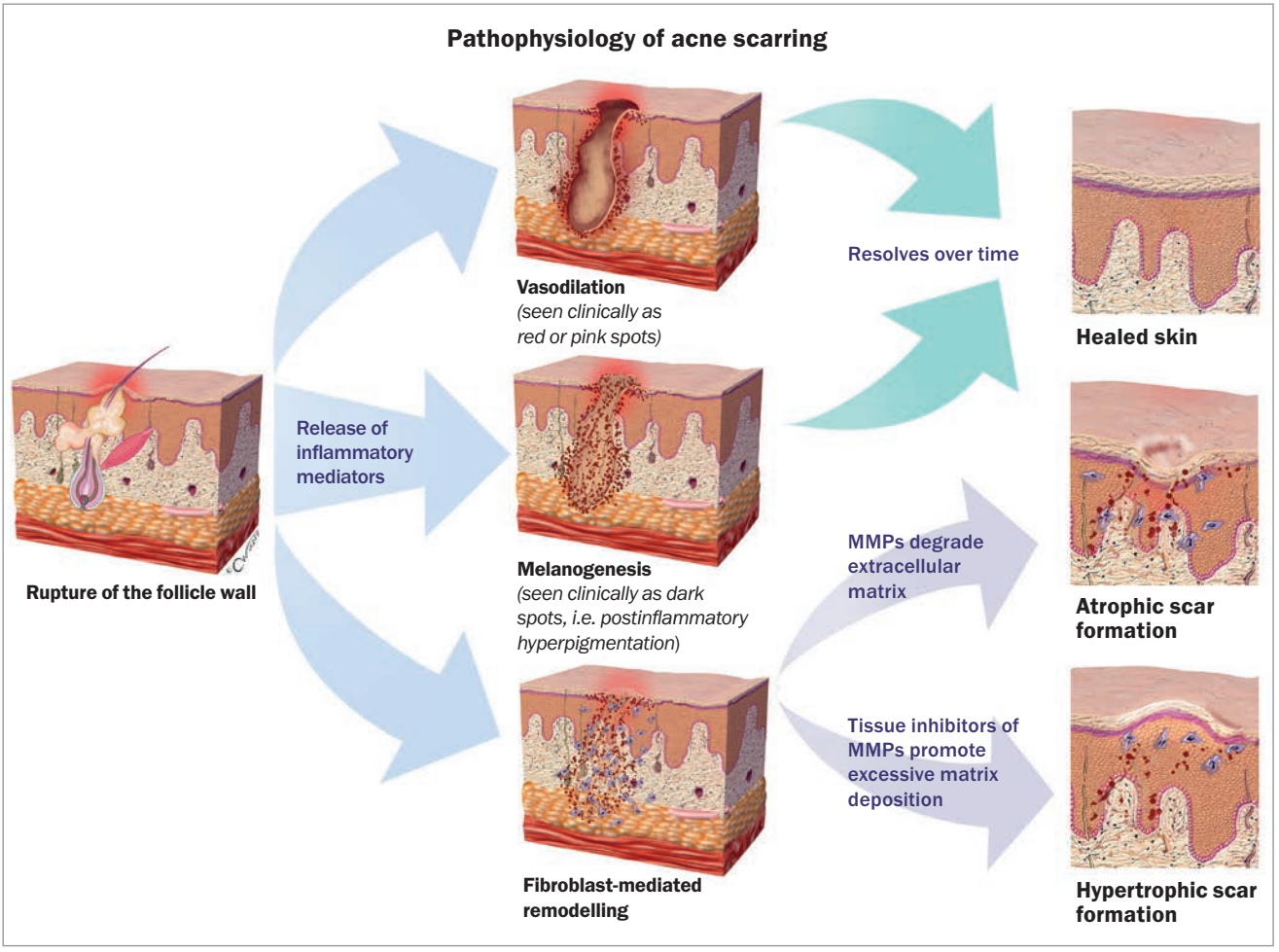

Figure 1. Pathophysiology of acne scarring. Rupture of the follicle wall triggers the release of inflammatory mediators, leading to transient redness or brown discolouration that resolves over time, or fibroblast-mediated remodelling, leading to scarring that can be permanent.
Abbreviation: MMPs = matrix metalloproteinases.

times more frequently than thicker (hypertrophic or keloid) scars. They are subdivided into icepick, boxcar and rolling scars, based on their shape and size.
- Hypertrophic and keloid scars typically develop on the back and shoulders.
- Papular scars most commonly occur on the jawline and trunk, presenting as firm, elevated lesions.

Who develops acne scarring?

Predicting which patients will develop acne scarring remains challenging. A recent meta-analysis identified three major risk factors: male sex, a positive family history of acne and acne severity.[2] Additional factors that have been identified include the duration of acne, lifestyle factors, lesion manipulation (squeezing) and acne relapse. Genetic factors may play a role in acne scarring, potentially associated with inherited innate immunity profiles. Patients who are prone to scarring may exhibit a prolonged adaptive immune response, leading to persistent inflammation and impaired wound healing.

Although severe acne is often associated with prolonged and intense inflammation, scarring can also occur in patients with mild acne. Therefore, early and effective treatment is essential for all patients with acne, regardless of the severity, to minimise the inflammation that drives scarring.

The higher risk of acne scarring in males compared with females may be because of anatomical differences in the sebaceous glands, but possibly also because of differences in healthcare-seeking behaviours, as women may be more likely to seek treatment earlier.

The importance of colour

It is essential to distinguish between PIE and PIH versus true acne scarring (Figure 3). Unlike scarring, PIH and PIE are transient and will resolve over time. Therefore, assessment for textural changes, such as skin atrophy (indentation) or thickening, is important in determining whether permanent scarring is present. Side lighting can be useful in assessing this, as it enhances the distinction between textural changes and changes in colour alone. It is also important to note hypopigmented marks or macules. These can also follow inflammatory acne, especially with repetitive squeezing of the acne lesions. This may result in focal and permanent loss of pigment without textural alteration.

Patients should be asked about a previous history of keloid and hypertrophic scarring. Patients with skin of colour are at a higher risk of developing keloid and hypertrophic scars, and this may be because of genetic factors.[5]

Patient assessment

Early assessment and treatment during the initial stages of acne can significantly reduce the risk of acne scarring. Patients should be informed about the risk of acne scarring and advised to avoid squeezing acne lesions, as this can lead to prolonged inflammation and subsequent scarring.

When examining the patient, existing scars should be assessed for and the degree of inflammation noted. Photographs taken at the time of presentation can be a valuable reference point for monitoring disease progression and treatment response. One study analysing acne scarring found that 94% of patients were dissatisfied with the information they received from their healthcare provider.[6] These patients expressed a desire for greater education from their doctors regarding available treatment options (46%), sequelae of acne and acne scarring on different skin types (44%), acne triggers (44%) and determination of acne severity (43%).[6] These findings highlighted the need for comprehensive patient education to improve satisfaction and engagement in acne management.

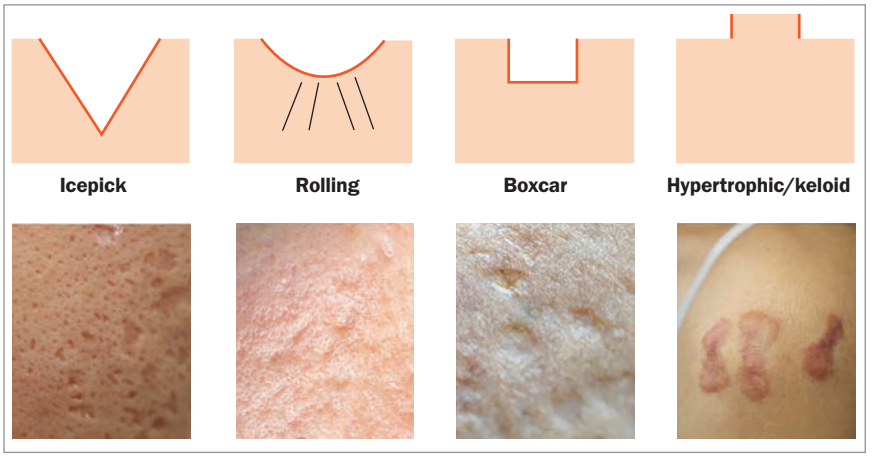

Figure 2. Acne scar types.

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Prevention and management of acne scarring

Timeline of treatment

Managing acne requires consistency, as noticeable improvement with any given treatment plan typically takes at least two to three months. Treating acne scarring is also a stepwise process, often requiring multiple treatment sessions spaced four to eight weeks apart, depending on the selected modalities.

Preventive treatment to reduce the risk of scarring

Preventive treatment for acne scarring aims to provide safe and effective early treatment for acne to minimise the risk of redness, pigmentary change and scarring. Topical retinoids are well established as effective treatments for acne, but several have also demonstrated efficacy in reducing atrophic acne scarring. As early as 1991, topical tretinoin 0.05%, applied daily for four months, has been reported to significantly improve superficial acne scars.[7] More recently, both adapalene and the fixed-dose combination of topical adapalene 0.3%/benzoyl peroxide gel 2.5% have been shown to improve atrophic acne scarring.[8]

The newest topical retinoid, trifarotene, has demonstrated both preventive and therapeutic effects on atrophic acne scarring. In a randomised, split-face, double-blind study, 121 subjects with moderate-to-severe facial acne and acne scars were treated with either trifarotene or vehicle once, daily for 24 weeks. Trifarotene reduced atrophic acne scars at week 24, and differences between both sides were noted as early as week 2.[9]

Treatment options for scarring

The management of acne scarring varies depending on the scar subtype (Figure 4). Although certain aspects of acne scar treatment, such as microneedling and radiofrequency therapy, are often performed by

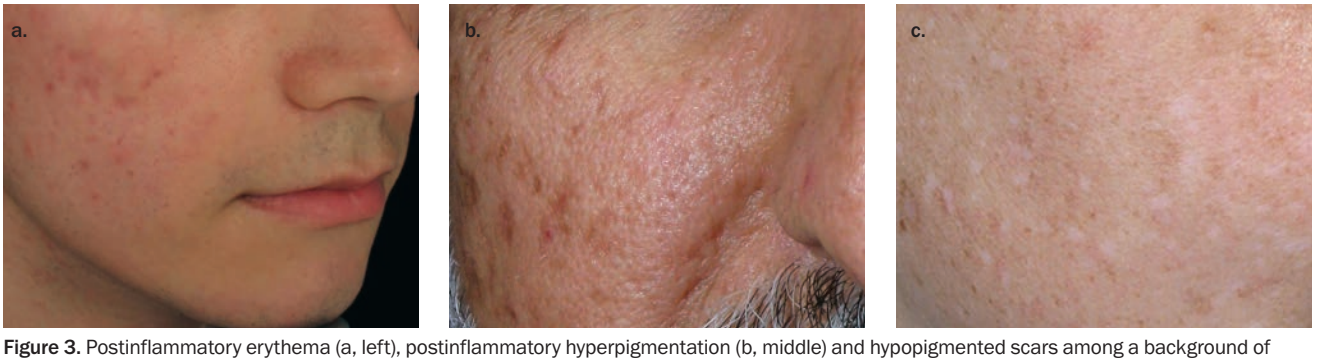

Figure 3. Postinflammatory erythema (a, left), postinflammatory hyperpigmentation (b, middle) and hypopigmented scars among a background of postinflammatory hyperpigmented changes (c, right).

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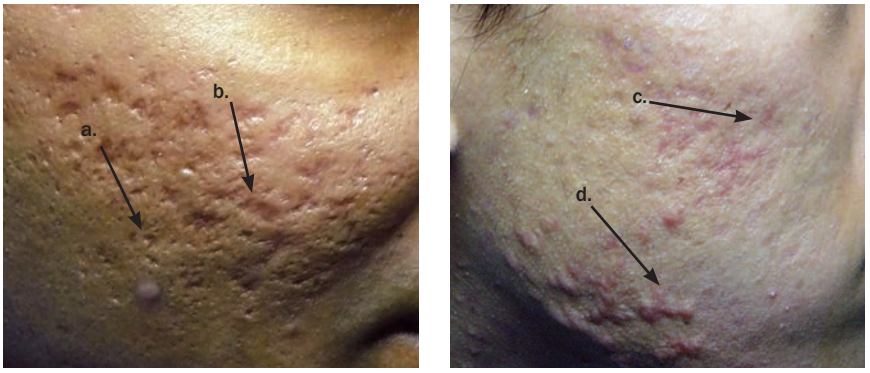

Figure 4. Atrophic (depressed) scars include (a) icepick, (b) boxcar and (c) rolling scars. Fibrotic (raised) scars include (d) hypertrophic and keloid scars.
Figures courtesy of Dr Adrian Lim. Figures reproduced with patient consent.

allied health professionals (e.g. nurses and dermal clinicians), referring patients to a dermatologist specialising in acne scarring can be highly beneficial. A specialist assessment enables a comprehensive treatment plan that incorporates a systematic approach, advanced techniques (as detailed below) and personalised treatment settings to optimise patient outcomes.

Treatment for hypertrophic versus atrophic scars

Hypertrophic and keloid scars are typically treated with intralesional corticosteroid injections, with or without the addition of 5-fluorouracil. The addition of 5-fluorouracil can be particularly beneficial for more resistant keloid scars and may help reduce the risk of steroid-related skin atrophy. Vascular laser treatments, such as pulsed-dye laser therapy, can be helpful as an adjunctive treatment, particularly to manage associated erythema and telangiectasias.

Atrophic scarring requires a thorough assessment of scar morphology and depth to guide treatment selection. The initial focus is often on addressing the deepest scars. Subcision, a surgical technique that most commonly uses a specialised tri-bevelled needle, is used to release fibrous bands tethering the base of the scar. This allows for elevation of the depressed area of scarring. Deeper, isolated scars may benefit from punch techniques, including punch excision or punch elevation.[10]

For mild-to-moderate atrophic scarring, a range of resurfacing energy-based devices are available. Radiofrequency is particularly suitable for darker skin types. Both non ablative and ablative laser resurfacing can be effective. Microneedling is another option, particularly for milder scarring. These treatments are based on the concept of creating controlled microscopic zones of injury to stimulate collagen remodelling, ultimately improving skin texture.[10,11]

Advanced treatments

Additional specialised techniques include trichloroacetic acid chemical reconstruction of skin scars (TCA CROSS), which involves focal application of high-concentration trichloroacetic acid (commonly 70 to 100%) to individual icepick scars. Dermal fillers may also be used to correct volume deficits, either by targeting individual scars with the 'tower technique' or by treating broader areas of atrophic scarring.[12]

An emerging approach involves transepidermal drug delivery. This can enhance healing and promote collagen remodelling through the application of growth factors, such as those found in platelet-rich plasma or insulin, following treatment with fractionated devices.[13]

Given the complexity of acne scarring, a multimodal treatment approach is often necessary to optimise outcomes. Although previous guidelines advised against cosmetic treatments in patients taking isotretinoin, this recommendation has evolved. With expert care by trained medical practitioners and individualised treatment settings, a range of interventions, excluding fully ablative laser and mechanical dermabrasion, can be safely performed.[14]

Early referral to a dermatologist specialising in acne scarring is key, ensuring comprehensive management of both active acne and residual scarring.

Conclusion

Scarring can occur in around half of patients with acne, even when the acne is mild. The risk of acne scarring and preventive measures should be discussed with all patients with acne. Treatment options for established acne scarring are varied and can be best facilitated by referral to a dermatologist to enable a comprehensive, multimodal approach, depending on the acne scar type. MT

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A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

COMPETING INTERESTS: Dr Gupta is a Board Member of the Australasian Society of Cosmetic and Procedural Dermatologists (ASCPD); is a Member of the All About Acne National Expert Team; and has received payment or honoraria for presentations from iNova and Pierre-Fabre. Dr See has received honoraria for consulting and speaking for Galderma, L'Oréal, SunPharma and Viatris; is co-chair of the All About Acne group and member of the Public Affairs Committee of the Australasian College of Dermatology.

MedicineToday Dermatology Collection 2025; 9(1): 3-6
First published 2025; 26(4): 25-29

Acne scarring

Why it occurs and what can be done

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Keratinocyte skin cancers

Updates on diagnosis and management

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Keratinocyte cancers, formerly known as non-melanoma skin cancers, comprise basal cell carcinoma and cutaneous squamous cell carcinoma. GPs are at the forefront of the detection and management of keratinocyte cancers, which are an important cause of morbidity and mortality in Australia. This updated summary for GPs incorporates the latest advances in management.

KEY POINTS

- Australia has one of the highest rates of skin cancer in the world, with keratinocyte cancers being the most common skin cancers encountered in general practice.
- The Cancer Council Australia *Clinical practice guidelines for keratinocyte cancer* are regularly updated and are a useful tool for GPs to provide evidence-based patient care.
- The 5-fluorouracil 0.5% and salicylic acid 10% solution is a new combined antimetabolite and keratolytic agent for targeted lesion-directed and/or small field-directed (up to 25 cm^2) therapy for actinic keratoses.
- Brachytherapy with rhenium-188 is now TGA-listed for the treatment of thin keratinocyte cancers.
- PBS-funded systemic therapies are now available for patients with locally advanced or metastatic keratinocyte cancers who are not suitable candidates for surgery or radiotherapy. These therapies include monoclonal antibodies (cetuximab and cemiplimab) for cutaneous squamous cell carcinoma, and hedgehog pathway inhibitors (sonidegib and vismodegib) for basal cell carcinoma.
- Patients with locoregional advanced keratinocyte cancers should be managed by a multidisciplinary team, comprising dermatologists, surgeons and radiation and medical oncologists.

Australia has one of the highest rates of skin cancer in the world, with keratinocyte cancers being the most common type. Keratinocyte cancers, formerly known as non-melanoma skin cancers, comprise basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC) (cSCC). Actinic keratosis (AK) is a potentially premalignant cutaneous lesion that may transform into cSCC if left untreated, although this is rare.

In 2021, keratinocyte cancers caused 760 deaths in Australia and was the most common cancer recorded as the principal diagnosis for hospitalisation.[1] An estimated 69% of Australians will undergo at least one excision for keratinocyte cancer in their lifetime, and this is likely to increase as the population ages.[2] In 2021 alone, the total cost to the Australian Government for new patients with keratinocyte cancers was $426.2 million.[3] However, statistics on the morbidity and mortality related to keratinocyte cancers are likely underestimated as they are not notifiable diseases in any state or territory except Tasmania.[1]

GPs have an important role in the prevention, early detection and management of keratinocyte cancers in Australia. Skin consultations account for about 17% of GP consultations, and skin cancers are the second most common reason for specialist referral.[4] Australia's high survival rate for skin cancers reflects the success of primary care services for the early detection and evidence-based treatment of skin cancers. GPs are also well

MedicineToday Dermatology Collection 2025; 9(1): 9-15
First published 2024; 25(8): 21-28

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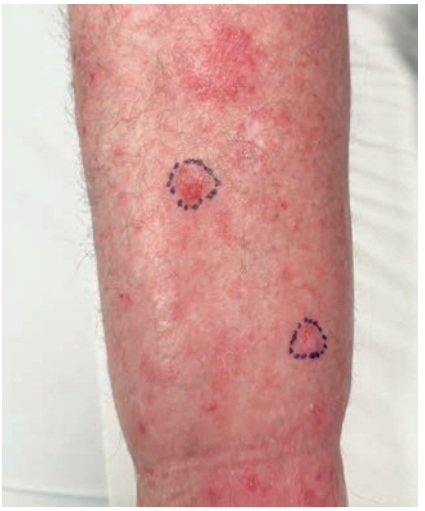


Figure 1. Multiple actinic keratoses on the lower leg, on a background of chronic sun damage.
Image courtesy of the authors. Image is published with patient consent.

positioned to educate patients on the importance of sun-safe behaviours and to detect skin cancers at the earliest opportunity through routine skin checks and opportunistic skin screening.

This update incorporates the latest guidelines and published literature on the diagnosis and management of keratinocyte cancers, to aid GPs with evidence-based treatment plans.

Actinic keratoses

AKs, also known as solar keratoses, are potentially premalignant lesions caused by damage to keratinocytes as a result of cumulative sun exposure. They are found on sites of chronic ultraviolet (UV) radiation exposure, most commonly on the face, scalp, ears and dorsal aspects of the limbs (Figure 1). The lesions progress to SCC at the rate of 0.075% to 0.1% per lesion per year, sometimes extrapolated to up to 10% over 10 years.[5] The spontaneous regression rate of AKs is also highly variable and has been reported to be about 15% to 63% per year.[1] Unfortunately, it is not possible to target higher-risk AKs as there are no clinically defining features that determine which AKs will progress to become cSCCs.

Associated factors

AKs are clinically significant, not only because they may progress to cSCC, but also because the presence of multiple AKs indicates significant, chronic UV radiation exposure. It is recommended that patients with multiple AKs undergo regular full skin examinations with their GP to assist in the early detection and management of skin cancers.

Presentation and diagnosis

AKs have varied clinical presentations. They are classically described as gritty macules, papules or plaques on an erythematous base, often with rough yellow or white scale. They can also present as hyperkeratotic, pigmented or atrophic lesions. The lesions are typically asymptomatic but may sting or itch.

The diagnosis of an AK is predominantly clinical. Biopsy should be considered if there is concern that the lesion may be an early cSCC or other keratinocyte cancer. Hallmark signs raising concern include tenderness, bleeding, inflammation and growth in height or thickness.

On biopsy, the distinction between an AK and a cSCC is the extent of keratinocyte atypia. Keratinocyte atypia is confined to the lower portion of the epidermis in an AK. In contrast, cSCC comprises keratinocyte atypia that occupies the entire epidermis and may infiltrate deeper into the dermis.

Treatment of actinic keratosis

Evidence-based treatment for AK is informed by the Cancer Council Australia's *Clinical practice guidelines for keratinocyte cancer* and the American Academy of Dermatology's *Guidelines of care for the management of actinic keratosis*.[6,7]

Lesion-directed treatment

The first-line modality for localised treatment of AK is liquid nitrogen cryotherapy. The duration of therapy varies depending on the lesion size and location, but a freeze of about 3 to 5 seconds as part of a single or double freeze–thaw cycle is generally recommended.[8] This usually causes erythema, oedema and, sometimes, a blister that heals over 7 to 10 days. Cryotherapy should be avoided if the diagnosis is uncertain, and prolonged cryotherapy should be avoided on the lower legs, where healing is poor.[9]

The 5-fluorouracil 0.5% and salicylic acid 10% solution has also been approved for use on targeted individual AKs (see Product Information for full details).

Curettage and cautery or electrodesiccation, and shave treatments may also help treat AK. However, these treatments are often reserved for larger, thicker lesions or if the diagnosis is uncertain.

Field-directed treatment

Field-directed treatment should be considered for areas that contain multiple AKs or lesions without distinct borders that allow for targeted localised treatment (Table 1).[7,9] Patient education about these therapies is paramount, as the therapies act, in part, by inducing an inflammatory reaction, including redness, soreness and crusting. Patients are best counselled about this before therapy, including being shown photographs of expected reactions (Figure 2a and 2b).

Squamous cell carcinoma

cSCC is the second most common skin cancer in Australia. The age-standardised incidence rate of cSCC is about 387 per 100,000 people aged 14 years and older.[10] The incidence increases steeply with age from mid-adulthood and appears higher in men than in women across all age groups. However, the current available evidence on national incidence rates is out of date and likely inaccurate because of a lack of statutory reporting of keratinocyte cancers.[2] The primary concern with cSCC is its ability to metastasise, with several large studies demonstrating a mortality rate of more than 70%.[11]

The most common sites of cSCC are the head and neck areas in men, and the upper limbs followed by the head and neck areas in women. After accounting for body surface area, the highest incidence of cSCC is on the face, particularly the lips, ears, nose, cheek and eyelids.[12]

TABLE 1. FIELD-DIRECTED TREATMENTS FOR ACTINIC KERATOSES[7,9]

Medication	Mechanism of action	Recommended regimen	Comments
5-fluorouracil cream	Antimetabolite that inhibits DNA and RNA synthesis in atypical cells	4% cream: applied topically once daily for four weeks 5% cream: applied topically once or twice daily for two to four weeks on the face or for three to six weeks on the limbs	4% or 5% formulations are some of the most common field therapies because of their affordable cost (about $70 per 20 g tube), ease of use and efficacy
5-fluorouracil 0.5% and salicylic acid 10% solution	Combined antimetabolite and keratolytic agent	Applied topically once daily to an area up to 25 cm^2 for up to 12 weeks	For targeted lesion- and/or small field-directed (up to 25 cm^2) therapy; this may be used as a regular treatment
Imiquimod 5% cream	Immune response modifier that activates toll-like receptor 7	Applied topically, three times a week on non-consecutive days for four weeks; if any lesions persist, the treatment can be continued for up to 16 weeks	Patient should be reviewed four weeks after starting treatment; inflammatory reactions can vary in severity between patients
Photodynamic therapy	Photodynamic reaction that produces cytotoxic oxygen free radicals	A photosensitising agent (either methyl aminolevulinate or aminolevulinic acid) is applied topically to the treatment area under occlusion for three hours; the area is then wiped clean and illuminated by red light for 7 to 9 minutes in the clinician's office, or immediately exposed to daylight for two continuous hours	Special training and equipment are needed to perform conventional photodynamic therapy, and its use is restricted to specialist centres
Diclofenac sodium gel 3%	Nonsteroidal anti-inflammatory agent	Applied topically twice daily for 60 to 90 days	Included in the *Therapeutic Guidelines* recommendations for mild lesions and for lesions in cosmetically sensitive areas

Risk factors

cSCC can arise de novo with no risk factors or triggers. However, most cSCCs arise in individuals with significant risk factors, including:[13]

- Fitzpatrick skin types I to III
- cumulative exposure to UV radiation
- male sex (male to female ratio of 3:1)
- increased age (average age of onset in the mid-60s)
- chronic inflammation or sites of previous trauma or scarring, especially in darker-skinned individuals
- immunosuppression, most significantly in patients with solid organ or stem cell transplant, with chronic leukaemia or on immunosuppressive agents
- infection with oncogenic human papillomavirus, particularly periungual and anogenital SCC
- rare hereditary cancer syndromes
- environmental exposures (e.g. arsenic, nitrosamines, alkylating agents)
- exposure to ionising radiation.

Presentation and diagnosis

cSCC has a spectrum of presentations. Bowen's disease, also known as cSCC in situ, typically presents as an erythematous patch or plaque with scale and, in rare cases, pigmentation. Without treatment, 2 to 5% of cases of Bowen's disease progress to involve the dermis, defined as invasive cSCC.[14] Invasive cSCC typically presents as an erythematous keratotic papule or nodule, which may be tender on palpation. On dermoscopy, invasive cSCC tends to have looped or hairpin and serpentine vessels. Regional lymph nodes should be examined, and suspected metastases should be confirmed via fine needle aspiration.

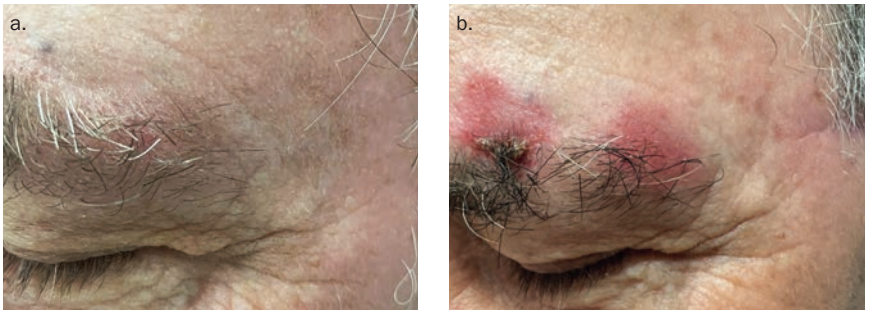


Figure 2a and b. Actinic keratoses (a, left) before treatment and (b, right) after treatment with 5-fluorouracil cream once daily for four weeks.
Images courtesy of the authors. Images are published with patient consent.

1. HIGH-RISK FEATURES OF KERATINOCYTE CANCERS AND TREATMENTS TO CONSIDER[15,16]

High-risk cSCC (any of the following criteria)

- Size ≥2 cm on the trunk or extremities, or ≥1 cm on the head, neck, hands, feet or genitalia
- Depth >6 mm or invasion beyond subcutaneous fat
- Ill-defined borders
- Recurrent tumour
- Immunocompromised status
- Prior radiation therapy
- Poor differentiation
- Perineural or lymphovascular invasion
- Rapid growth
- Neurological symptoms

High-risk BCC (any of the following criteria)

- Size ≥2 cm on the trunk or extremities, or ≥1 cm on the head, neck, hands, feet or genitalia
- Ill-defined borders
- Recurrent tumour
- Immunocompromised status
- Prior radiation therapy
- Aggressive subtype (e.g. infiltrating, sclerosing/morphoeic or micronodular)
- Perineural invasion

Treatment options to consider

- Referral to a specialist or multidisciplinary team
- Mohs micrographic surgery
- Radiotherapy
- Systemic therapy for patients who are not suitable candidates for curative surgery or radiotherapy

Abbreviations: BCC = basal cell carcinoma; cSCC = cutaneous squamous cell carcinoma.

The diagnosis of cSCC is established via biopsy. On histopathological examination, Bowen's disease shows keratinocyte atypia involving the full thickness of the epidermis. If invasive cSCC is suspected, the biopsy should be deep enough to determine the extent of dermal involvement. The pathology report should include a synoptic checklist of information useful for prognosis, including the tumour subtype, degree of differentiation, tumour thickness and presence or absence of perineural, vascular or lymphatic spread.[6] Key factors indicative of higher risk and poorer prognosis for cSCC are summarised in Box 1.[15,16]

Treatment of invasive cSCC

Surgery

Surgical treatment options for cSCC include local excision and Mohs micrographic surgery. Low-risk lesions can be treated with surgical excision, curettage and cautery, or punch excision. Lateral and deep margins must be adequate to ensure complete excision. Adequate deep margins are particularly important, as inadequate deep margins significantly increase the risk of recurrence.[17] For the best cosmetic result, tumours should be excised along relaxed skin tension lines, but along a line that avoids distortion.

For patients with cSCC with features of poor prognosis, referral to a multidisciplinary team or to a specialist for assessment and treatment should be considered (Box 1).[18]

Radiotherapy

Radiotherapy for cSCC has improved significantly in the past few decades. Modified fractionation schedules and more precise fractionation techniques allow for an improved balance between targeting tumour cells and minimising effects on normal tissue. Radiotherapy for cSCC may be considered for patients who are not appropriate surgical candidates, such as in cases of frailty, comorbidities or high surgical or bleeding risk. Referral to a radiation oncologist as part of multidisciplinary care should be considered for patients with stage T3 or T4 primary tumours, persistent or recurrent cSCC, and following incomplete surgical excision as an alternative to re-excision.

Systemic treatment

Locoregional advanced cSCC represents an advanced stage of disease that may present de novo or after previous surgery and radiotherapy.[19] The goal of treatment is to clear local disease and prevent further recurrence or regional metastasis. Surgery, radiotherapy, chemotherapy or a combination of treatments may be needed. Patients should be assessed on a case-by-case basis in a multidisciplinary setting.[6]

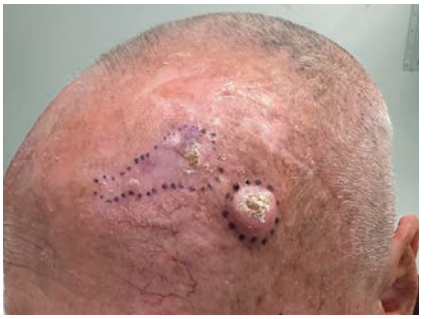


Figure 3. Two cSCCs on the left lateral forehead: biopsy proven moderately differentiated SCC medially and well differentiated SCC laterally.
Abbreviations: cSCC = cutaneous squamous cell carcinoma; SCC = squamous cell carcinoma.
Image courtesy of the authors. Image is published with patient consent.

Systemic drug treatments should be considered for patients with locoregionally advanced or metastatic SCC who are not suitable candidates for surgery or radiotherapy.[20] Both cetuximab, an epidermal growth factor receptor inhibitor, and cemiplimab, a programmed cell death protein-1 inhibitor, are PBS listed for the treatment of metastatic or locally advanced cSCC in patients who are unsuitable for curative surgical resection or radiotherapy, and who have a WHO performance status of 0 (fully active) or 1 (restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature).

Chemoprophylaxis

Chemoprophylaxis agents, including acitretin, capecitabine and vitamin B3 (nicotinamide), have been used in practice to reduce the risk of keratinocyte cancers in solid organ transplant recipients who develop multiple or high-risk keratinocyte cancers.[6] A 2022 Australian study involving 22 solid organ transplant recipients showed that acitretin, a synthetic retinoid, appears

to be well tolerated and effective in reducing keratinocyte cancers for at least five years.[21] However, these therapies are not without adverse effects and decisions should be made by dermatologists experienced in their use for this purpose.[22]

Basal cell carcinoma

BCC has the highest incidence of all cancers in Australia and accounts for 70% of all keratinocyte cancers.[1] The most recent (2011–14) reports of BCC incidence in Australia estimate an annual incidence of 770 affected people per 100,000.[23] However, when the incidence of lesions is considered, the rates are considerably higher. BCC incidence rates are highest on the face, followed by the upper limbs, trunk and lower limbs. Among the facial sites, BCCs most commonly occur on the nose, followed by the forehead and temple, then the cheeks and perioral region and then the ears (Figure 3).[24]

Risk factors

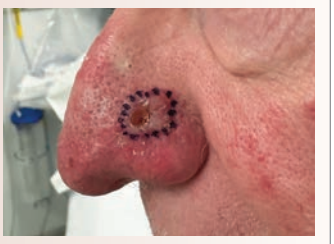
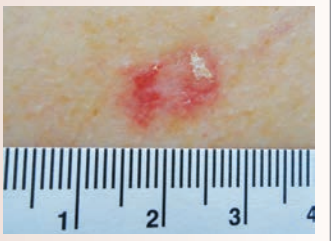
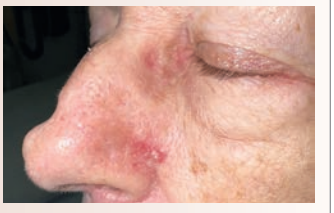
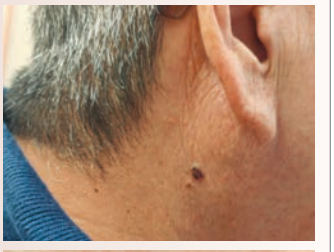
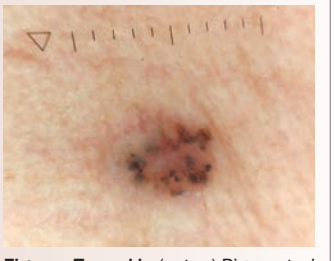
As with cSCC, exposure to UV radiation is the greatest risk factor for BCC. However, unlike SCC, the risk is associated with intense episodes of burning rather than cumulative exposure.[25] Other risk factors include:[6]

- exposure to artificial UV radiation, including psoralen and UVA radiation
- exposure to ionising radiation
- exposure to arsenic
- presence of rare hereditary syndromes (e.g. naevoid BCC syndrome [Gorlin's syndrome], Bazex–Dupré–Christol syndrome, Rombo syndrome).

Presentation and diagnosis

Evaluation of a suspected BCC entails a comprehensive clinical examination supplemented with dermoscopy. BCCs are usually diagnosed via biopsy. The clinical features and histopathology for the different subtypes of BCC are outlined in Table 2.[6] Not all clinical and histological features may be present for a specific lesion.

TABLE 2. CLINICAL AND HISTOLOGICAL FEATURES OF THE MOST COMMON SUBTYPES OF BCC[6]

Histological subtype	Clinical features	Photographic example
Nodular	• Most common type of BCC on the face • Shiny, translucent (pearly) papule or nodule • Raised, rolled edges • Central depression, crusting, ulceration or umbilication • Blood vessels across the surface (e.g. telangiectasia and arborising vessels on dermoscopy)	 **Figure 4.** Nodular BCC of the left nasal alar.
Superficial	• Commonly occurs on the trunk or limbs • Well-circumscribed macule or patch, or thin papule or plaque • Pale or varying degrees of erythema • Scaling or slightly shiny • Thin, translucent rolled edges	 **Figure 5.** Superficial BCC on the mid-back.
Morphoeic/ sclerosing	• White or yellow scar-like plaque • Ill-defined borders • Rarely ulcerates or bleeds • Firm induration on palpation	 **Figure 6.** Morphoeic BCC of the left nasal alar groove.
Pigmented	• Pigmented plaque or nodule • Absent pigment network • Multiple blue-grey globules or ovoid nests • Structureless or leaf-like areas of pigment, especially in the periphery • Blood vessels across the surface such as linear or arborising telangiectasia • Spoke-wheel areas with radial projections of pigment from a well-circumscribed dark centre • Focal ulceration	  **Figures 7a and b.** (a, top) Pigmented BCC of the neck. (b, bottom) Dermoscopy image of the same pigmented BCC.

Abbreviation: BCC = basal cell carcinoma.
Images courtesy of the authors. Images are published with patient consent.

2. WHEN TO CONSIDER REFERRAL TO A SPECIALIST OR MULTIDISCIPLINARY TEAM[6]

GPs should consider referral for the following indications.

- If the diagnosis is uncertain or there are doubts about appropriate treatment
- If the recommended treatment is beyond the skills of the practitioner
- For cancers with any high-risk features (see Box 1)
- For cancers of a large size
- For cancers in technically difficult or high-risk anatomical locations (e.g. ears, nose, eyelids)
- If there are cosmetic concerns
- For recurrent or persistent cancers
- If signs suggestive of metastatic spread are present, such as palpable regional lymph nodes
- If there is perineural or lymphovascular invasion
- In the presence of immunosuppression or skin-related comorbidities (e.g. scleroderma, xeroderma pigmentosa)

BCCs rarely metastasise, and the main clinical concern is local destruction. If allowed to progress, BCCs can cause significant morbidity and represent a significant burden on healthcare services. Key factors indicative of higher risk and poorer prognosis for BCC are summarised in Box 1.[15,16]

Treatment of BCC

Treatment options for low-risk BCC

Small, low-risk, superficial BCC may be treated with cryotherapy, imiquimod cream or photodynamic therapy. Cryotherapy is performed with a double freeze–thaw cycle of 20 to 30 seconds. This causes a significant blister that heals in about three to four weeks. It can lead to hypopigmentation; therefore, it is important to counsel patients about this. Long-term follow up is essential, as late recurrences may occur.[6]

Similarly, topical treatment with imiquimod 5% cream is more intensive than for AKs, with therapy applied by the patient once daily, on five consecutive nights per week for six weeks.[26] The degree of inflammation is variable and depends partly on the specific skin lesion and genetic factors. If severe inflammation occurs, patients may need to take a break from therapy for a week or two to allow time for the reaction to settle before continuing treatment. Skin biopsy is required for PBS-reimbursed prescription of imiquimod 5% cream. There is usually a good cosmetic outcome with little scarring after imiquimod treatment. Several studies and clinical trials have shown that imiquimod is superior to 5-fluorouracil in treating superficial BCCs.[26,27]

Photodynamic therapy may be considered for superficial and thin nodular BCCs. Two treatment sessions, one week apart, are usually required, with the lesions first descaled or debulked before applying the photosensitising agent.

Brachytherapy utilising the beta emitter radioisotope rhenium-188 is now TGA-listed (but not PBS-funded) for the treatment of thin BCC and cSCCs (<3 mm thick) in a single treatment session.[28] The area requiring treatment is covered with a protective foil before the rhenium-188 compound is applied on top using a special applicator and left in place for 30 to 180 minutes. Although studies have shown that healing and the rates of remission are favourable, the caveat is that long-term data, while being accrued, are lacking.[28,29]

Surgical treatment options

Surgery is usually the first-line therapy for nonsuperficial BCCs (Box 1). It usually involves elliptical excision of the lesion and repair of the defect by side-to-side (primary) closure. Very large lesions or lesions in anatomically difficult areas may require flap or skin graft repair. Curettage and electrodessication may be considered as an option for some lesions.

Referral to a specialist is recommended for the consideration of other treatment options, such as Mohs micrographic surgery and postsurgical adjuvant treatments, for lesions with features of poor prognosis in certain cases (Box 1).[6]

Mohs micrographic surgery is a highly specialised and meticulous surgical technique. It involves histopathological examination of frozen sections of almost the entire peripheral and deep margins of the excised tissue, in contrast with standard specimen processing, where only 0.1 to 1% of the surgical margin is examined. Mohs micrographic surgery may be considered an alternative to surgical excision for the following types of BCCs:[6]

- aggressive histological subtypes (e.g. infiltrating, micronodular, sclerosing)
- residual or recurrence following previous treatment
- poorly defined clinical border
- located in an anatomically difficult area or an area of large size, especially on the face.

Radiotherapy

Radiotherapy using curative doses is an alternative treatment for BCC if the patient declines surgery or surgery is inappropriate because of patient factors including frailty, tumour-related factors (e.g. if tissue conservation or cosmesis is a high priority, such as in BCC of the eyelid) or treatment-related factors (e.g. concurrent anticoagulant therapy). For patients with a stage T3 or T4 primary BCC or persistent or recurrent BCC, referral to a radiation oncologist for an opinion regarding radiation therapy should be considered.

Systemic therapy

Metastatic BCC is rare. If suspected, confirmation is required via biopsy. Patients with complex locally advanced disease are best treated by a multidisciplinary team that includes surgeons, dermatologists, radiation oncologists and medical oncologists. For patients who are not suitable candidates for surgery or radiotherapy, oral therapy with a hedgehog pathway inhibitor (sonidegib or vismodegib) should be considered.[30] Both agents have similar efficacy and are listed on the PBS for the treatment of metastatic or locally advanced BCC, for which neither surgery nor curative radiotherapy is appropriate.

When should a GP refer?

GPs are well positioned to educate patients on the importance of sun-safe behaviours, to detect skin cancers at the earliest opportunity and to provide initial management. Recommendations on when to consider referring patients for specialist or multidisciplinary care are outlined in Box 2.

Patients requiring specialised management, including photodynamic therapy, Mohs micrographic surgery and brachytherapy, may be referred to a dermatologist. Referrals to plastic surgery and surgical oncology specialists are appropriate for lesions that require complex surgical management or have higher-risk features. For patients who are unable to undergo surgery because of lesion features or comorbidities, referral for a radiation oncology opinion is appropriate. For complex tumours and metastatic tumours, referral to a multidisciplinary team that includes dermatologists, surgeons and medical and radiation oncologists is recommended for planning and management.

Conclusion

Keratinocyte cancers are the most common cancers encountered in Australia, and GPs play a crucial role in their detection and early management. Full skin examination is recommended for patients at risk of skin cancers, as many areas of the skin cannot be adequately monitored by patients themselves. Prevention through sun-safe education, early detection and appropriate treatment can help reduce the impact these cancers have on patients' lives and the healthcare system. MT

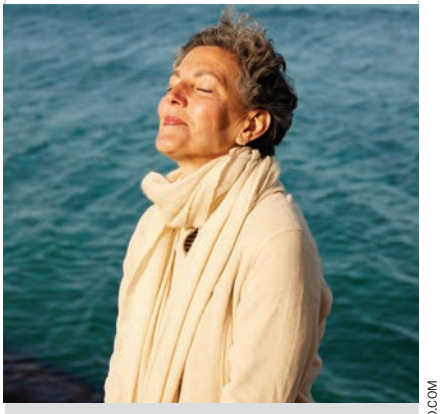
References

A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

COMPETING INTERESTS: Dr Miao and Dr Phan: None. Associate Professor Shumack receives advisory board payments from Oncobeta.

ONLINE CPD JOURNAL PROGRAM

What are three common sites for actinic keratoses?



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MedicineToday Dermatology Collection 2025; 9(1): 9-15
First published 2024; 25(8): 21-28

Keratinocyte skin cancers

Updates on diagnosis and management

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Psoriasis

Systemic treatment options for adults

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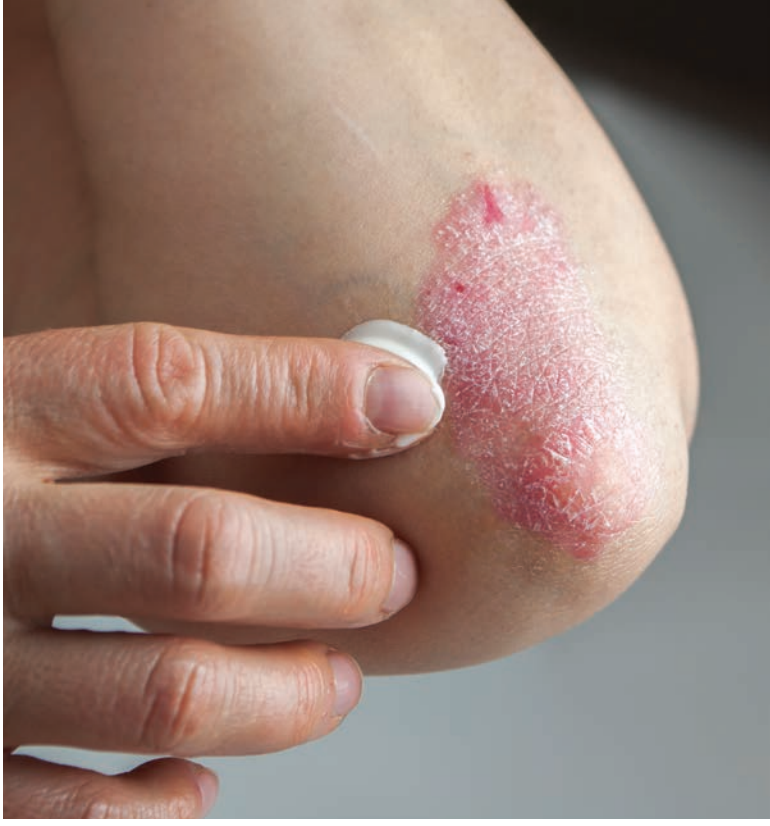
Mild psoriasis can usually be managed using topical agents, but moderate-to-severe psoriasis typically requires systemic therapies. There are several nonbiologic and biologic therapies available in Australia for psoriasis.

KEY POINTS

- Chronic plaque psoriasis can be classified as mild, moderate or severe disease based on the body surface area affected, psoriasis area severity index, effect on quality of life and location on high-impact sites.
- Psoriasis is not purely a cutaneous disease and has multiple associated comorbidities, including psoriatic arthritis, metabolic syndrome, cardiovascular disease, diabetes, obesity and inflammatory bowel disease.
- GPs play a key role in identifying and managing psoriasis and any disease or treatment complications, as well as any associated comorbidities in patients.
- Nonbiologic systemic treatment options for patients with moderate-to-severe psoriasis include methotrexate, ciclosporin, acitretin, apremilast, deucravacitinib and ultraviolet B phototherapy.
- Patients must fulfil specific criteria for severe chronic plaque psoriasis to qualify for treatment with a biologic agent in Australia through the PBS.
- Biologic systemic treatment options available in Australia include tumour necrosis factor-alpha inhibitors (infliximab, adalimumab, certolizumab), interleukin (IL)-12/23 inhibitors (ustekinumab), IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab) and IL-23 inhibitors (risankizumab, guselkumab, tildrakizumab).



Chronic plaque psoriasis affects about 2% of the population. The severity can be determined based on the percentage of body surface area (BSA) affected, psoriasis area severity index (PASI) and effect on quality of life. A BSA of less than 3% is considered mild disease, 3 to 10% is considered moderate and greater than 10% is considered severe disease.[1] Plaque psoriasis with a PASI score greater than 10 is considered at least moderate in severity. Newer definitions include high- and low-impact sites. High-impact sites include the face, scalp, palms, soles and genital areas, and are associated with a poorer quality of life.[2] This article provides an overview of nonbiologic and biologic systemic treatment options for psoriasis in adults.

Comorbidities of psoriasis

Psoriasis is a systemic inflammatory condition, rather than a purely cutaneous disease, and is associated with multiple comorbidities. It is important to identify these comorbidities, as they can be reversible and, if untreated, can result in significant morbidity and mortality.

Psoriatic arthritis (PsA) affects up to 42% of all patients with psoriasis.[3] There are different types of PsA including distal interphalangeal, asymmetric oligoarticular, symmetric polyarthritis,

MedicineToday Dermatology Collection 2025; 9(1): 17-24
First published 2024; 25(9): 29-35

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spondylitis and arthritis mutilans types. PsA questionnaires, such as the Psoriasis Epidemiology Screening Tool, Psoriatic Arthritis Screening and Evaluation, and Early Psoriatic Arthritis Screening Questionnaire, can help detect early symptoms of PsA and help clinicians in deciding whether a rheumatology referral is required. Clinical signs that can indicate an increased risk of developing PsA include enthesitis, dactylitis (sausage digits), scalp or flexural psoriasis and nail changes, such as pitting, onycholysis and subungual hyperkeratosis.

Psoriasis is also associated with metabolic syndrome, cardiovascular disease, diabetes and obesity. Psoriasis is an independent risk factor for myocardial infarction, stroke and peripheral vascular disease because of the involvement of common inflammatory mediators and cytokines. Patients with severe psoriasis are twice as likely to develop diabetes and three times more likely to develop heart failure than those without psoriasis. For every 10% increase in the BSA affected by psoriasis, there is an additional 20% risk of developing diabetes.[4] Obesity is also an independent risk factor for psoriasis and PsA. Weight loss improves pre-existing psoriasis and prevents new-onset psoriasis.[5] Psoriasis also occurs in almost 10% of patients with Crohn's disease. Patients with psoriasis are almost 2.5 times more likely to have Crohn's disease and have 1.7 times the risk of developing ulcerative colitis.[6]

Role of GPs in managing moderate-to-severe psoriasis

GPs play a key role in managing psoriasis. They are in the unique position of knowing the clinical guidelines for different comorbidities and have often established longer-term relationships with patients.

Prompt referral to a dermatologist is suggested if the psoriasis is unresponsive to topical therapies, there is a significant impact on the patient's quality of life or there is moderate to severe disease with a greater than 10% BSA involvement. In the context of moderate-to-severe psoriasis, GPs can:

- identify and manage any comorbidities
- assess patients for potential complications of psoriasis, including metabolic syndrome, cardiovascular disease, arthritis and mental health disease
- ensure patients are up to date with their malignancy screens and vaccinations.

GPs can also prescribe certain continuing treatments for psoriasis following initiation by a dermatologist, as well as monitoring for treatment response and treatment complications. Live vaccines should not be given to patients who are taking immunosuppressive or immunomodulatory agents.

Pregnancy and breastfeeding

Psoriasis typically improves in pregnancy but can worsen postpartum. Owing to a lack of data, there is no international guideline on the safety of administering biologics in pregnant and breastfeeding women, as biologics can be actively transported across the placenta, especially in the late second and third trimesters. A multidisciplinary approach with the treating dermatologist and obstetrician is recommended, as untreated severe psoriasis can result in negative pregnancy outcomes. Live vaccines should not be administered to a newborn exposed to a biologic in utero (particularly in the second half of gestation) because of the risk of dissemination. The Table provides an overview of the safety of psoriasis treatments in pregnant and breastfeeding women.

Systemic medications for psoriasis

Most patients can manage their psoriasis using topical agents, but moderate-to-severe disease typically requires systemic therapies.[1] There are a range of nonbiologic and biologic therapies for psoriasis available in Australia.

Methotrexate, ciclosporin, apremilast and deucravacitinib can be used for PsA. Tumour necrosis factor (TNF)-alpha inhibitors and interleukin (IL)-17 inhibitors have been approved and used successfully in patients with both psoriasis and PsA. Some of the IL-23 inhibitors (risankizumab and guselkumab) have been approved for the treatment of PsA, although they have limited efficacy in axial disease. Patients with a high body mass index (BMI) are less likely to respond to biologics and more likely to withdraw from the drug because of their lower efficacy.[7] Overweight and obese patients may require higher doses or an increased frequency of injections to achieve the same effect as that in patients of a healthy weight.

Patients with chronic plaque psoriasis must fulfil certain criteria to qualify for a biologic agent in Australia through the PBS. The patient must be at least 18 years of age and be treated by a dermatologist. The patient must have had psoriasis for at least six months and, at the time of application, must have severe chronic plaque psoriasis affecting the whole body (PASI score >15), or have severe chronic plaque psoriasis of the face, palm of a hand or sole of a foot (at least 30% involvement, or at least two of the three PASI symptom subscores indicating severe or very severe erythema, thickness and scaling).

Patients must have tried and failed (alternatively, have a contraindication or toxicity to) two of six systemic treatments for a minimum of six weeks, as listed in Box 1.

Nonbiologic systemic treatment options for adults with psoriasis

Methotrexate

Methotrexate is a dihydrofolate reductase inhibitor that is widely available and affordable, with anti-inflammatory and antiproliferative properties.[8] It can be used for psoriasis and PsA as either monotherapy or in conjunction with biologics.[9] Methotrexate can be administered as an oral, intramuscular or subcutaneous preparation for psoriasis and PsA. The usual oral dose

TABLE. SAFETY AND SPECIAL CONSIDERATIONS OF PSORIASIS TREATMENTS FOR WOMEN WHO ARE PREGNANT OR BREASTFEEDING

Treatment	Women who are pregnant	Women who are breastfeeding	Special considerations
Ultraviolet B phototherapy	Safe	Safe	Folic acid supplements are suggested
PUVA phototherapy	Contraindicated	Contraindicated	
Methotrexate	Contraindicated	Contraindicated	Teratogenic
Ciclosporin	Safe	Safe	Must treat in conjunction with obstetrician, as reports of premature births and lower births have been reported. Neonatal ciclosporin levels may also need to be monitored if breastfeeding.
Acitretin	Contraindicated	Contraindicated	Teratogenic
Apremilast	Insufficient data	Insufficient data	
Deucravacitinib	Insufficient data	Insufficient data	

Abbreviation: PUVA = psoralen and ultraviolet A.

is between 10 and 25 mg/week, although in clinical practice, the dose ranges from 2.5 to 25 mg/week. Folic acid (e.g. 5 mg/week, although the dosing varies in clinical practice) is commonly prescribed at least 24 hours after the methotrexate dose to reduce gastrointestinal and immunosuppressive effects. Parenteral administration of methotrexate reduces the common gastrointestinal symptoms.

A minimum of 10 mg/week for at least six weeks is the dose as per PBS criteria to be eligible for a biologic agent. A test dose of 5 mg/week is sometimes used to identify early methotrexate toxicity, such as bone marrow failure, although this practice may only be beneficial in patients at increased risk of methotrexate toxicity, such as older individuals or those with impaired renal function.[10]

About 45% of patients achieve PASI 75 (75% reduction in PASI score from baseline) at weeks 12 to 16 with methotrexate treatment.[11] Other studies have shown similar outcomes, with a range of 7.5 mg/week to 15 mg/week achieving PASI 75 at week 12 in 39 to 75% of patients.[8]

Common side effects of methotrexate include nausea and vomiting (18%), oral ulcers (11.1%), upper respiratory tract infections (10.2%), abnormal liver function test results (10%), leucopenia (3.4%), infections and pneumonitis.[11]

Ciclosporin

Ciclosporin is an oral calcineurin inhibitor that reduces T-cell function and inhibits the synthesis of interleukin (IL)-2. It is used to treat dermatological conditions such as psoriasis, eczema and lupus. The typical dose ranges between 2 and 5 mg/kg/day; however, the optimal dose to achieve disease control is 5 mg/kg/day with 58 to 71% achieving PASI 75 at weeks 12 to 16. Failure to achieve an adequate response to a lower dose (2 mg/kg/day) is required to be eligible for a biologic agent.

A significant benefit of ciclosporin is it can quickly bring psoriasis under control, as it has a rapid onset of action. It is used for a short treatment course (e.g. six months, although this can vary among clinicians), as long-term use is associated with hypertension and nephrotoxicity. Some common side effects of ciclosporin include hypertension, renal dysfunction, headaches, gastrointestinal issues (nausea, diarrhoea and abdominal discomfort) and paraesthesia.[9] Regular renal function testing and blood pressure monitoring are essential with ciclosporin, with deterioration of at least 10% from baseline necessitating at least temporary cessation of the drug. Other potential side effects include hyperkalaemia, headache, hirsutism, gingival hyperplasia, malignancy and risk of infection. Ciclosporin is metabolised and, therefore, is associated with drug interactions through the cytochrome P450 pathway, including CYP3A4.[12]

Acitretin

Acitretin is a second-generation retinoid used in plaque psoriasis, pustular psoriasis and palmoplantar psoriasis. It reduces the proliferation of epidermal keratinocytes, inhibiting the IL-6-induced T helper (Th)1/Th17 inflammatory cell pathways while downregulating the expression of interferon-gamma.[9]

At week 12, PASI 75 was shown to be achieved in 47% and 69% of patients treated with doses of 25 mg and 35 mg, respectively.[13] The effect of acitretin is augmented with concomitant phototherapy. Acitretin is contraindicated in women of childbearing potential because of the drug's teratogenicity. Acitretin can be esterified into the lipophilic etretinate in the presence of alcohol; therefore, women should avoid pregnancy for at least three years after the discontinuation of acitretin. The drug is, therefore, commonly only prescribed in men and postmenopausal women. An advantage of acitretin is that it is not an immunosuppressive agent and can be used in patients with a history of infections or malignancies, especially skin cancers. Common side

1. SYSTEMIC TREATMENTS THAT ADULTS WITH PSORIASIS MUST HAVE TRIED AND FAILED BEFORE TREATMENT WITH BIOLOGICS

- Phototherapy (UVB or PUVA): at least three treatments per week
- Methotrexate: at least 10 mg weekly
- Ciclosporin: at least 2 mg/kg/day
- Acitretin: at least 0.4 mg/kg/day
- Apremilast: 30 mg twice/day
- Deucravacitinib: 6 mg daily

Abbreviations: PUVA = psoralen and ultraviolet A; UVB = ultraviolet B.

effects of acitretin include photosensitivity, transient liver function test abnormalities and hyperlipidaemia, as well as mucocutaneous side effects (e.g. xerosis, cheilitis, epistaxis, fragile and brittle skin and nails) and telogen effluvium.[14]

Apremilast

Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 that does not suppress the immune system and does not need blood monitoring. It reduces the production of proinflammatory cytokines (including TNF, IL-17, IL-23 and IL-22) by reducing the intracellular concentration of cyclic adenosine monophosphate. It is PBS listed for patients with severe psoriasis who have failed to respond to, a contraindication to or a severe intolerance to methotrexate. The initial dose is 10 mg, which is titrated up over six days to a maximum of 30 mg twice daily. Dosing adjustment may be required in patients with severe renal impairment.

The common side effects are gastrointestinal issues (diarrhoea, nausea), headache and nasopharyngitis, with some reports of depressive symptoms and suicidal ideation. Apremilast is effective for chronic plaque psoriasis, as well as scalp and genital psoriasis.[15]

More patients achieved PASI 75 at week 8 when treated with apremilast and ultraviolet B (UVB) phototherapy compared with UVB phototherapy alone ($p<0.03$), with no statistically significant difference in PASI 90.[16] Randomised controlled trials have shown that 28.8 to 33.1% of patients taking apremilast achieved PASI 75 compared with 5.3 to 5.8% taking placebo at week 16.[17,18]

GPs can prescribe apremilast if directed to continue treatment (not initiate treatment) by a dermatologist or a dermatology registrar in consultation with a dermatologist.

Deucravacitinib

Deucravacitinib is an oral, tyrosine kinase 2 inhibitor that inhibits the IL-23 signalling pathway, which is effective in treating psoriasis and PsA. It has been shown to be more effective than apremilast and placebo in achieving PASI 75 and 90 at weeks 16 and 24, respectively. PASI 75 was achieved at week 16 in 53% of patients treated with deucravacitinib compared with 39.8% treated with apremilast and 9.4% with placebo.[19]

Similar to the PBS criteria for apremilast, deucravacitinib can be prescribed to patients with severe psoriasis who have failed to respond to, a contraindication to or a severe intolerance to methotrexate. The dose is 6 mg once daily. Common side effects include nasopharyngitis, upper respiratory tract infections, headache, skin infections (e.g. herpes simplex virus, varicella zoster virus), acne and hypertension. Given it is an immunosuppressive agent, it is important to perform an immunosuppressive screen prior to starting treatment and monitor for infections including herpes zoster disease.

As with apremilast, GPs can prescribe deucravacitinib if directed to continue treatment (not initiate treatment) by a dermatologist or a dermatology registrar in consultation with a dermatologist.

Ultraviolet B phototherapy

Phototherapy consists of treatments with ultraviolet A (UVA) or UVB wavelengths. UVA machines are no longer commonly used in Australia because of the associated increased risk of skin cancers. UVA can be combined with psoralens (topical or oral) (PUVA) for more effective clearance of psoriasis and other skin conditions, but there is a risk of the onset of cutaneous and systemic side effects including nausea, headache, hypertrichosis, peripheral oedema, lentigines and skin cancers.

Narrowband UVB phototherapy is an effective and frequently used treatment for psoriasis, typically administered three times per week, with few adverse events at a wavelength of 311 to 313 nm. The effect is equivalent or near equivalent to that of PUVA, as it clears psoriasis and results in long-term remission.[20] To date, narrowband UVB phototherapy is not associated with an increased risk of skin cancer.[21]

Biologic systemic treatment options for adults with psoriasis

Screening for biologics

There is no international consensus on screening tests that should be performed before prescribing a biologic, but it is suggested to perform a full blood count, measurement of electrolyte levels, renal and liver function tests, measurement of fasting serum lipid levels and antinuclear antibody (ANA) positivity testing if prescribing a TNF inhibitor. An immunosuppressive screen can consist of tuberculosis testing and HIV, hepatitis B and C, varicella, measles and *Strongyloides* serology. A chest x-ray is required to exclude latent tuberculosis. Box 2 lists some common immunosuppressive screening assessments to be performed before initiating biologics in adults with psoriasis.

There is no consensus regarding the exact timing of live vaccines; however, a patient taking an immunosuppressive agent, including a biologic, should not receive a live vaccine during treatment with the immunosuppressant and for three months after the last dose. An immunosuppressant or biologic can be administered one month after the live vaccine dose.

Tumour necrosis factor-alpha inhibitors

The TNF-alpha inhibitors, including etanercept, infliximab and adalimumab,

2. COMMON IMMUNOSUPPRESSIVE SCREENING ASSESSMENTS IN ADULTS WITH PSORIASIS BEFORE INITIATING BIOLOGICS

History

- Infections: hospitalisation for infections, recurrent infections
- Malignancies: types, dates, treatment
- Travel: countries visited and dates, exposure to tuberculosis
- Age- and sex-related malignancy screening (e.g. mammogram, cervical screening test, colonoscopy, prostate, etc.)
- Infusion reactions
- Vaccine history
- Pregnancy and family planning
- History of heart failure; other past medical history
- History of inflammatory bowel disease

Examination

- Body mass index, body weight and abdominal circumference
- Full skin examination to assess for skin cancers

Blood tests

- Full blood count; electrolytes, urea and creatinine levels; liver function tests; comprehensive metabolic panel; C-reactive protein levels; erythrocyte sedimentation rate
- Antinuclear antibody, extractable nuclear antigen, double-stranded DNA levels
- Lipid profile, glycated haemoglobin
- HIV serology; hepatitis B and C serology; cytomegalovirus serology; Epstein–Barr virus serology; measles, mumps and rubella and varicella zoster serology; syphilis serology; *Strongyloide*s serology; tuberculosis test

Imaging

- Chest x-ray

were among the original biologics for psoriasis and are still used today. In general, they are effective for psoriasis and PsA, but they also have other indications such as inflammatory bowel disease, hidradenitis suppurativa, rheumatoid arthritis and ankylosing spondylitis. TNF-alpha inhibitors have been used for psoriasis at specific sites including scalp, nail and palmoplantar psoriasis. Side effects of TNF-alpha inhibitors include paradoxical pustular psoriasis, palmoplantar psoriasis or pustulosis, lupus, opportunistic infections, reactivation of tuberculosis or hepatitis, non-melanoma skin cancer or lymphomas, demyelinating disease and worsening heart failure.

Newer biologics are preferred to the TNF-alpha inhibitors as first-line treatment because they are more effective and are associated with fewer side effects. Etanercept is used for paediatric and adult chronic plaque psoriasis, or those with scalp, nail, pustular, erythrodermic and inverse psoriasis at doses of 50 mg twice per week for 12 weeks, followed by a maintenance dose of either 50 mg/week or 50 mg twice per week. Etanercept is a recombinant TNF-alpha receptor protein fused with the Fc portion of immunoglobulin (Ig)G1. In terms of efficacy, at week 12, PASI 75 has been shown to be achieved in 33% and 49% of patients taking the drug at doses of 50 mg/week and 50 twice per week, respectively.[1]

Infliximab is a chimeric monoclonal antibody consisting of a murine variable region and human IgG1-alpha constant region, which neutralises the effects of TNF-alpha and is administered as an intravenous infusion of 5 mg/kg at weeks 0, 2 and 6 as an induction, followed by every eight weeks as maintenance, although higher doses (e.g. up to 10 mg/kg) or an increased frequency (e.g. every four weeks) is sometimes used for better disease control. With rapid onset, 80% and 57% of patients receiving 5 mg/kg intravenously have been shown to achieve PASI 75 and PASI 90 at week 10, respectively.[22] Subcutaneous infliximab (120 mg every two weeks, regardless of weight) has recently become available for patients who have had two or more doses of intravenous infliximab.

Adalimumab is given as a subcutaneous injection for psoriasis, PsA and hidradenitis suppurativa. The dose is 80 mg subcutaneously in week 0, 40 mg in week 1 and followed by 40 mg every fortnight as maintenance. At week 16, PASI 75 is achieved in 71% of patients treated with adalimumab compared with 7% of those treated with placebo.[23]

Certolizumab is a PEGylated, humanised monoclonal antibody, which is TGA approved, but not PBS listed, for psoriasis. Given its molecular structure, it is not actively transported across the placenta and is safe in pregnancy. It is administered subcutaneously at a dose of 400 mg every two weeks.

Interleukin-12/23 inhibitors

Ustekinumab is a human monoclonal antibody targeting the common p40 subunit of IL-12 and IL-23. The dose is weight dependent: 45 mg if the patient's body weight is 100 kg or less, or 90 mg if the patient's body weight is greater than 100 kg, administered subcutaneously at week 0 and 4, and then every 12 weeks as maintenance. At week 12, PASI 75 was shown to be achieved in 66.7 to 67.1% of patients at a dose of 45 mg and 66.4 to 75.7% of patients at a dose of 90 mg.[1]

The IL-17 inhibitors, secukinumab and ixekizumab, have been shown to be more effective than ustekinumab. Secukinumab 300 mg was found to be more effective than ustekinumab in achieving PASI 75 at week 16 (79% *vs* 57.6% of patients). In another randomised controlled trial, those treated with ixekizumab were more likely to achieve PASI 90 at week 12 (72.8%) compared with the ustekinumab group (42.2%).[1]

The durability of the response of biologics is important, as a loss of effect over time may reduce treatment adherence and affect a patient's quality of life. Ustekinumab has a longer drug survival than TNF-alpha inhibitors, with lower rates of discontinuation.[24]

Interleukin-17 inhibitors

Secukinumab is a human IgG1 monoclonal antibody that binds to IL-17A and

inhibits its interaction with the IL-17 receptor. It is used to treat psoriasis, PsA, hidradenitis suppurativa and ankylosing spondylitis. The initiation dose for psoriasis is 300 mg via subcutaneous injection weekly for five weeks, followed by 300 mg monthly. Phase III randomised controlled trials assessing the efficacy of secukinumab in moderate-to-severe psoriasis have shown that PASI 75 was achieved at week 12 in 77.1 to 81.6% of patients receiving the 300 mg dose, 67 to 71.6% of patients receiving the 150 mg dose and 4.5 to 4.9% of patients receiving placebo.[25]

Secukinumab has also been found to be effective for palmoplantar psoriasis. At week 16, 33.3% of patients taking 300 mg and 22.1% of those taking 150 mg achieved a palmoplantar Investigator's Global Assessment response of 0 or 1.[26]

Ixekizumab is a humanised IgG4 monoclonal antibody that binds to IL-17A and prevents it from interacting with its receptor. It is administered as a subcutaneous dose of 160 mg in week 0, followed by 80 mg every fortnight for the first 12 weeks and then 80 mg every four weeks. At week 12, 84.2% of those treated with ixekizumab achieved PASI 75 compared with 53.4% with etanercept and 7.4% in the placebo group. Ixekizumab is also more effective in achieving PASI 90 at week 12 than ustekinumab.[27]

Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits both IL-17A and IL-17F. It is administered subcutaneously via a prefilled pen at a dose of 360 mg (2×160 mg) at weeks 0, 4, 8, 12 and 16, and thereafter every eight weeks. Bimekizumab has been shown to be more effective for moderate-to-severe psoriasis than secukinumab (which selectively inhibits IL-17A alone). In a trial, 62% of participants in the bimekizumab group and 49% of participants in the secukinumab group achieved PASI 100 at week 16. At week 48, 67% of participants treated with bimekizumab had a PASI 100 response, compared with 46% of participants treated with secukinumab.[28] Similarly, bimekizumab has been shown to be more effective for moderate-to-severe psoriasis than placebo, adalimumab and ustekinumab. At week 16, 86.2% of participants in the bimekizumab group achieved PASI 90, compared with 47.2% of participants with adalimumab.[29] At week 16, 85% of those treated with bimekizumab achieved PASI 90 compared with 50% of those treated with ustekinumab.[30]

Il-17 inhibitors are associated with mucocutaneous candidiasis and are not effective for treating inflammatory bowel disease. Most cases of candidiasis affect the oral cavity, are mild in nature and can be treated with topical clotrimazole, miconazole, amphotericin lozenges or nystatin for seven to 14 days. More moderate to severe infections may require oral fluconazole for seven to 14 days or even cessation of treatment. It may be prudent to avoid IL-17 inhibitors in patients with a personal history of inflammatory bowel disease.

Interleukin-23 inhibitors

IL-23 inhibitors, including risankizumab, guselkumab and tildrakizumab, specifically target and inhibit the p19 subunit of IL-23 and are more effective than placebo.

Risankizumab is a humanised IgG1 monoclonal anti-IL-23, administered as 150 mg subcutaneously at weeks 0 and 4, and then every 12 weeks, the effects of which are superior to those of placebo at week 16.[31] Risankizumab was also shown to be more effective than adalimumab at weeks 16 and 44, ustekinumab at weeks 16 and 52 and secukinumab at week 52.[32] At week 16, 73% of participants achieved PASI 90 compared with 2% receiving placebo.[33] At week 16, 55.9% of those treated with risankizumab achieved PASI 90 compared with 5.1% receiving apremilast.[34]

Risankizumab has demonstrated durability and safety. An ongoing phase III open-label extension study designed to evaluate the long-term safety and efficacy of risankizumab has shown that more than 75% of patients achieved PASI 90 and more than 40% achieved PASI 100 after 16 weeks of risankizumab treatment.[35] After 52 weeks, more than 86% of patients achieved PASI 90 and more than 58% of patients achieved PASI 100. Data up to 172 weeks showed that 85.5% of patients achieved PASI 90 and 54.4% achieved PASI 100 with risankizumab treatment. The most common adverse effects include nasopharyngitis (31%) and upper respiratory tract infections (20%).[33]

Tildrakizumab is an IL-23 inhibitor administered as 100 mg subcutaneously at weeks 0 and 4, and then every 12 weeks. Clinical studies have shown that at week 12, 64% of participants treated with 100 mg achieved PASI 75 compared with 6% receiving placebo.[36]

Guselkumab is an IL-23 inhibitor administered as 100 mg subcutaneously at weeks 0 and 4, and then every eight weeks. A trial has shown that 86.3 to 91.2% of participants treated with guselkumab achieved PASI 75 at week 16 compared with 68.5 to 73.1% with adalimumab and 5.3 to 8.1% with placebo.[1]

Common side effects of IL-23 inhibitors include nasopharyngitis, upper respiratory tract infection, headaches and fatigue.

Future directions

The cost of biologics can burden the healthcare system and economy. When drugs lose their patent protection, the introduction of biosimilars can reduce drug costs and improve accessibility while providing similar efficacy rates to those of the originators.[37] A biosimilar is a biological product with an active product that is derived from a biological source. It is structurally similar and should have the same efficacy as the originator biological medication. Due to the complexity of biological molecules, biosimilars are not identical to the originator biologic but undergo testing to ensure the safety, efficacy and immunogenicity are similar.

Janus kinase inhibitors are small-molecule inhibitors that affect intracellular signalling and may have potential beneficial effects in psoriasis. Trials of topical and oral Janus kinase inhibitor agents are ongoing.

Conclusion

In summary, there are a range of non-biologic and biologic systemic treatments available for patients with moderate-to-severe psoriasis in Australia. GPs play an important role in identifying patients who would benefit from systemic treatments from a dermatologist, as well as in managing any disease complications and comorbidities. MT

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A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

COMPETING INTERESTS: Dr Daniel: None. Dr Nguyen has received support from Sanofi and AbbVie for attending investigator meetings. Associate Professor Shumack has received speaker payment from BMS. Associate Professor Foley has received research grants to the institution from AbbVie, Amgen, BMS, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, Sun Pharma and UCB Pharma; is or has been a consultant for Apogee, Aslan Pharmaceuticals, Eli Lilly, Galderma, Janssen, LEO Pharma, Pfizer; has received payment or honoraria for lectures, presentations, speakers' bureaus and educational events from AbbVie, Amgen, Boehringer-Ingelheim, BMS, Eli Lilly, Janssen, Novartis, LEO Pharma, Pfizer, Sanofi, Sun Pharma and UCB; has received personal payments from Pfizer; has received support to attend meetings from Eli Lilly, Sun Pharma and Boehringer-Ingelheim; is or has been a (paid) Advisory Board member for AbbVie, Amgen, Boehringer-Ingelheim, BMS, Eli Lilly, Galderma, GSK, Janssen, Novartis, LEO Pharma, Mayne Pharma, Pfizer, Sanofi, Sun Pharma and UCB; and has received drug samples for patients and medical writing services from AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Sanofi, Sun Pharma and UCB.

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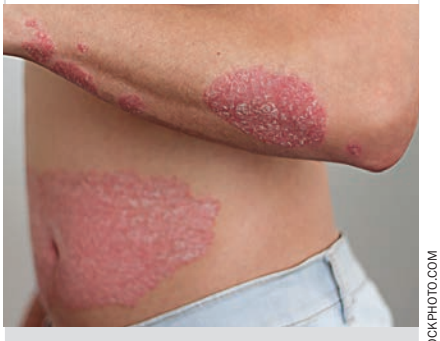
What percentage of the body surface area is affected in moderate psoriasis?



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MedicineToday Dermatology Collection 2025; 9(1): 17-24
First published 2024; 25(9): 29-35

Psoriasis

Systemic treatment options for adults

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Atopic dermatitis
New and emerging treatments

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Atopic dermatitis is a chronic relapsing and remitting disease. Patients typically receive treatment with counselling, trigger avoidance, emollients, wet dressings and topical corticosteroids. Conventional systemic agents may be required for severe disease but are often associated with significant adverse events. Recently, the treatment landscape for these patients has changed dramatically with the PBS listing of two targeted systemic treatments: dupilumab and upadacitinib. Other emerging treatments are on the horizon, offering promising options for those with severe recalcitrant disease.

KEY POINTS

- Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder worldwide, resulting from skin barrier disruption and a genetic predisposition.
- The mainstay of treatment for mild-to-moderate AD includes topical corticosteroids, topical calcineurin inhibitors and trigger avoidance.
- Conventional treatment of moderate-to-severe AD includes phototherapy and systemic immunosuppression.
- Novel systemic treatments that are PBS listed for moderate-to-severe AD include dupilumab (a human monoclonal antibody that blocks interleukin-4 and interleukin-13 signalling) and upadacitinib (a Janus kinase-1 selective small molecule inhibitor).
- Emerging targeted treatments offer promising options for patients with AD who have severe recalcitrant disease.

Atopic dermatitis (AD), also known as eczema, is the most common inflammatory skin condition worldwide, affecting about one in 10 individuals. It is a chronic relapsing and remitting condition seen in all age groups, although it tends to begin in infancy within the first year of life.[1] About 30% of infants and 10% of adults experience AD.[1-3] AD is often clustered with other allergic hypersensitivity diseases (allergic rhinitis and asthma, often known as the atopic triad), which all have similar mechanisms of pathogenesis.[4] Several longitudinal studies also provide evidence to support the atopic march – that is, the progressive development of AD, food allergy, allergic rhinitis and asthma throughout childhood.[5-7]

MedicineToday Dermatology Collection 2025; 9(1): 27-33
First published 2025; 26(3): 49-55 Updated June 2025

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Untreated symptomatic AD can have a negative impact on patients' quality of life. The unrelenting itch-scratch cycle leads to sleep disturbance and chronic fatigue. Continuous itch affects concentration and school performance in children. The mental health comorbidities of AD (e.g. attention deficit hyperactivity disorder, anxiety, depression, low self-esteem, conduct disorder and autism) are well established.[8-10] Importantly, school performance is compromised by chronic fatigue, behavioural issues and absenteeism, which severely impacts future life courses. Assertive proactive management of AD is paramount.

The past decade has seen an increase in advanced therapeutic options becoming available for AD in Australia through clinical trials and more recently listed on the PBS. This article provides an overview of treatment option pathways, which includes new topical and systemic agents and those on the near horizon. Many of these emerging therapies have surpassed phase 3 clinical trials and are already in use for patients overseas with chronic severe AD (Figure 1).[11-16]

Pathogenesis

The pathogenesis of AD is complex and multifactorial. AD is a result of both genetic and environmental factors and immune system dysregulation.[17,18] Evidence to date suggests that AD is

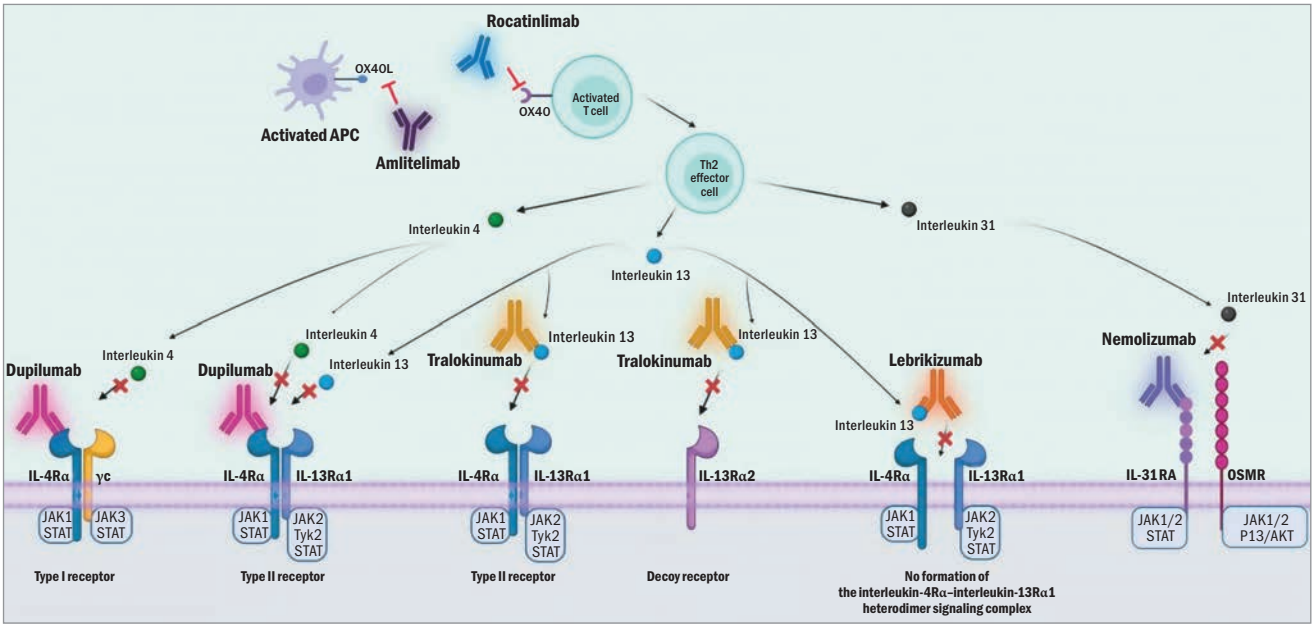

Figure 1. Mechanisms of action of biologic drugs for atopic dermatitis: dupilumab, tralokinumab, lebrikizumab, nemolizumab, rocatinlimab and amlitelumab.

Abbreviations: APC = antigen-presenting cell; IL-31RA = IL-31 receptor A; IL-4Rα = IL-4 receptor alpha chain; IL-13Rα1 = IL-13 receptor alpha 1 chain; IL-13Rα2 = IL-13 receptor alpha 2 chain; JAK = Janus kinase; OSMR = oncostatin M receptor; PI3/AKT = phosphoinositide 3-kinase/protein kinase B; STAT = signal transducer and activator of transcription; Th2 = T helper 2; Tyk2 = tyrosine kinase 2; γc = γc chain.

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driven by an overactive T helper 2 (Th2) response. This Th2 dominance leads to the production of various cytokines, such as interleukin (IL)-4, IL-5, IL-13 and IL-31, which contribute to a dysregulated inflammatory response, contributing to skin barrier disruption.[17] In response to the compromised skin barrier, keratinocytes produce cytokines such as thymic stromal lymphopoietin, IL-25 and IL-33, which further augments the Th2 response. These inflammatory cytokines also orchestrate the itch sensation by activating cutaneous sensory nerve fibres.[1,17]

Together, this heightened inflammatory cycle reduces the expression of filaggrin that maintains skin barrier integrity. There is a well-established association between filaggrin mutations and AD, although this is not a causal link, as many patients with filaggrin mutations do not develop AD.[17,18] Reduced levels of expression of other components of the epidermis, such as loricrin, involucrin and ceramides, also contribute to the skin barrier deficits that are a hallmark feature of AD.[17,19]

The impaired skin barrier in AD allows for increased transepidermal water loss, enabling allergens to enter more easily, triggering immunoglobulin E sensitisation.[19,20] Triggers for AD can include common allergens such as food, dust mites, environmental allergens (e.g. pollen, grass and mould), irritants (e.g. chlorine, sex hormones, latex) and even changes in weather can trigger an eczema flare.[20,21] A disrupted skin barrier also provides a portal for pathogen entry. Secondary skin infections with *Staphylococcus aureus* and herpes simplex virus further disrupt the skin barrier and further exacerbate AD.[20,21]

Clinical presentation

AD is generally a clinical diagnosis; however, the clinical presentation of AD varies tremendously. Infants can present with AD on the face and there can be extensor involvement such as on the trunk or back.[22,23] However, in adolescents and adults, AD typically presents over flexural areas such as the antecubital and popliteal fossae. Flare-ups of AD can present as intensely pruritic, erythematous, weeping oedematous lesions sometimes associated with crusting. Erosions and excoriations are common, and lichenification or thickening of the skin is a sign of disease chronicity.[19,22,23]

Disease severity scales most relevant to healthcare practitioners in Australia are the Eczema Area and Severity Index (EASI) and Physician Global Assessment (PGA). A minimum rating on these two scales (a baseline EASI of at least 20 and PGA of 4) is required for a PBS subsidy if considering a patient for treatment with an advanced targeted therapy. Other scales have been validated and used in research settings including the Scoring Atopic Dermatitis (SCORAD) index and the Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score that aims to objectively describe the clinical features of AD. To measure the impact of AD on sleep, mood and quality of life, the Patient-Oriented Eczema Measure and Dermatology Quality of Life Index (DLQI) severity scale have been developed.[19] For prescribing new

targeted therapies in Australia, the DLQI score is required at baseline and is then repeated with each continuous prescription application.

Treatment

Physical therapies and antibiotics

AD is a relapsing disease. General management recommendations for patients with AD include avoiding irritants such as perfumed products and avoiding exposure to triggers (Box 1).[1,24] Moisturising at least twice daily is recommended to maintain the integrity of the skin barrier.[19,25] Daily bathing or luke warm showers are recommended to reduce bacterial skin load and are limited to a five-minute duration to avoid skin flares.[1,19,24,25] Wet dressings may reduce skin irritation and protect the skin from further trauma but can be cumbersome and time consuming to apply and cause irritation if left overnight.[1,25-27] Bleach baths may be recommended to avoid secondary skin infections.[1,23,25,26,28] Other physical therapies, such as controlled exposure to narrowband ultraviolet light therapy, are also considered for AD because of their immunosuppressive effects and ability to enhance the epidermal barrier.[24]

AD-affected skin can be colonised by *S. aureus*; therefore, a positive culture from a swab alone cannot differentiate between colonisation and active infection. The decision to treat with systemic antibiotics depends on the clinical relevance, ideally with antimicrobial sensitivities confirmed through culture.[1,29] Skin swabs (viral and bacterial) are recommended in circumstances where a secondary skin infection is suspected, to confirm the diagnosis and guide treatment choice.

Topical corticosteroids

The mainstay of treatment for AD is the use of topical corticosteroids to reduce inflammation (Box 2).[2] The recommended potency of topical corticosteroids depends on the severity and location of the AD. A mild-potency topical corticosteroid is recommended for the face and flexures (e.g. axilla, inframammary, inguinal, cubital or popliteal fossa, genitals) and high potency for thickened, lichenified areas and the palms and soles.[1] The potency of corticosteroids is well documented.[30] Topical corticosteroids can be applied directly onto skin, or in conjunction with emollients, which are generally applied over topical corticosteroids on inflamed skin.

Clobetasol 0.05% ointment and cream, the most ultrapotent topical corticosteroid, is now PBS listed from 1 May 2025, available in a 30g tube.

Long-term inappropriate use of corticosteroids can lead to skin atrophy, striae, rosacea, telangiectasias and purpura.[30] A standard unit used for topical corticosteroid application is the fingertip unit (FTU), which covers the area of two adult hands (i.e. 1 FTU = 0.5 g = 2 palms = 2% of an adult's body surface area).[31,32] The recommended FTUs for adequate effectiveness is well documented.[31,32] However, there is a plethora of misinformation about the safety of topical corticosteroids in the media leading to a suboptimal treatment response.[33] Reassurance and regular clinical reviews can help overcome treatment barriers.

It is important to select an appropriate base for the topical therapy. Creams are reserved for hair-bearing areas or patient comfort, whereas ointments will increase the topical steroid potency and minimise stinging (thus prescribed for severe flares with major excoriations).

Alternative topical therapies to corticosteroids

Alternative topical therapies to corticosteroids for AD available in Australia are calcineurin inhibitors and crisaborole.

Topical calcineurin inhibitors include tacrolimus ointment (0.03% and 0.1% strengths) and pimecrolimus cream (1% strength). These topical calcineurin inhibitors are naturally produced by *Streptomyces* bacteria and inhibit T-cell activation, reducing the inflammatory response in AD.[34] Topical pimecrolimus 1% is PBS listed for the treatment of AD and is safe to use in sensitive areas such as the eyelids and face in children over the age of 3 months.[35] To date, access to topical tacrolimus requires compounding in Australia but the 0.1% tacrolimus ointment is TGA approved for the treatment of moderate-to-severe AD, and is due for release soon.

Crisaborole 2% is a nonsteroidal topical ointment that inhibits the activity of phosphodiesterase-4 (PDE-4), the levels of which are elevated in patients with AD. The reported barriers are cost and tolerability.[36] It is approved by the TGA for the treatment of mild-to-moderate AD in patients 2 years of age and older; however, it is not currently

1. PHYSICAL THERAPIES FOR ATOPIC DERMATITIS

Trigger avoidance
- Avoiding hot showers and the use of cosmetics, fragrances and detergents

Cool compresses
- Short-term use for flares
- Generally two to three times per day for one week
- Left on for five to 10 minutes

Wet dressings
- Short-term use for flares
- Generally two to three times per day for one week
- Left on for one to two hours; remove when dry
- Wet dressings can be used over topical corticosteroid treatments to enhance absorption

Bleach baths
- 12 mL household bleach (4% sodium hypochlorite) per 10 L of water
- Five-minute soak daily during active flare (usually daily for one month, then three times a week for one month, then once a week for one month)
- Bath oil may be added
- Bath temperature: 28 to 30°C

Narrowband ultraviolet B (phototherapy)
- Controlled exposure to a narrow peak of ultraviolet light (311 nm), three times weekly, reassessed every six to 12 weeks
- Used in conjunction with topical or systemic treatments
- Accessed via referral to specialist dermatologist or major public health service

2. TOPICAL, ORAL AND SUBCUTANEOUS TREATMENTS FOR ATOPIC DERMATITIS

Topical*

Topical corticosteroids

***Mild*†**
- Hydrocortisone 0.5–1%
- Desonide 0.05%

Moderate
- Methylprednisolone aceponate 0.1%
- Triamcinolone acetonide 0.02%
- Betamethasone valerate cream 0.02%, 0.05%
- Clobetasone butyrate 0.05%

Potent
- Betamethasone dipropionate 0.05%
- Betamethasone valerate ointment 0.1%
- Mometasone furoate 0.1%

Ultrapotent
- Betamethasone dipropionate 0.05% in optimised vehicle
- Clobetasol propionate 0.05% (PBS listed from 1st May 2025)

Nonsteroidal topical treatments†
- Calcineurin inhibitors
  - Pimecrolimus 1% (PBS listed for AD)
  - Tacrolimus 0.1%, 0.03% (compounded); both considered safe in children from 3 months of age[35]
- PDE-4 inhibitor
  - Crisaborole 2% (TGA approved for mild-to-moderate AD in patients 2 years of age and older, but is not currently PBS listed)

Emerging therapies (not currently TGA approved)
- Delgocitinib 2% (pan JAK inhibitor)
- Tapinarof 1% (aryl hydrocarbon receptor agonist)

Emollients plus
- Emollients containing ceramides
- Emollients containing other nonprescription beneficial ingredients

Oral

Oral corticosteroid avoidance
- Prednisolone is rarely used and reserved only for emergency settings under very close supervision

Corticosteroid-sparing agents
- Ciclosporin‡
- Methotrexate
- Azathioprine
- Mycophenolate mofetil

JAK inhibitors
- Upadacitinib (selective JAK-1 inhibitor)
  - 15 mg to 30 mg once daily
  - PBS listed for patients over 12 years of age for chronic severe AD
- Abrocitinib (selective oral JAK-1 inhibitor)
  - 100 to 200 mg once daily
  - TGA approved for moderate-to-severe AD but not PBS listed

Subcutaneous

Novel targeted treatments
- Dupilumab (IL-4Rα monoclonal antibody that blocks IL-4/IL-13 signalling)
  - loading dose: 600 mg (week 0)
  - maintenance: 300 mg every 2 weeks
  - PBS listed for patients aged 12 years and older with chronic severe AD

Emerging treatment (TGA approved)
- Lebrikizumab (IL-13 monoclonal antibody)
  - loading dose: 500 mg (at weeks 0 and 2)
  - induction: 250 mg every 2 weeks (until week 16)
  - maintenance dose: 250 mg every 4 weeks
  - TGA approved for patients 12 years of age and older with moderate-to-severe AD but not currently PBS listed

Emerging treatments (not currently TGA approved)
- Tralokinumab (IL-13 monoclonal antibody)
- Nemolizimab (IL-31Rα antagonist)
- Rocatinlimab (OX40 monoclobal antibody)
- Amlitelimab (OX40 ligand monoclonal antibody)

Abbreviations: AD = atopic dermatitis; JAK = Janus kinase; PDE-4 = phosphodiesterase-4.

* Treatment times depend on the severity of disease. AD should be treated until inflammation is settled with supervision.
† Preferred for sensitive areas such as the face, axilla and groin.
‡ Ciclosporin is the only conventional systemic agent that is TGA approved and PBS listed for AD.

PBS listed (available for purchase in 60 g at a nonsubsidised private price).

Oral corticosteroids and conventional systemic agents

Oral corticosteroids are rarely required for management of severe AD. Patients with a severe flare can be managed with wet dressings and must be prescribed sufficient quantities of topical therapies. Moreover, these patients require a prompt review for initiation of a systemic therapy. Corticosteroid-sparing agents, such as methotrexate and ciclosporin, may be considered; however, with the increasing availability of targeted treatments, these systemic treatments are no longer the mainstay of treatment for severe AD because of their potential for severe life-threatening side effects (e.g. myelosuppression and hepatotoxicity with methotrexate; and hypertension and renal failure with ciclosporin).[37]

Novel targeted therapies approved and PBS subsidised for use in Australia

Patients with severe refractory cases of AD may be referred to a dermatologist to access novel systemic treatments. Practical considerations when referring patients to dermatologists for more advanced therapies are outlined in Box 3.

Dupilumab

Dupilumab is a human monoclonal antibody that binds IL-4Rα and inhibits signalling mediated by IL-4 and IL-13, key drivers of the inflammatory response of a variety of Th2-mediated diseases, including AD, asthma, rhinosinusitis, nasal polyposis and eosinophilic oesophagitis.[38] It is administered fortnightly as a subcutaneous injection (300 mg, after a loading dose of 600 mg). It is generally well tolerated. Commonly reported side effects include

conjunctivitis, injection-site reactions, nasopharyngitis, headache and oral herpes simplex virus reactivation.[39] Rarer adverse effects that have been reported include seronegative arthritis and enthesitis, de novo psoriasis, paradoxical head and neck dermatitis and worsening of alopecia areata.[40-42] Recent literature has raised the possibility of an increased risk of cutaneous T cell lymphoma, although further research is needed as reported data appear to be inconclusive.[43,44]

Dupilumab has been listed on the PBS since March 2021 for the treatment of chronic severe AD in patients aged 12 years and older who have failed to respond to optimally prescribed topical treatments. It is approved internationally for use in infants as young as 6 months of age, and real-world data already exist for children.[44] Skin areas before and after treatment with dupilumab are shown in Figures 2 to 5.

Upadacitinib

Upadacitinib is an oral small molecule that selectively inhibits the signalling of Janus kinase (JAK)-1, which is a key intracellular mediator of Th2 cytokine signalling integral to AD pathogenesis. Upadacitinib has been PBS listed since March 2022 for patients over 12 years of age with chronic severe AD and has been successfully used to control inflammation in a range of inflammatory conditions including rheumatoid arthritis, psoriatic arthritis and inflammatory bowel disease.[46] A head-to-head study comparing the efficacy of upadacitinib with dupilumab in adults with moderate-to-severe AD showed that upadacitinib was slightly superior to dupilumab. At week 16, 61.6% of patients treated with 30 mg upadacitinib achieved 90% improvement in the EASI (EASI90) versus 40.3% with 300 mg dupilumab.[47] Upadacitinib was more rapid at improving itch symptoms compared with dupilumab.[46]

Upadacitinib is a well-tolerated, convenient, once-daily oral treatment, but requires close monitoring because of its immunosuppressive effect. Side effects include acne, upper respiratory tract infections, headache, gastrointestinal disorders, urinary tract infections and opportunistic infections such as herpes zoster reactivation.[48] Haematological abnormalities such as anaemia, thrombocytosis, elevated transaminases and creatine kinase levels and changes in lipid profile have been noted in some patients following the initiation of treatment and require monitoring.

Major serious adverse effects have been described with general JAK inhibition and include cardiovascular events such as venous thromboembolism, stroke and increased risk of malignancy. The TGA has therefore recommended that JAK inhibitors should not be prescribed in patients who are aged over 65 years with a history of cardiovascular disease or at risk of cancer unless there are no alternative treatments. These recommendations are presented as a black box warning in the US , which were triggered by reported outcomes with tofacitinib (a small molecule with nonspecific JAK inhibition [JAK-1, JAK-2, JAK-3 and tyrosine kinase 2] prescribed in rheumatological patients).[49] Shingrix and pneumococcal vaccination should be administered to all patients considering treatment with JAK inhibitors.

Emerging topical therapies

Delgocitinib

Delgocitinib is a topical pan-JAK inhibitor for moderate-to-severe hand dermatitis.[50] Internationally, it is a 2% formulation, applied twice daily. To date, in Australia, compounding of this agent is unavailable. The medication is expecting TGA approval in late 2025. Pooled analysis of the DELTA 1 and 2 trials (phase 3) showed that 20% and 29% of patients treated with delgocitinib , respectively, achieved treatment success with improved hand eczema severity scores and DLQI scores after 16 weeks compared with 10% and 7% of patients who received the cream vehicle (placebo arm), respectively.[51]

Tapinarof

Tapinarof 1% is a novel nonsteroidal topical aryl hydrocarbon receptor (AhR) agonist applied once daily, which was originally approved by the US Food and Drug Administration for psoriasis. AhR is a cytoplasmic receptor that is ubiquitously expressed, and holds key roles in gene expression, cellular homeostasis and immune responses.[52] Its anti-inflammatory effect is mediated by the downregulation of Th2 cytokines, reducing oxidative stress and improving the skin barrier. The phase 3 ADORING trials demonstrated favourable

3. CONSIDERATIONS FOR REFERRAL TO A DERMATOLOGIST

Patient factors
- Compliance issues or concerns with topical therapies
- Psychosocial impact (missed school or work, impact on relationships)

Disease factors
- Impact on sleep and high itch scores (>4 on Visual Analogue Scale)
- Severe regional presentation (face, hand, feet), refractory to 4 weeks of daily topical corticosteroids or topical calcineurin inhibitors
- Severe generalised presenation, refractory to 4 weeks of daily topical corticosteroids or topical calcineurin inhibitors
- Diagnostic challenges (mimickers e.g. scabies, tinea, psoriasis, contact allergy)

Complications
- Eczema herpeticum (secondary herpes simplex infection)
- Impetiginised eczema (secondary staphylococcal infection)
- Erythroderma, dyspigmentation, lichenification

Key PBS criteria* for targeted therapies (dupilumab and upadacitinib)
- Physician Global Assessment baseline score of at least 4
- Eczema Area and Severity Index baseline score of at least 20
- DLQI baseline score of any value† but a score of 6 or more indicates the disease is having a moderate effect on the patient's life
- Chronic severe AD lesions present for at least 6 months (affecting either the whole body or the face and hands)

Abbreviation: DLQI = Dermatology Life Quality Index.

* These PBS criteria serve only as a guide, as many patients with refractory disease who do not meet all the criteria will still benefit from a specialist assessment. Variations of this scoring system are used overseas for the prescription of advanced targeted therapies.

† For continuing prescription in Australia, patients need to demonstrate an improvement in DLQI score of at least 4 points compared with baseline (thus logically the minimum baseline DLQI must be ≥4).

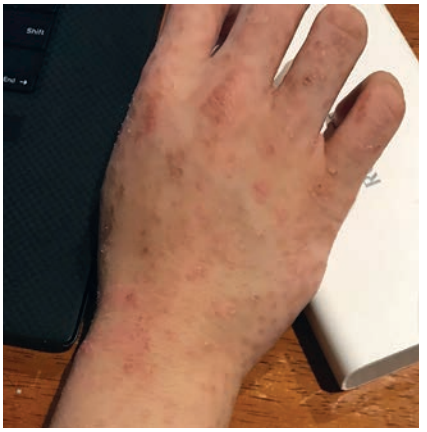

Figure 2a. Right hand of patient A before dupilumab treatment.
Image published with patient consent.

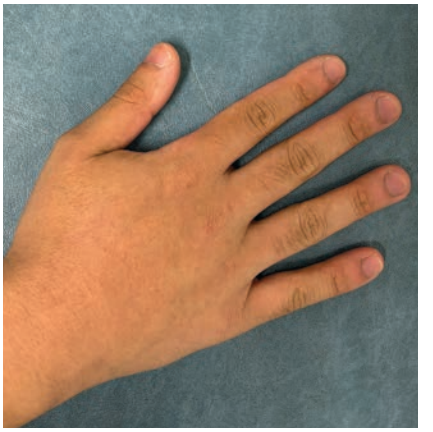

Figure 2b. Right hand of patient A after dupilumab treatment.
Image published with patient consent.

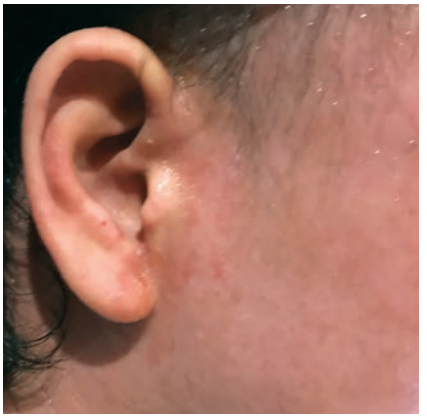

Figure 3a. Right lateral face of patient A before dupilumab treatment.
Image published with patient consent.

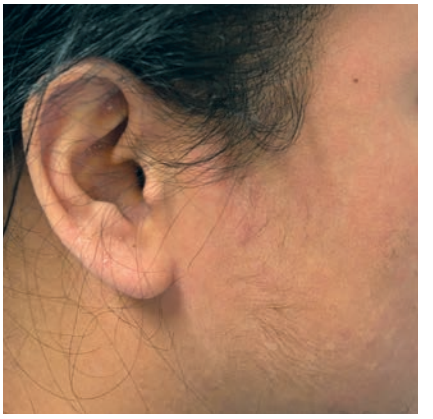

Figure 3b. Right lateral face of patient A after dupilumab treatment.
Image published with patient consent.

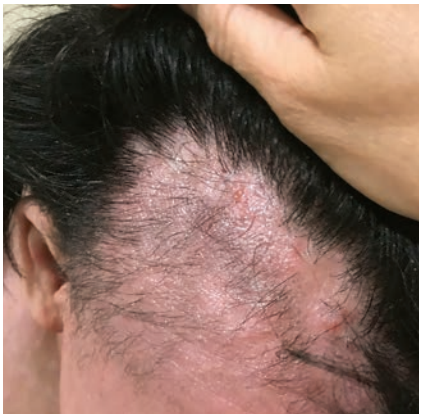

Figure 4a. Right frontal scalp of patient A before dupilumab treatment.
Image published with patient consent.

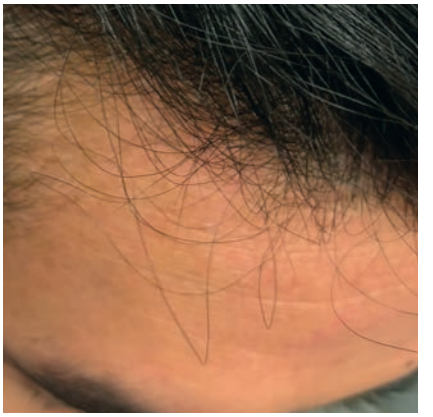

Figure 4b. Right frontal scalp of patient A after dupilumab treatment.
Image published with patient consent.

tolerability, safety and efficacy with the use of tapinarof in patients with AD from the age of 2 years. After eight weeks of therapy, an improvement of 75% in EASI (EASI75) was achieved in 56% of patients versus 23% for vehicle.[15,53] Common adverse events, although minimal, include folliculitis, headache and nasopharyngitis.

Emerging oral and subcutaneous therapies

Abrocitinib

Abrocitinib is a selective oral JAK 1 inhibitor used for the treatment of moderate-to-severe AD. It is TGA approved for moderate-to-severe AD and recently was recommended for a PBS listing (November 2024) for adult patients with chronic severe AD. In a phase 3, double-blind, clinical trial, abrocitinib at a dose of either 200 mg or 100 mg once daily resulted in a significantly improved EASI75 response for moderate-to-severe AD than placebo at weeks 12 and 16, comparable with dupilumab at the study end point.[54] However, the 200 mg dose of abrocitinib was superior to dupilumab with respect to itch response at week 2.[54] The most commonly reported side effects associated with this treatment included nausea, acne and herpes zoster infection.[54]

Lebrikizumab

Lebrikizumab is a selective anti IL-13 human monoclonal antibody that is effective for AD particularly because of its slow dissociation rate.[55] Lebrikizumab prevents the formation of the IL-13Rα/IL4Rα complex, thus blocking IL-13 signalling (via binding to only the IL-13 α1 chain), which is thought be the key driver of inflammation in AD. Two phase 3 clinical trials have shown that in adults and adolescents with moderate-to-severe AD, treatment with lebrikizumab monotherapy every two weeks improved skin clearance compared with placebo over a 16-week induction period.[56] An EASI75 response was seen in 58.8% of patients receiving lebrikizumab compared with 16.2% for placebo.[57] Most side effects were mild in severity, with conjunctivitis and

herpes zoster infections most commonly reported.[56,57] Lebrikizumab is TGA approved for the treatment of moderate-to-severe AD in patients 12 years of age and older, but the drug is currently not listed on the PBS (it received a recommendation for a PBS listing in March 2024).

Tralokinumab

Tralokinumab is also a selective anti IL-13 human monoclonal antibody, which is different to lebrikizumab in that it blocks the binding of IL-13 to both receptor chains. Phase 2 studies have shown that tralokinumab was superior to placebo at 16 weeks of treatment and was well tolerated, with most responders not requiring any rescue medication such as topical corticosteroids for the duration of the study.[58] Selective IL-13 agents appear to be better tolerated compared with IL-4/-13 inhibitors owing to fewer ocular adverse effects and fewer injection-site reactions.

Nemolizumab

Nemolizumab is an IL-31Rα antagonist that prevents binding of IL-31 to its receptor. IL-31 has been implicated in the pathophysiology of multiple Th2-mediated atopic disorders. Notably, IL-31 has been identified as one of the main drivers of pruritus that characterises AD, exacerbating skin barrier disruption.[59] Two replicate phase 3, double-blind, randomised clinical trials (ARCADIA 1 and ARCADIA 2) have demonstrated that nemolizumab 30 mg improved eczema assessment scores, itch and sleep at 16 weeks in adolescent and adult patients with moderate-to-severe AD.[60] Generally, the treatment was well tolerated with minimal adverse effects, although those commonly reported were nasopharyngitis and upper respiratory tract infections.[60] Moreover, there was no increased rates of conjunctivitis, herpes zoster infections or de novo cases of asthma reported.

Rocatinlimab and amlitelimab

The expression of OX40-positive T cells is increased in patients with AD compared with healthy controls. OX40 is present on sensitised T cells after antigen-specific activation, leading to the expression of OX40 on the surface of effector and memory cells, thereby promoting T cell survival and memory.[61] It is not expressed in naïve T cells. Moreover, OX40 expression is increased in pathogenic T cells. In skin biopsies of AD lesions, OX40 and OX40 ligand-positive cells were co-localised in the dermis, lending strong support for their role in AD pathogenesis.[61,62] The OX40 and OX40 ligand interaction has been reported to enhance cell mobility, promote an effector T cell phenotype, increase cytokine production and conversely, suppress the action of T regulatory cells.[63,64]

Rocatinlimab is an anti-OX40 monoclonal antibody that binds to OX40 present on an activated CD4-positive, CD8-positive T cell.[63] It reduces the number and inhibits the expression of OX40-expressing pathogenic T cells. A phase 2 clinical trial has shown that rocatinlimab treatment improved EASI scores by 60% compared with placebo (15%) over the duration of the study period. The most efficacious response was noted in the group that received 300 mg, fortnightly.[65] The most common adverse effects were pyrexia, chills, headache, aphthous ulcers and nausea.[65]

Amlitelimab is a OX40 ligand monoclonal antibody that binds to the OX40 ligand on antigen-presenting cells. In a phase 2a multicentre study, amlitelimab showed improvements in EASI scores of 80%, compared with 50% in the placebo arm.[66] Adverse effects noted with this treatment included headache, hyperhidrosis, pyrexia, iron-deficiency anaemia and elevated aspartate aminotransferase levels.[66]

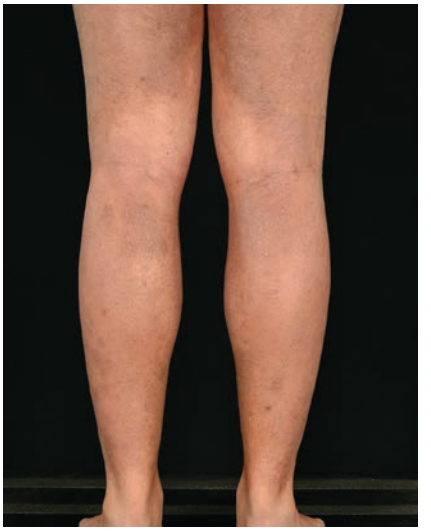

Figure 5a. Posterior legs of patient B, skin type 3, before dupilumab treatment.

Figure 5b. Posterior legs of patient B, skin type 3, after dupilumab treatment.

Conclusion

AD is a complex, multifactorial disease with a relapsing and remitting course. An improved understanding of the pathogenesis of AD has contributed to an array of novel therapeutics.[67] In the era of precision medicine, specific targeted treatments for AD offer promise to patients who have not responded to conventional management. Although some agents are not yet PBS listed in Australia, many are in fact already in use overseas for patients with chronic severe AD with 'real world' experience being compiled. This will certainly shed light on the safety and efficacy of these novel therapeutics over years to come. MT

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A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

COMPETING INTERESTS: None.

MedicineToday Dermatology Collection 2025; 9(1): 27-33
First published 2025; 26(3): 49-55

Atopic dermatitis
New and emerging treatments

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A teenage boy with patchy hair loss after a haircut

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Test your diagnostic skills in our regular dermatology quiz. What is the cause of this worsening hair loss, which occurred after a trip to a barbershop?

Case presentation

A 14-year-old boy presents with a 12-month history of hair loss on his scalp. The hair loss began after a haircut at a barber shop and has been gradually worsening, with the affected areas becoming mildly itchy.

The patient is otherwise well. He has no significant medical history and is not taking any regular medications. He lives with his family, who are all well and not showing any skin or hair changes.

On examination, patchy alopecia is observed on the patient's occipital and nuchal scalp (Figure 1a). The affected areas are mildly erythematous with overlying scale and speckled with black dots. Trichoscopy reveals fine perifollicular scale as well as comma, corkscrew and zigzag hairs (Figure 1b). The remainder of the examination is unremarkable.

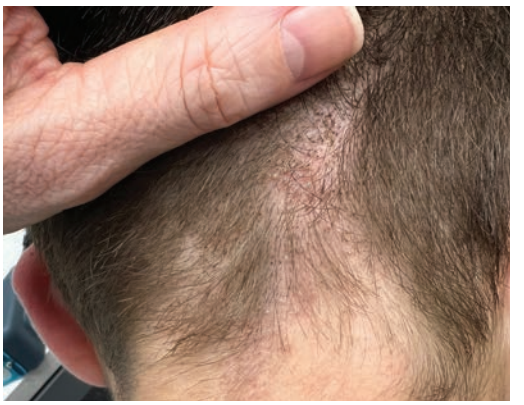

Figure 1a. The case patient at presentation, with patchy alopecia of the occipital and nuchal scalp.
Images published with patient consent.

Figure 1b. Trichoscopy of the affected area showing a fine perifollicular scale and corkscrew hairs.

Differential diagnoses

Conditions to consider among the differential diagnoses include the following.

Scalp psoriasis

Scalp psoriasis, which affects individuals of all age groups and both genders, is seen in about 80% of people with psoriasis.[1] A chronic inflammatory condition in genetically predisposed individuals, psoriasis is a T-cell immune-mediated disorder that leads to hyperproliferation of keratinocytes, resulting in thickened skin and scale. Environmental triggers, which include stress, smoking, alcohol, infections and certain medications, can exacerbate the condition.[2] It is particularly common in Caucasians and about one-third of patients have a family history of the condition.[3]

Scalp psoriasis typically presents as erythematous, scaly plaques on any part of the scalp, but it can extend to the hairline, forehead, nape of the neck, and area behind the ears.[4] The plaques may be covered with thick, silvery-white scale that can lead to noticeable flaking resembling dandruff. Patients may complain of pruritus or, in severe cases, localised alopecia.[5]

The diagnosis is primarily clinical. Scalp psoriasis can occur in isolation or with other manifestations of psoriasis – nail pits, onycholysis and oil spots, as well as hyperkeratosis over the extensors, can be useful clues. A scalp biopsy is usually not required but, if performed, a histological examination shows parakeratosis, acanthosis and inflammatory infiltrates.[6]

This was not the correct diagnosis for the case patient, who did not have erythematous plaques with silvery white scale on his scalp and no manifestations elsewhere to suggest psoriasis.

Discoid lupus erythematosus

Discoid lupus erythematosus (DLE), the most common subtype of cutaneous lupus erythematosus, is an autoimmune condition with both genetic and environmental aetiology. It can affect both males and females and occurs in people of any age

MedicineToday Dermatology Collection 2025; 9(1): 35-37
First published 2025; 26(3): 57-59

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but is most commonly seen in young to middle-aged women and patients with skin of colour and certain ethnicity (African, Asian and Hispanic descent). Risk factors include a history of smoking, certain medications, preceding viral infections, stress and a personal or family history of other autoimmune diseases.[7] Ultraviolet light exposure is an important trigger because DLE is a photosensitive disorder.[8]

DLE presents as well-defined erythematous patches or plaques commonly affecting sun-exposed areas. As the condition progresses, the lesions can develop atrophic scarring that presents as hyper- or hypopigmentation. Scalp involvement has been reported in around 60% of patients with DLE.[9] Scalp plaques have adherent, thick scale that may cause follicular hyperkeratosis and can lead to destruction of the hair follicles, resulting in scarring alopecia.[10] Patients may complain of pruritus or tenderness and notice that lesions tend to worsen with sun exposure.[8]

A scalp biopsy may be performed to confirm a diagnosis of DLE, showing epidermal atrophy, follicular plugging, basal cell degeneration and a lymphocytic infiltrate around hair follicles.[11] Direct immunofluorescence testing of lesional skin will frequently reveal immune complex deposition at the dermoepidermal junction.

Although DLE often remains localised to the skin, between 5 and 15% of patients develop systemic lupus erythematosus.[12] Serological testing for autoimmune diseases, such as the antinuclear antibody (ANA) and extractable nuclear antigen (ENA), is often performed to assess for systemic involvement but is frequently negative in patients who have isolated cutaneous DLE.[13]

This was not the correct diagnosis for the case patient. Trichoscopy revealed nonscarring alopecia and did not show any follicular plugging. In addition, he did not have any risk factors for an autoimmune aetiology.

Seborrhoeic dermatitis

Seborrhoeic dermatitis is a common inflammatory skin condition affecting people of all ages and ethnicities.[14] The aetiology is believed to be multifactorial, involving a complex interplay of genetic predisposition, immune response and hormonal factors. Colonisation of the skin by the commensal yeast *Malassezia* species is believed to be pivotal in the pathogenesis, stimulating inflammation that precipitates flares of seborrhoeic dermatitis.[15] Triggers include cold weather, stress, nutritional deficits (e.g. B-group vitamins, zinc, essential fatty acids and vitamin D), hormonal changes, immunosuppression and certain medications (e.g. immunosuppressants, antipsychotics, lithium and androgenic medications), as well as some neurological disorders, such as Parkinson's disease and epilepsy.[16,17]

Seborrhoeic dermatitis presents as poorly defined, erythematous, scaly patches with little or no pruritus.[18] On the scalp, there are often greasy, thin, yellowish scales that may adhere to hair shafts. There is no associated scarring or permanent hair loss. In adults, seborrhoeic dermatitis mainly affects areas that are rich in sebaceous glands, such as the face (especially the eyebrows, glabella, nasolabial folds and skin around the ears), scalp, axilla, chest, genitals (pubic area, perianal region, the labia majora in females and the scrotum in men) and the skin folds. In infants, the condition usually affects the scalp (cradle cap), axilla and groin folds.

The diagnosis of seborrhoeic dermatitis is primarily based on the clinical characteristics. Trichoscopy reveals thin, yellowish scales and diffuse erythema.[19] If the diagnosis is unclear, a scalp biopsy may be performed and will typically reveal parakeratosis, spongiosis and mild perivascular infiltrates; however, this is seldom required.[20]

Seborrhoeic dermatitis is not the correct diagnosis for the case patient. The typical yellowish scaling was not present and would not explain the corkscrew hairs.

Tinea capitis

This is the correct diagnosis. Tinea capitis is an infection of the scalp and hair caused by dermatophytic fungi, primarily from the *Trichophyton* and *Microsporum* genera. In Australia, the most common causative species are *Microsporum canis* (zoophilic) and *Trichophyton tonsurans* (anthropophilic).[21] Tinea capitis is contagious and can be spread by direct contact with an infected person or via contaminated objects, such as hairbrushes, hats, pillows, towels and furniture, where the fungal spores may remain viable for months.[22] In addition, zoophilic fungi can be transmitted from infected animals, including pets: *M. canis* can be acquired through contact with an infected cat or kitten and *Trichophyton mentagrophytes* is commonly associated with guinea pigs.

Although tinea capitis affects people of all ages, it is primarily seen in young children. Risk factors include crowded living conditions, communities where people are in close contact (e.g. schools), poor hygiene, warm humid environments and animal contact.[23] Tinea capitis can be linked to barbershops, especially if proper hygiene practices are not maintained.

The clinical features of tinea capitis depend on the causative species and host inflammatory response. The most common presentation is a fine scaly patch on the scalp with associated alopecia. The area may be erythematous (which may be minimal or pronounced) or grey in colour. Itch and tenderness are variable and depend on the level of inflammation. Other presentations include kerion (a painful, erythematous and boggy plaque with associated alopecia and pustules) and favus (yellow, crusted areas associated with matted hair).

Trichoscopy is a useful tool in the diagnosis of tinea capitis.[24,25] Common findings include the following:

- comma-shaped hairs, which are curved and broken
- black dots (hairs that are broken at the level of the scalp)
- corkscrew hairs (spiral-shaped),

which are commonly seen in cases caused by *Trichophyton* species
- zigzag hairs, with several bends
- morse code-like hairs (irregularly broken hair shafts that resemble dashes and dots)
- scaling, which may be diffuse, fine, yellowish, grey or white (perifollicular and/or coating affected hairs)
- perifollicular erythema.

A diagnosis of tinea capitis is based on findings from the clinical examination and confirmed by laboratory investigations. A Wood's lamp examination can be helpful, as certain *Microsporum* species fluoresce bright green under ultraviolet light.[26] However, not all causative fungi (including most *Trichophyton* species) fluoresce, so a negative Wood's lamp test does not rule out a diagnosis of tinea capitis.

Microscopy and culture are recommended.[24] Scrapings of scalp and scale scrapings and plucked hairs are easy to collect for testing. A diagnosis of tinea capitis is confirmed by visualisation of hyphae and spores in a potassium hydroxide preparation and the specific organism identified by fungal culture, which can take up to four weeks. Treatment should not be delayed, but the results of fungal culture can help to guide management if the patient is not responding to empirical therapy.

Management

The mainstay of treatment for tinea capitis is systemic antifungal therapy. Topical antifungal preparations are generally ineffective because they do not penetrate the hair follicles where the infection is located. First-line therapy is griseofulvin 500 mg daily (or 10 to 20 mg/kg daily in children) for six to eight weeks.[27] Alternatively, terbinafine 250 mg daily (or 62.5 mg daily in children under 20 kg and 125 mg daily in children 20 to 40 kg) for four weeks can also be prescribed.[27] Griseofulvin is more effective for *Microsporum* whereas terbinafine is more effective for *Trichophyton*. For patients who cannot tolerate griseofulvin or terbinafine and patients who have extensive or refractory cases of tinea capitis, itraconazole or fluconazole may be selected.[28]

Adjunctive topical therapies are often recommended to reduce fungal spore shedding and risk of reinfection. Antifungal shampoos containing ketoconazole or selenium sulfide should be used two to three times weekly during the course of treatment.[29]

The patient's close contacts, particularly household members, should be screened and treated if necessary.[28] Patients and caregivers should be educated about hygiene practices and the contagious nature of the condition. To prevent spread, items that are in contact with the hair (including hair grooming tools, hats and pillows) should be thoroughly cleaned and not shared with other people. In cases of zoophilic infection, the family pets should be checked by a veterinarian.

Outcome

A clinical diagnosis of tinea capitis was made and the patient commenced empirical treatment with terbinafine 250 mg daily for four weeks. This agent was chosen because a *Trichophyton* species was suspected to be the causative organism, in light of contact with a barbershop. The diagnosis was explained and he was educated about the importance of cleaning his hair grooming tools, hats and pillows and not sharing these with others until his condition resolved. For hair washing, he was advised to use a shampoo containing 2% ketoconazole. None of his family members showed signs of tinea capitis. The diagnosis was confirmed by light microscopy and the result of fungal culture, returned four weeks later, confirmed the growth of *T. tonsurans*. Eight weeks later, the patient had no signs of infection and his hair regrowth was excellent. MT

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A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

COMPETING INTERESTS: None.

MedicineToday Dermatology Collection 2025; 9(1): 35-37
First published 2025; 26(3): 57-59

A teenage boy with patchy hair loss

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A widespread erythematous targetoid eruption

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Test your diagnostic skills in our regular dermatology quiz. What is the cause of these asymptomatic lesions?

Case presentation

A 16-year-old girl presents with a widespread skin eruption of sudden onset. The lesions are asymptomatic but the eruption was preceded by a flu-like illness (fevers, chills, malaise) by one day. The patient does not have any medical history of note. She does not take regular prescription medications, denies using any over-the-counter preparations, and has not had any recent vaccinations.

On examination, raised, erythematous papules coalescing into plaques are observed on the patient's trunk, arms and legs (Figure 1a). The eruption extends bilaterally to the palms, soles and vulval skin but the oral and ocular mucosal surfaces are not involved. The lesions are noted to blanch with pressure. On closer inspection, some of the lesions look like 'targets', with a central dusky area surrounded by a paler outer ring and sharply demarcated border (Figure 1b).

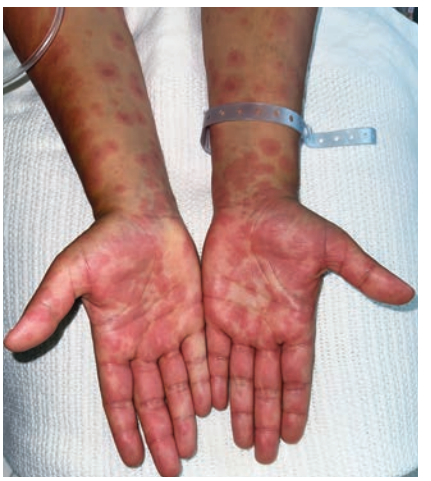

Figure 1a. The diffuse eruption of erythematous papules and plaques on the trunk, arms and legs, which extends to the palms and soles (case patient).

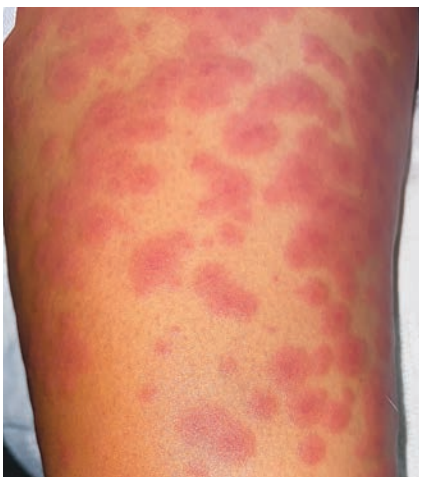

Figure 1b. Some of the lesions have a targetoid appearance (a central dusky area surrounded by a paler outer ring and a sharply demarcated border).

Differential diagnoses

Conditions to consider among the differential diagnoses include the following.

Viral exanthems

Viral exanthems, a common presentation in both children and adults, are widespread eruptions that accompany viral infections. Viral exanthems may be triggered directly by a viral infection itself or indirectly, such as by a hypersensitivity reaction to the virus.[1]

Certain exanthems may be diagnosed on the basis of their distinctive morphology, including chickenpox (varicella-zoster virus), measles (measles virus), rubella (rubella virus), roseola (human herpes virus types 6 and 7), erythema infectiosum (parvovirus B19) and hand, foot and mouth disease (coxsackievirus). However, viral exanthems often present nonspecifically and can be a diagnostic challenge.[2] Helpful clues when evaluating patients include associated systemic symptoms, immunisation history and contact with infected or unwell individuals.[3]

In general, viral exanthems are self-limiting and treatment is supportive. It is more important to make a definitive diagnosis in pregnant women and immunocompromised or unvaccinated people, as well as in children who may have been exposed to such groups.[4]

For the case patient, her history of systemic symptoms preceding the rash make a viral exanthem a top differential diagnosis. However, the targetoid appearance of the lesions may point to an alternative diagnosis.

Urticaria

Urticaria ('hives') is characterised by an eruption of pruritic lesions that may be localised or widespread. It is often

MedicineToday Dermatology Collection 2025; 9(1): 38-40
First published 2024; 25(4): 58-60

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polymorphic and usually includes wheals (raised, oedematous plaques with a skin-coloured or pale centre surrounded by an area of erythema). These lesions are typically transient and migratory, disappearing from one location before reappearing elsewhere, so changes in the shape and distribution of the rash over time is one of the keys to the diagnosis.[5] The condition is caused by activation of cutaneous mast cells, which release chemical mediators, predominantly histamine, that increase vascular permeability in the surrounding tissue and cause the typical oedematous appearance of urticarial lesions.[6]

Urticaria may be classified as acute (less than six weeks duration, often lasting hours to days) or chronic (more than six weeks duration). Most cases of acute urticaria are idiopathic. However, there are many known triggers, including:

- viral or bacterial infections
- allergy to foods or medications
- contact or irritant dermatitis
- vaccination
- insect bites and stings.

Acute urticaria is not the correct diagnosis for the case patient, whose eruption had a fixed distribution.

Sweet syndrome

Sweet syndrome (acute febrile neutrophilic dermatosis) is an uncommon skin disorder associated with fever and other systemic symptoms, including malaise, arthralgia, myalgia and headache. Other organs may also be affected, most commonly the eyes, where it may manifest as conjunctivitis or episcleritis.[7]

Sweet syndrome most commonly occurs in middle-aged women but other population groups may be affected. The cause is not completely understood, but studies have shown that it is often triggered by an insult to the immune system, such as an acute systemic infection, malignancy (particularly haematological malignancy) or drug exposure. Susceptibility is increased in people with an underlying chronic condition or immunodeficiency.[8]

The skin rash of Sweet syndrome has a sudden onset and appears as widespread, erythematous vesicles, papules, nodules and/or plaques, typically distributed on the neck and limbs. The lesions may be small initially but tend to grow and may coalesce to form larger, irregular plaques. They are characteristically painful and tender and may last for days to weeks.[9]

Sweet syndrome may be diagnosed clinically but is usually confirmed with skin biopsy. Given the disease associations, further investigations for underlying malignancy or autoimmune conditions are usually recommended, with the choice of these made with consideration of each patient's demographic and risk factors.[10]

Sweet syndrome is not the correct diagnosis for the case patient, whose rash was not painful or tender. The lesions of Sweet syndrome tend to be juicy in appearance. Additionally, the patient is not within the age group that is most commonly affected.

Erythema multiforme

This is the correct diagnosis. Erythema multiforme is an immune-mediated skin disorder that presents as a symmetrical, erythematous eruption. Its characteristic targetoid lesions have concentric rings of colour variation: a central darker area, surrounding pale ring, and sharply demarcated border. The eruption may be widespread and typically includes the palms and soles. Erythema multiforme is classified as minor (affecting the skin only) and major (also involving oral, urogenital or, rarely, ocular mucosa).[11] The mucosal lesions may present as blisters, which can burst to form painful erosions. Patients are typically aged 20 to 30 years.

About 90% of cases of erythema multiforme are associated with infections, with herpes simplex virus type 1 (HSV-1) the most common.[12] The presence of herpes labialis ('cold sore'), either preceding or occurring together with the eruption, may be a useful clue to this precipitant. Other infectious triggers include *Mycoplasma pneumoniae*, cytomegalovirus, Epstein–Barr virus and influenza virus. An infectious cause may be suspected in patients who report a prodrome of systemic symptoms including fever, malaise and myalgia. Noninfectious causes include medications (e.g. antibiotics, antiepileptics, NSAIDs), vaccines, pregnancy and coexisting conditions such as inflammatory bowel disease and malignancy.[13-15] However, in many cases the cause remains unknown.

A diagnosis of erythema multiforme is usually made clinically. Serological testing for infectious causes is sometimes performed, which can help to direct treatment. When there is doubt about the diagnosis, a skin biopsy can be helpful to rule out more serious conditions such as autoimmune blistering diseases, namely bullous pemphigoid.[12] The histopathological findings of erythema multiforme include apoptotic keratinocytes, basal vacuolar change, spongiosis, epithelial necrosis and, sometimes, blisters.[16]

Management

Mild and uncomplicated cases of erythema multiforme are typically self-limiting and resolve within four to six weeks. Supportive treatment includes oral antihistamines and topical corticosteroids or a short course of oral prednisone to alleviate pruritus and discomfort. Oral mucosal lesions may be painful and can be treated with oral antiseptic mouthwashes and topical corticosteroids.[17] The use of all potential inciting medications should be stopped.

If HSV infection is suspected to be the cause then oral antiviral therapy should be given early to reduce the severity and duration of the rash.[18] Treatment options are aciclovir (400 mg five times daily for seven days), famciclovir (500 mg twice daily for seven days) or valaciclovir (1 g twice daily for seven days).[19] If *Mycoplasma pneumoniae* infection is suspected then appropriate antibiotic therapy is warranted.

In patients with recurrent erythema multiforme that is HSV-associated or idiopathic, antiviral prophylaxis has been shown to be effective in reducing the frequency and severity of episodes.[20] Current

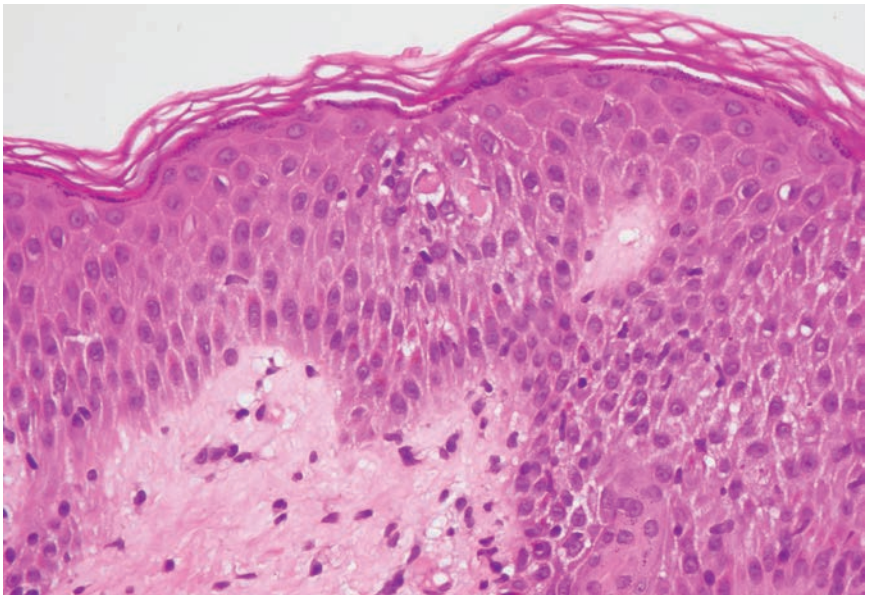

Figure 2. Histopathology of the biopsy specimen (case patient), showing lichenoid inflammation with basal vacuolar change and scattered apoptotic keratinocytes (magnification 400×).

treatment recommendations include aciclovir (400 mg twice daily), famciclovir (250 mg twice daily) or valaciclovir (500 mg twice daily), for six months or more.[12] In patients who respond, the duration of continuous antiviral therapy may be extended.[12]

For patients with erythema multiforme major, the spectrum of severity is wide. For those who have extensive and severe oral mucosal involvement, oral intake may be affected and admission to hospital may be appropriate for close monitoring and parenteral rehydration.[11] For patients with eye involvement (rare), early consultation with an ophthalmologist for assessment and management is crucial to prevent long-term complications.[21]

Outcome

The case patient was given a provisional diagnosis of erythema multiforme. Because of her young age and the extensive nature of the eruption, a punch biopsy was performed; the histological findings confirmed the diagnosis (Figure 2). Serological testing, including a viral panel, was performed but did not reveal an infectious precipitant. A clear cause for erythema multiforme was not identified.

The patient was treated supportively with betamethasone dipropionate (0.05% ointment applied twice daily for seven to 10 days) and loratadine (10 mg as needed) to alleviate pruritus. At a follow-up visit one month later, her rash had cleared with only a few areas of postinflammatory hyperpigmentation remaining. She was advised to present to her GP if she experiences a similar episode in the future. MT

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COMPETING INTERESTS: None.