DECEMBER 2022 VOL 6 NO 2

A MEDICINE TODAY PUBLICATION

Dermatology Collection

PEER REVIEWED UPDATES FOR MEDICAL PRACTITIONERS

Reprints in Dermatology

Scalp pruritus – scratching for answers

An introduction to field therapies for photoageing

Rosacea: a thorny problem with a rosy outlook

Pruritic papules in a 10-month-old boy

Diffuse linear streaks on the trunk and limbs

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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 December 2022 Dermatology Collection covers a range of dermatological presentations and conditions.

Scalp pruritus is a frequent presentation to general practice that has a broad range of causes, some that are commonly managed in general practice and others that require dermatologist assessment. Read about how to differentiate between causes on history and examination, and the various treatment options available.

The global market for antiageing products is estimated at over $40 billion and, with an ageing population, treatments are being more highly sought after. Field therapies – treatments that address the visible signs of photoageing – include topical therapies, cosmeceuticals, chemical peels and laser, light and other nonlaser modalities. Read about the general concepts of photoageing and some of the field therapies available.

Rosacea affects up to 5.5% of the global population and is a common condition managed in general practice. Its symptoms can be distressing for patients and appropriate treatment can improve their quality of life. Review the diagnostic features, differential diagnosis and treatment options for rosacea.

Finally, test your diagnostic skills with two Dermatology Clinic articles. What are the differential diagnoses and causes of the lesions in these case presentations of a 10-month-old boy with a pruritic papular eruption and a 65-year-old man with diffuse linear streaks on his trunk and limbs?

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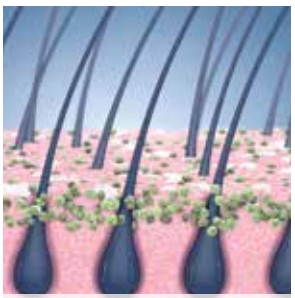

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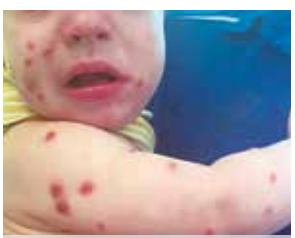

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Scalp pruritus

Scratching for answers

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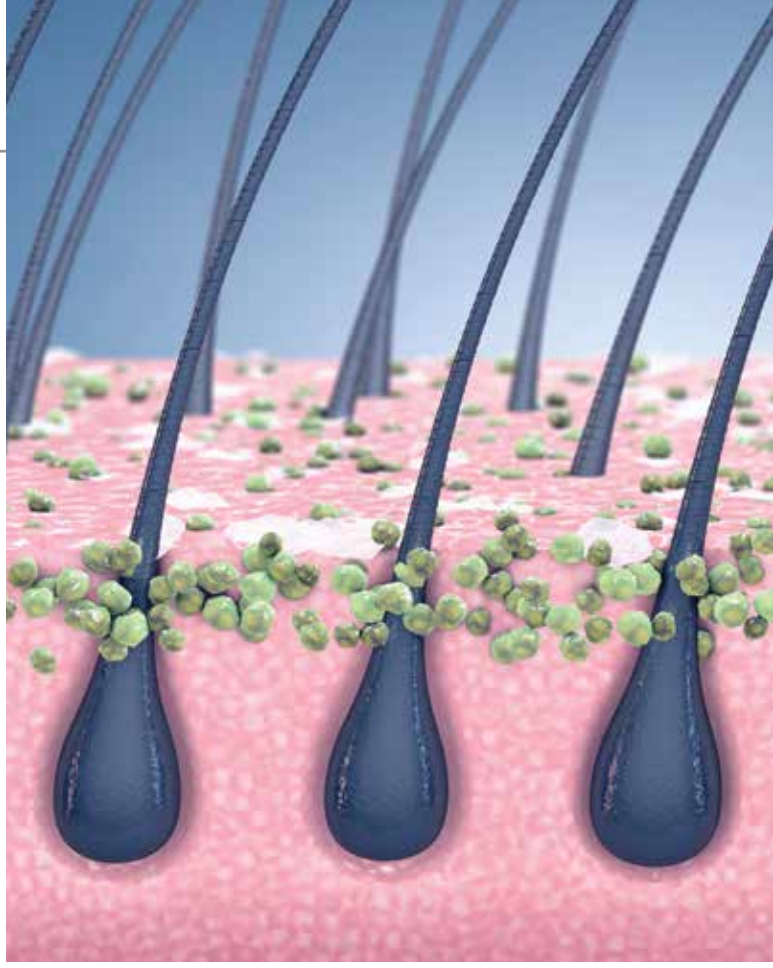
Scalp itch is common in people of all ages. Treatment depends on an accurate diagnosis. Causes range from everyday skin conditions such as seborrhoeic dermatitis, psoriasis and head lice to rare disorders such as dermatitis herpetiformis and trigeminal trophic syndrome.



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KEY POINTS

- Scalp pruritus is a feature of many common dermatological conditions, including seborrhoeic dermatitis, psoriasis, pediculosis capitis, atopic dermatitis or eczema, lichen simplex chronicus and contact dermatitis.
- Scalp pruritus may also be a prominent feature of rare conditions such as dermatitis herpetiformis, lichen planopilaris and trigeminal trophic syndrome.
- Pruritus of the scalp can occur without any discernible skin changes; psychological issues can exacerbate or manifest as scalp pruritus.
- Scalp pruritus can be a diagnostic and therapeutic challenge; distinguishing features in the patient's history should be sought and physical examination should include whole-body skin inspection.
- Sometimes a therapeutic trial is required before the diagnosis is established.
- A definitive cause for scalp pruritus is not always found; these patients may benefit from symptomatic antipruritic treatments.
- Referral to a dermatologist is recommended when the diagnosis remains unclear or the disease does not respond to treatment. Early dermatology referral is essential for patients with dermatitis herpetiformis, lichen planopilaris and alopecia.

Scalp pruritus is a frequent presentation to GPs. This article outlines the clinical features and treatment of common dermatological conditions associated with scalp pruritus, as well as some rare but important causes of this condition. A summary of the common causes of scalp pruritis is listed in Table 1; a summary of less common causes of scalp pruritus are listed in Table 2.

Common causes of scalp pruritus

Seborrhoeic dermatitis

Clinical features

Seborrhoeic dermatitis is a common dermatosis with a predilection for sites of increased sebum production, including the scalp, ears, face, central chest and major body folds (Figures 1a and b). Although the cause of seborrhoeic dermatitis

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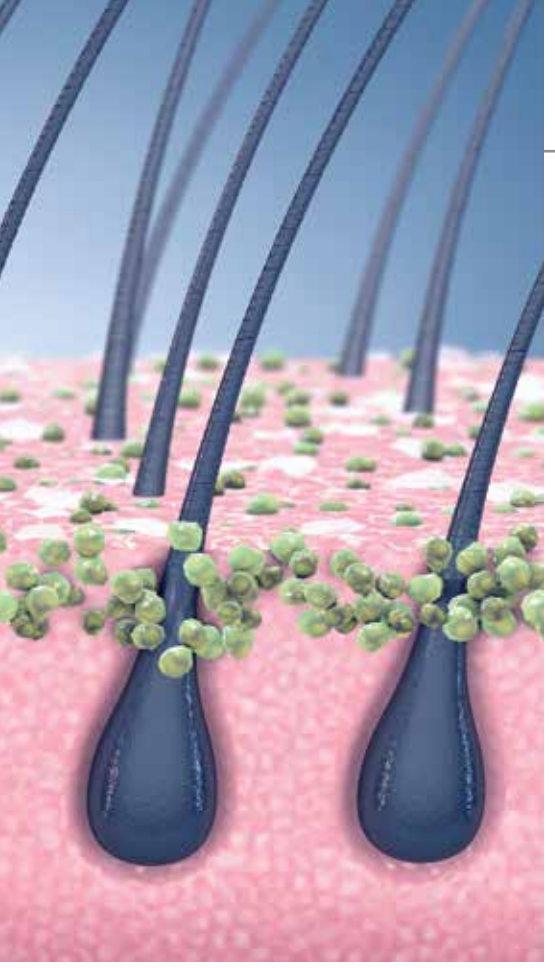
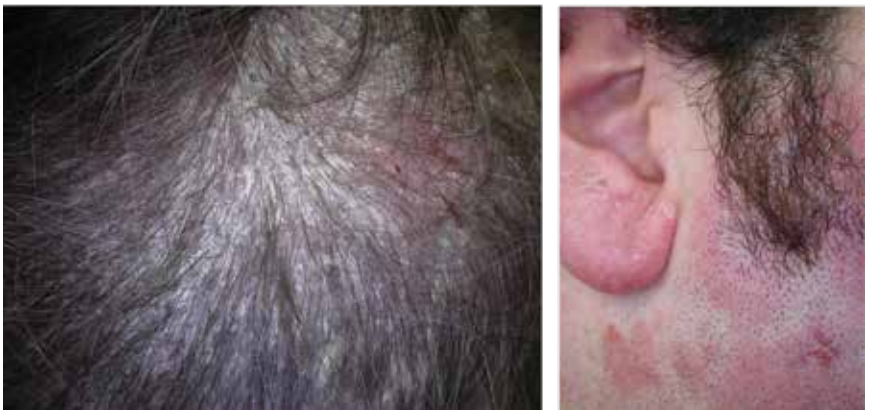




Figures 1a and b. Seborrhoeic dermatitis. a (left). Loosely adherent scales on the scalp. b (right). Facial rash associated with seborrhoeic dermatitis.

remains unknown, the commensal yeast *Malassezia furfur* has been implicated in its pathogenesis.

Infantile and adult forms are distinguishable. The infantile form, commonly known as 'cradle cap', occurs in the first three months of life and is self-limiting. The adult form tends to begin in late adolescence and persist into adulthood, with peak prevalence in the third and fourth decades.

Seborrhoeic dermatitis has an estimated prevalence of 3% in the general population. For reasons that are not completely understood, seborrhoeic dermatitis is more common in individuals with HIV infection and neurological disorders, notably Parkinson's disease. Indeed, severe or recalcitrant seborrhoeic dermatitis may be the presenting sign in patients with HIV infection.

In its mildest form, seborrhoeic dermatitis of the scalp is referred to as dandruff (also called pityriasis capitis), and is characterised by diffuse, fine white scaling without inflammation. With more extensive disease, greasy yellow to salmon-coloured scales overlay patches of inflamed skin (Figure 1a). Areas of affected skin may be asymptomatic or extremely itchy. Seborrhoeic dermatitis can mimic psoriasis but, in the latter, plaques are well demarcated, thicker and more inflamed (Figures 2a and b). The presence of nail changes and plaques elsewhere on the body in psoriasis can help differentiate it from seborrhoeic dermatitis (Figure 2c).

Seborrhoeic dermatitis may be associated with blepharitis and facial rash (Figure 1b). The rash may extend to involve the postauricular region with fissuring, as can otitis externa. Other areas, such as the axillae and groin, may show a glazed erythema with little scaling.

Treatment

Seborrhoeic dermatitis is a chronic relapsing condition, and patients need to be reminded that treatment aims to control, not cure. In mild cases, regular use of an antidandruff shampoo is usually effective. Examples are shown in the Box. The shampoo should be massaged into the scalp and left for about five minutes before rinsing out. Washing the shampoo out too soon or not using it often enough are common causes of treatment failure. For more difficult cases, a topical antifungal preparation such as a ketoconazole cream may be used in addition to a shampoo. The cream is mixed with water and massaged into the scalp at night and washed out the next morning.

Patients with a greater degree of inflammation will benefit from the addition of a topical corticosteroid. Corticosteroid lotions are the easiest form to apply to hair-bearing areas and include methylprednisolone aceponate 0.1% and mometasone furoate 0.1% lotions. These can be used as needed.

When the scalp is thickly covered with scale, preparations such as extemporaneously compounded coal tar and keratolytics such as liquor picis carbonis (LPC) 3 to 6% with salicylic acid 3% in aqueous cream are beneficial.

Systemic antifungal agents such as itraconazole, terbinafine or fluconazole should be reserved for patients with severe or unresponsive disease. The quality of evidence examining the clinical efficacy of oral treatments in patients with seborrhoeic dermatitis is low, and there is no direct comparison between treatments.[1]

Psoriasis

Clinical features

Psoriasis is a chronic, immune-mediated papulosquamous skin condition that is common in Australia, with an estimated prevalence of 2 to 6%. Psoriasis is a polygenic disorder that is influenced by a variety of environmental factors, such as trauma, medication and infection. The classic features – erythema, thickening

TABLE 1. COMMON CAUSES OF SCALP PRURITUS

Cause	Key features on history	Key features on examination	Treatments
Seborrhoeic dermatitis	• Infantile form occurs in the first three months; is self-limiting • Adult form begins in late adolescence and persists into adulthood • May be asymptomatic or itchy • More common in people with HIV and neurological disorders	• Mild: fine white scaling; known as dandruff • More severe: greasy yellow to salmon-coloured scales overlying patches of inflamed skin • May extend to posterior auricular area • May be associated with blepharitis and facial rash • Scales and hair casts glide easily along the hair shaft	• Aim is control, not cure • Mild: regular use of antidandruff shampoo • More difficult: add on topical antifungal (i.e. ketoconazole) • More inflammation: add on topical corticosteroid (i.e. methylprednisolone aceponate or mometasone furoate) as needed • Thick and scaly scalp: coal tar and keratolytics • Severe: systemic agents (i.e. itraconazole, terbinafine, fl conazole)
Psoriasis	• Associated with comorbidities, such as psoriatic arthritis, cardiovascular disease, metabolic syndrome, mental health disorders, malignancies and immune-related disorders	• Well demarcated, erythematous plaques with adherent silvery scale • May extend beyond hairline and to posterior auricular area • May have nail changes and plaques elsewhere on body	• Mild: tar and salicylic acid-based shampoos • Moderate to severe: topical corticosteroids • More severe: add dithranol 0.1 to 0.2% to tar/salicylic acid preparation • Treatment resistant: add on systemic therapy, such as methotrexate, acitretin, ciclosporin, apremilast or biologic therapy
Pediculosis capitis (head lice)	• Presents with itch that is prominent over the occipital and parietal scalp	• Can be diagnosed by direct visualisation of tan to brown eggs, which are difficult to dislodge from hair shafts, or lice	• First-line: topical pediculicides (i.e. permethrin, malathion); reapply after seven days • Wet comb with fine-toothed comb to physically remove nits • Treatment-resistant: add on oral ivermectin 200 mcg/kg; repeat after seven days
Lichen simplex chronicus	• Secondary to repetitive scratching or rubbing • Predisposing factors: atopic dermatitis, neuropathic pruritus, anxiety, obsessive compulsive disorder	• Solitary or multiple dry, scaly plaques with leathery appearing skin • Occurs at sites accessible to scratching (i.e. occipital scalp, posterior neck, lower legs)	• Aim is to break the itch-rub cycle • Topical corticosteroids (i.e. methylprednisolone aceponate or mometasone furoate) • Treatment resistant: add on intralesional triamcinolone acetonide • Manage psychological stressors • Biopsy if diagnosis unclear

and scale – are the result of abnormal keratinocyte proliferation and differentiation, vascular dilation and a population of inflammatory cells within the dermis and epidermis.

The scalp is involved in more than half of patients with psoriasis, and in some instances this may be the sole manifestation. Scalp psoriasis is characterised by well-demarcated erythematous plaques that have an adherent silvery scale. Lesions may advance beyond the hairline and extend to involve the retroauricular area (Figures 2a and b). In milder cases, scaling may be diffuse and nonspecific, and resemble pityriasis capitis. Psoriasis of the scalp seldom results in alopecia.

Psoriasis is a systemic disease process associated with a number of comorbidities. Psoriatic arthritis is the major systemic manifestation, affecting up to 30% of patients, and scalp psoriasis is a sign of increased risk of psoriatic arthritis. Patients have an increased risk of developing metabolic syndrome, cardiovascular disease, mental health issues, inflammatory bowel disease and certain malignancies, such as non-melanoma skin cancers, thus it is important to screen for and manage this vast range of comorbidities.[2]

Treatment

Medicated shampoos may be effective for mild cases of scalp psoriasis. These preparations contain active ingredients such as tar and salicylic acid. For moderate to severe scalp psoriasis, topical corticosteroids are the mainstay of treatment. Potent and very potent topical corticosteroids are suitable for scalp psoriasis. Start with a topical corticosteroid lotion such as mometasone furoate 0.1% or methylprednisolone aceponate 0.1%; these can be applied to the scalp after shampooing and left overnight. Topical corticosteroid treatment is more efficacious when combined with calcipotriol, a vitamin D derivative.[3] A combination product containing calcipotriol and betamethasone was available on PBS; however, it has recently been discontinued. Another treatment

ANTIDANDRUFF MEDICATED SHAMPOOS: ACTIVE INGREDIENTS AND EXAMPLES OF PRODUCTS

Selenium sulfide
- Selsun products

Zinc pyrithione
- Cedel Anti-Dandruff Medicated Shampoo
- Head & Shoulders Anti Dandruff Shampoos and Anti Dandruff Conditioners
- Neutrogena T/Gel Daily Control 2-in-1

Ketoconazole (1 to 2%)
- Nizoral anti-dandruff shampoo
- Sebizole shampoo

Coal tar
- Ionil T Shampoo
- Neutrogena T/Gel Therapeutic Shampoo

Polytar liquid
- Sebitar Scalp Cleansing Treatment

Salicylic acid
- Neutrogena T/Gel Anti-Dandruff Conditioner

option is clobetasol propionate 0.05% shampoo, which is also available on the PBS for this indication. This is applied to the scalp for five to 15 minutes, then rinsed out, initially daily then once to twice a week for maintenance.

Patients with thickened plaques and adherent scale require a keratolytic preparation. This is usually left on overnight and washed out the next morning. A typical preparation may include a combination of a tar (e.g. 3 to 10% LPC) and salicylic acid 3 to 5% (maximum 10%) in aqueous cream, extemporaneously compounded.

In more severe cases, dithranol at a concentration of 0.1 to 0.2% can be added to compounded preparations for overnight application to the scalp. Higher concentrations of dithranol (0.5 to 1%) can be used for short contact treatment, applied and left for no more than 30 minutes before being washed off. Short-contact treatment can be very irritating to inflamed skin. Preparations containing dithranol and tars should be used with caution by fair-haired individuals as they can stain the hair. Dithranol's propensity to cause red–brown staining and skin irritation has contributed to a decline in its use.

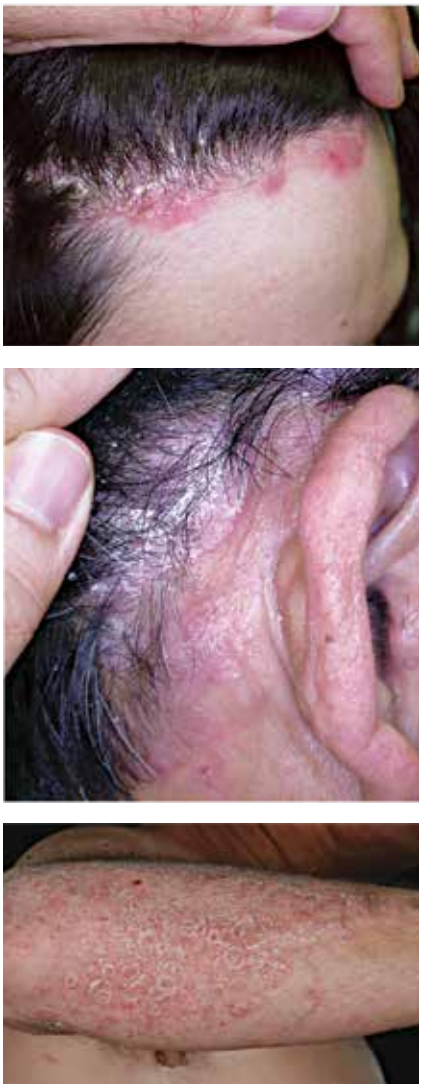
Systemic therapy, such as methotrexate, acitretin, ciclosporin, or biologic therapy, can be used in patients with treatment-resistant scalp psoriasis. Methotrexate can be prescribed by GPs; however, other systemic therapies, such as ciclosporin, acitretin (except in Western Australia) and apremilast must be prescribed and managed by a dermatologist. Referral to a dermatologist is indicated when topical treatments and methotrexate (if the GP is comfortable prescribing this) are unable to provide adequate disease control and additional therapy is required.

Biologic therapy including tildrakizumab (IL-23 inhibitor), guselkumab (IL-23 inhibitor), risankizumab (IL-23A inhibitor), etanercept (TNF inhibitor), adalimumab (TNF-alpha inhibitor), infliximab (TNF-alpha inhibitor), secukinumab (IL-17A inhibitor), and ixekizumab (IL-17A inhibitor) be used in severe scalp and generalised psoriasis.[4] Biologic therapy is PBS subsidised for severe, treatment resistant psoriasis and must be prescribed by a specialist dermatologist.

Pediculosis capitis (head lice)

Clinical features

Infestation of the scalp by the head louse is common, especially in children. Infestation is typically acquired by direct head-to-head contact, after which the female louse lays eggs (nits) – usually five to 10 per day – cemented to the base of hair shafts. Viable eggs appear tan to brown, whereas empty eggs are clear to white. Nits are difficult to dislodge from hair shafts, distinguishing them from seborrhoeic scales and hair casts, which glide easily along the shaft. Clinically, patients with head lice present with itch that is prominent over the occipital and parietal scalp, where infestation tends to be greatest. Papules are occasionally observed (Figure 3a). There may be secondary impetiginisation and hairs matted down by exudates.



Figures 2a to c. Large silvery scales of psoriasis developing just around the hairline (a, top) and in the occipital and retroauricular areas (b, middle). c (bottom). Patients with scalp psoriasis often have psoriatic plaques on other areas of the body.

Diagnosis is through direct visualisation of eggs or adult lice (Figure 3b). These are best detected by combing the hair systematically with a fine-toothed comb.

Treatment

There is a lengthy list of treatments available for head lice, but little high-quality evidence comparing their effectiveness.

Topical pediculicides remain the choice of treatment in Australia. First-line topical agents include permethrin 1%, malathion 0.5% or 1% and pyrethrins 0.165% piperonyl butoxide 1.65%.[5] Chemical pediculicides have limited ovicidal activity and thus a second application, seven days after the first, is advisable to kill newly hatched nymphs.

Oil-based pediculicides are an alternative. Examples include melaleuca (tea tree) oil 10% plus lavender oil 1% and eucalyptus oil 11% plus lemon tea tree oil 1%. Lotions or liquid preparations are preferred because they are more effective than shampoos. The entire family should be treated at the same time to prevent cross infection.

A fine-toothed comb is required to remove nits. Evidence supports 'wet combing' combined with a lavish amount of hair conditioner as an effective treatment for lice.[6] Conditioner is applied to wet hair in order to 'stun' the lice and then swept in a systematic fashion through the hair with a fine-toothed comb.

Wet combing should be used the day after application of a topical pediculicide to assess treatment success. If the pediculicide has been applied appropriately then the detection of live lice indicates treatment resistance. Widespread pesticide resistance has emerged and patterns vary with geographic location, even between schools in the same city.[7] When pesticide resistance is suspected, swapping to an alternative topical pesticide is recommended. For head lice infestations refractory to topical treatment options, oral ivermectin 200 mcg/kg is prescribed as a single dose, with a repeat dose given seven days later.[8] This should still be combined with topical therapies.

Lichen simplex chronicus

Clinical features

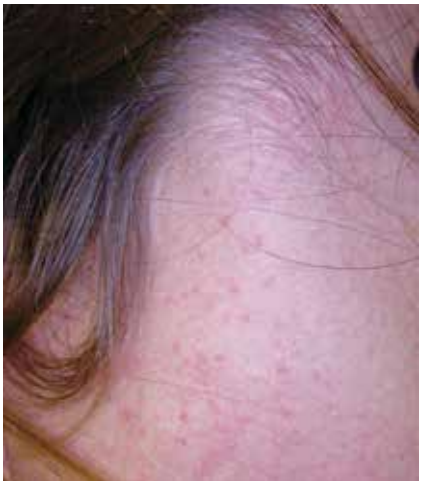
Lichen simplex chronicus is a secondary skin disorder, in which repetitive scratching or rubbing gives rise to lichenified plaques (Figure 4). These can be solitary

TABLE 2. LESS COMMON CAUSES OF SCALP PRURITUS

Cause	Key features on history
Tinea capitis	• Occurs primarily in children
Contact dermatitis	• Often first affects the ears, forehead, neck or face • Caused by irritants or allergens (i.e. hair dyes or treatments) • Irritant dermatitis appears after the first exposure; allergy-related dermatitis requires sensitisation and develops after repeated exposure
Endogenous or atopic eczema	• Usually associated with a generalised eczema flare rather than just isolated to the scalp
Lichen planopilaris	• Itchy and tender, or asymptomatic • May be localised to the scalp or present elsewhere • Results in scarring alopecia
Folliculitis	• Frequently associated with *Staphylococcus aureus*, *Malassezia* spp, and the mite *Demodex folliculorum*
Acne necrotica	• May have cicatricial (scarring) alopecia
Trigeminal trophic syndrome	• Complication of trigeminal nerve injury • Anaesthesia and dysaesthesia in the trigeminal nerve distribution • Irresistible desire to pick skin
Dermatitis herpetiformis	• Associated with gluten-sensitive enteropathy • Intensely itchy
Scabies	• Only usually involves scalp in infants, young children and older and immunosuppressed people
Psychosomatic disorders	• History may identify psychosocial stressors, anxiety or depression
Idiopathic pruritus capitis	• May not be associated with identifiable disease

Key features on examination	Treatments
• Two main patterns: – ectothrix (annular patches of partial alopecia) – endothrix (hair breaks off level with follicular orifice, giving rise to 'black dot' tinea capitis in patients with dark hair) • Varies from fine scale to boggy, purulent mass	• To confirm diagnosis, pluck six to eight hairs for fungal culture and microscopy • Oral antifungals are required (i.e. terbinafine, griseofulvin) • Also use ketoconazole or selenium sulfide shampoo to help prevent spread • Repeat culture at the end of treatment
• May be erythematous, vesicular and weeping	• Patch testing to identify allergens (can be performed at specialist dermatology centres) • Avoid triggers • Topical corticosteroid treatments • Oral prednisolone for severe cases
• May be diffusely red, vesicular and weeping • Hair may be matted • May have temporary alopecia	• Prevention: eliminate triggers, keep skin moisturized, wet dressings, bleach baths • Topical corticosteroid treatments • Systemic therapies (i.e. dupilumab, upadacitinib) for severe cases
• Early lesions: perifollicular erythema, scale, violaceous papules • Older lesions: follicular plugging and scarring	• Treat early to prevent scarring and hair loss • First-line: potent topical corticosteroids and intralesional corticosteroids • Systemic therapy for severe cases
• Monomorphic papules and pustules	• Wound swab for cultures and sensitivities – if *S. aureus*, use topical clindamycin lotion or oral flucloxacillin – if *Malassezia*, use antifungal shampoo – if *Demodex*, use topical permethrin cream or oral ivermectin
• Recurring crops of pruritic, red-brown papules with central necrosis • Resolve with varioliform scars • Occur on anterior hairlines and areas of increased sebum production	• Anti-staphylococcal antibiotics (i.e. tetracyclines, macrolides) • Isotretinoin
• Crescenteric ulceration of nasal rim, sparing nasal tip • Can affect the scalp and forehead	• Protective barriers and pharmacological therapies for neuropathic pain • Skin flaps and grafts
• Papulovesicles that occur in herpetiform clusters • Most commonly over extensor surfaces of elbows, dorsal forearms, knees, buttocks and scalp • Secondary erosions from vigorous scratching	• Needs referral to both a dermatologist and gastroenterologist • Biopsy to find subepidermal blisters and granular IgA deposits in papillary dermis • Dapsone, topical corticosteroids, gluten-free diet
• Pruritic, erythematous papules that become excoriated • Vesicles, indurated nodules, eczematous dermatitis and bacterial infections are common • Scabetic 'burrows'	• Topical permethrin cream, applied twice (one week apart) • Treat all household contacts • Hot wash and tumble dry bedclothes and linen
• Varied presentation	• Treat underlying stressor
• Varied presentation	• Consider stressors, ageing, neuropathic causes, systemic diseases, malignancy, medications • Basic investigations (i.e. FBE, UEC, TFTs, iron studies, BGL, CXR) • Trial empirical therapy (i.e. tar-based shampoos, antihistamines)

Abbreviations: BGL = blood glucose level; CXR = chest x-ray; FBE = full blood examination; TFTs = thyroid function tests; UEC = urea, electrolytes and creatinine level.



Figures 3a and b. Pediculosis capitis. a (left). Erythematous, pruritic papules on the nape of the neck. b (right). Dermoscopic view of an empty louse egg shell (nit) adherent to the hair shaft.

or multiple. Lesions have a dry or scaly surface, and normal skin markings are accentuated giving the skin a 'leathery' appearance. Rubbing may result in secondary broken hair shafts or apparent alopecia. Skin changes occur at sites accessible to scratching, including the occipital scalp and posterior neck. Involvement of the lower legs, scrotum or vulva and extensor forearms should be sought.

Figure 4. Lichen simplex chronicus, with plaques extending a distance from the hair margin.

Lichen simplex chronicus is common in adults with atopic dermatitis. Other predisposing factors include neuropathic pruritus and psychological conditions such as anxiety and obsessive compulsive disorder.

Lichen simplex chronicus can be diagnosed through its characteristic clinical appearance. If there is diagnostic uncertainty then examination of a skin biopsy specimen can help exclude lichen planus, lichen amyloidosis and psoriasis.

Treatment

The primary objective in treating lichen simplex chronicus is to break the itch–rub cycle. Potent topical corticosteroid lotions such as methylprednisolone aceponate and mometasone furoate are the mainstay of treatment. In patients with resistant lichen simplex chronicus, topical corticosteroids can be used in combination with intralesional triamcinolone. It is important to manage psychological stressors that perpetuate compulsive scratching and rubbing.

Less common causes of scalp pruritus

Tinea capitis

Tinea capitis is a dermatophyte infection of the scalp that occurs primarily in children. The causative organism varies with geographic location. In Australia, *Microsporum canis* and *Trichophyton tonsurans* predominate. There have been increasing reports of tinea capitis caused by *Trichophyton soudanense* (Figure 5), *Trichophyton violaceum* and *Microsporum audouinii* in immigrant children from East Africa, and confirmation of transmission to local populations.[9]

The two main patterns of tinea capitis invasion are: ectothrix and endothrix. In ectothrix infection (e.g. *M. canis* infection), arthroconidia (fungal spores) surround and destroy the cuticle, resulting in annular patches of partial alopecia. In endothrix infection (e.g. *T. tonsurans* infection), the arthroconidia are found within the hair shaft. This weakens the cuticle, and the hair breaks off level with the follicular orifice giving rise to 'black dot' tinea capitis in patients with dark hair. Inflammation varies from a fine scale to kerion formation, characterised by a boggy, purulent mass.

Clinical diagnosis of tinea capitis can be difficult owing to its varied presentation. An approach is to consider and exclude a fungal infection in patients (especially children) with hair loss and scale. To confirm the diagnosis, six to eight hairs should be plucked for fungal culture and microscopy.[9] A Wood's lamp is helpful in identifying tinea capitis only when the causative organism fluoresces (e.g. *M. canis*), as not all dermatophytes exhibit this phenomenon.

Treatment of tinea capitis requires oral antifungals, as topical therapy alone is rarely successful. Current evidence supports terbinafine for empiric treatment of tinea capitis caused by *Trichophyton* or griseofulvin for tinea capitis caused by *Microsporum* spp.[10] Oral griseofulvin is given at a recommended dose of 20 mg/kg/day up to 500 mg orally for a minimum of six to eight weeks, or until a clinical and mycological cure is achieved. Terbinafine is given to adults at a dose of 250 mg once daily, and to children at a recommended dose of 62.5 mg (body weight

Figure 5. Tinea capitis caused by *Trichophyton soudanense*.

under 20 kg) or 125 mg (body weight 20 to 40 kg) once daily for four weeks.[11-13] Terbinafine is available on the PBS for children with tinea capitis only when initial treatment with griseofulvin has failed. Side effects are comparable between griseofulvin and terbinafine; nasopharyngitis, headache and pyrexia are most common.[14] Concurrent use of ketoconazole or selenium sulfide shampoo can help prevent spread.[10] Alternative oral agents include itraconazole and fluconazole, but these are suboptimal choices for Trichophyton infections.[11] Culture should be repeated at the end of treatment to confirm microbiological cure.

Contact dermatitis

Scalp pruritus can be caused by contact dermatitis, due to either an irritant or an allergen. The scalp is relatively resistant to contact dermatitis because of rapid epidermal turnover and a thick epidermis and stratum corneum. It is also well protected by hair. Often the ears, forehead, neck or face are affected first.

Major allergens are found in hair dyes (e.g. paraphenylenediamine), bleaches, permanent wave solutions and hair creams. Potential irritants include bleaching agents (the most common irritant), agents containing thioglycolates for permanently waving hair and blow drying the hair.

Clinically, the scalp may be erythematous, vesicular and weeping (Figure 6). The timing of onset can help differentiate irritant and allergic contact dermatitis; irritant contact dermatitis appears after the first exposure, whereas allergic contact dermatitis requires sensitisation and develops after repeated exposure.

Patch testing is generally useful for diagnosing the substance responsible. In addition to avoidance of triggers, treatment with a topical corticosteroid is usually all that is needed. Oral prednisolone can be used for patients with severe contact dermatitis.

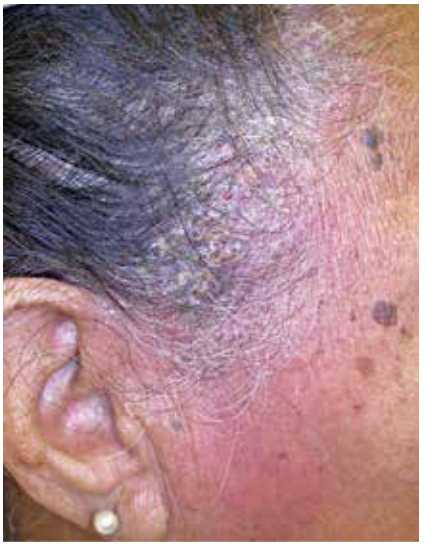


Figure 6. Hair dye allergy, showing erythema with excoriation and crust.

Endogenous or atopic eczema

Eczema involves the scalp usually in the setting of a generalised flare rather than as an isolated presentation. The scalp may be diffusely red, vesicular and weeping. The hair may become matted and temporary alopecia may occur.

Eliminating triggers, keeping skin moisturised and using wet dressings and bleach baths as needed are the mainstays of preventative management. Treatment with topical corticosteroids can be considered. An alcohol-based lotion is useful in the presence of thickened, matted hairs but can be strongly irritating. A potent corticosteroid cream (betamethasone dipropionate, methylprednisolone aceponate or mometasone furoate) diluted with water is a more acceptable alternative. In an eczematous flare, there is usually increased colonisation or infection with *Staphylococcus aureus*, and successful treatment often requires concurrent oral antibiotics. Biologic and advanced targeted systemic treatments are now available, including dupilumab and upadacitinib, and must be prescribed by a dermatologist. Dupilumab is a monoclonal antibody that inhibits interleukin 4 and is administered subcutaneously. Upadacitinib is a janus kinase 1 (JAK1) inhibitor administered once daily as an oral tablet. Both agents are PBS subsidised for chronic severe atopic dermatitis that is inadequately controlled with topical pharmacotherapies.[15-17]

Lichen planopilaris

Lichen planopilaris is a rare inflammatory scalp condition that results in scarring alopecia. Early lesions consist of perifollicular erythema, scale and violaceous papules. Later, there is follicular plugging that is replaced by scarring. There is an absence of follicular openings within foci of hair loss (Figure 7). The scalp is often itchy and tender but can be asymptomatic. Activity may be localised to the scalp or present elsewhere on the body, where it serves as a diagnostic clue.

Early treatment is necessary to avoid scarring and permanent hair loss, and patients should be referred to a dermatologist. Potent topical corticosteroids are the first-line treatment, generally in combination with intralesional corticosteroids. Rapidly progressive and extensive disease requires systemic therapy.

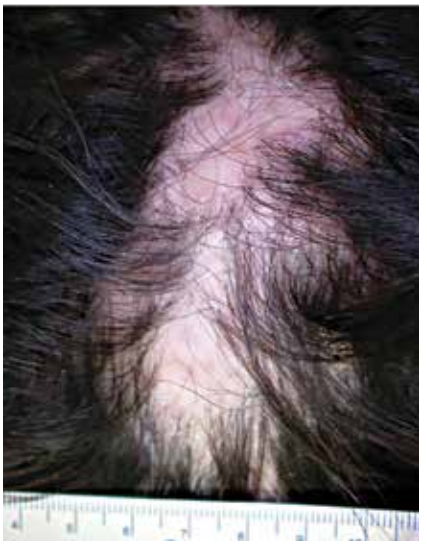


Figure 7. Lichen planopilaris resulting in cicatricial alopecia.

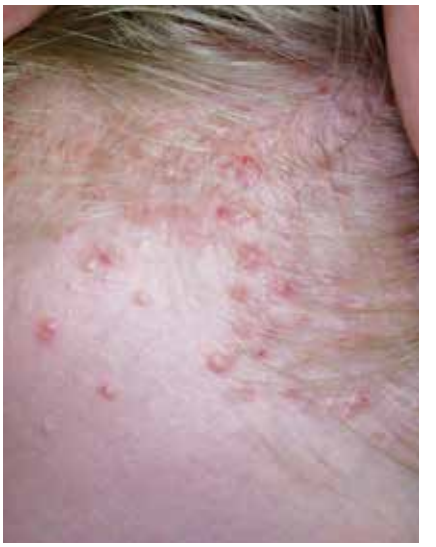


Figure 8. Follicular papules and pustules of *Malassezia* folliculitis.

Folliculitis

Pruritus of the scalp associated with monomorphic papules and pustules raises the possibility of folliculitis, a disorder with infectious (most commonly) and non-infectious aetiologies. Frequent causes of infectious folliculitis include *S. aureus, Malassezia* spp. (Figure 8) and the mite *Demodex folliculorum*.

When culture reveals *S. aureus* infection, treatment with topical clindamycin lotion or oral flucloxacillin is recommended. Topical therapy with antifungal shampoo is usually effective for *Malassezia* folliculitis, although occasionally a course of oral antifungal therapy may be needed. *Demodex* folliculitis may be treated with topical permethrin cream or oral ivermectin.

Acne necrotica

Acne necrotica presents with recurring crops of pruritic, red-brown papules that undergo central necrosis and resolve with varioliform scars. Lesions are distributed around the anterior hairline and areas of increased sebum production on the face and trunk.[18] Cicatricial alopecia may result. Patients respond to antistaphylococcal antibiotics, including tetracyclines and macrolides. Positive responses to isotretinoin have been reported.[19]

Trigeminal trophic syndrome

Trigeminal trophic syndrome is a complication of trigeminal nerve injury. Anaesthesia and dysaesthesia in the sensory distribution of the trigeminal nerve trigger an irresistible desire to pick the skin, with resultant ulceration. Crescentic ulceration of the nasal rim with sparing of the nasal tip is characteristic, but other sites, including the scalp and forehead may be affected (Figure 9). Treatment centres around the use of protective barriers and pharmacological therapies for neuropathic pain. Long-term treatment success has been reported with skin flaps and grafts.

Dermatitis herpetiformis

Dermatitis herpetiformis is a rare autoimmune skin disease associated with gluten-sensitive enteropathy. It is characterised by intensely pruritic papulovesicles that occur in herpetiform clusters, most often over the extensor surfaces of the elbows, dorsal forearms, knees, buttocks and scalp. Vesicles are disturbed by vigorous scratching, and secondary erosions and excoriations predominate.

The diagnosis of dermatitis herpetiformis is confirmed by detection of subepidermal blisters and granular IgA deposits in the papillary dermis through direct immunofluorescence of a skin biopsy specimen. Serology may aid in the diagnosis.

Dermatitis herpetiformis is usually treated with dapsone, topical corticosteroids and a gluten-free diet. Patients should be referred to a dermatologist and a gastroenterologist.

Scabies

Scabies involves the scalp usually only in infants, young children and older or immunosuppressed patients. Other sites that are involved are the palms of the hands, soles of the feet, neck and flexural areas. The rash is typified by pruritic erythematous papules that become excoriated. Vesicles, indurated nodules, eczematous dermatitis and secondary bacterial infection are also common. The pathognomonic scabetic 'burrow' is a greyish white, thread-like structure, 1 to 10 mm long, found on the extremities. The mite has a characteristic 'jet with contrail' or 'hang glider' appearance on dermoscopy.

Treatment consists of two applications, one week apart, of topical permethrin 5% cream. It is essential to treat household contacts at the same time as the patient to prevent cross infection. Bedclothes and linen should be hot washed and tumble dried to prevent fomite transmission. Oral ivermectin is PBS subsidised for treatment-resistant scabies. Two doses of 200 mcg/kg should be administered with fatty food, with the first on day one and the second sometime between day eight and 15.[20]

Psychosomatic disorders

Psychosocial stressors, anxiety or endogenous depression can manifest as various dermatological complaints, including scalp pruritus. Direct questioning may

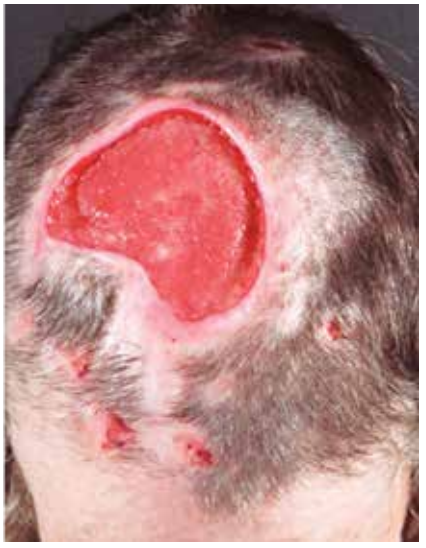


Figure 9. Trigeminal trophic syndrome.

reveal such precipitants in the absence of clear organic disease.

Idiopathic pruritus capitis

Scalp pruritus may occur in the absence of identifiable disease. Unexplained scalp pruritus can occur during periods of stress and as a manifestation of ageing (pruritus of senescence). Neuropathic pruritus (e.g. burning scalp syndrome, notalgia paraesthetica and postherpetic neuralgia) should be considered in patients with localised itch on non-inflamed skin, especially if they have accompanying dysaesthesia, such as numbness or a burning sensation.

Early dermatology referral is essential for patients with dermatitis herpetiformis, lichen planopilaris and other types of scarring alopecia

Scalp pruritus often occurs in the context of generalised whole-body pruritus. The medication history may reveal a pharmacological cause. Common triggers include opioids, NSAIDs, antihypertensive drugs, especially thiazide diuretics, lipid-lowering drugs, such as statins, and antibiotics. In rare cases, generalised pruritus is associated with an underlying disease process, including malignancy. In patients with lymphoma, pruritus can be associated with systemic symptoms such as night sweats and weight loss.

Investigations for patients with chronic pruritus on noninflamed skin who do not respond to therapy depend on the clinical findings. Basic investigations can include a full blood count, measurement of electrolytes, thyroid function tests, iron studies and chest radiography.

In patients with unexplained scalp pruritus, empirical treatment may be helpful. Tar-based shampoos are useful as they have antipruritic properties. If itch persists then systemic therapies may be used, including antihistamines and antidepressants such as doxepin and selective serotonin reuptake inhibitors.

Is there a role for punch biopsy in the work-up for scalp pruritus?

Biopsies can be very helpful in reaching a diagnosis; however, scalp biopsies are ideally performed in a controlled setting (e.g. by a dermatologist) because of the associated risk of bleeding and the need for dermatopathologist expertise in interpreting the results. Biopsies can be useful in differentiating conditions such as psoriasis from eczema, and for diagnosing lichen simplex chronicus, lichen planopilaris and, occasionally, folliculitis. A scalp biopsy is useful for diagnosing dermatitis herpetiformis; however, ideally the biopsy would be taken from a more typical body site other than the scalp.

When should patients be referred?

Referral to a dermatologist is recommended in cases of persistent diagnostic uncertainty and disease that does not respond to treatment. Early dermatology referral is essential for patients with dermatitis herpetiformis, lichen planopilaris and other types of scarring alopecia.

Conclusion

Scalp pruritus is a common symptom that can be associated with a range of dermatological conditions. It is important to identify distinguishing features in the patient's history and examination results to make an accurate diagnosis. Sometimes, a therapeutic trial is needed before the diagnosis is known. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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Scalp pruritus

Scratching for answers

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An introduction to field therapies for photoageing

BELINDA LAI MD
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Photoageing caused by chronic sun exposure manifests with skin changes such as rhytids, lentigines, coarse texture and neoplasia. A wide range of field therapies are available to address visible signs of photoageing and, potentially, subclinical photodamage. These include sunscreens for primary prevention, topical retinoids and alpha-hydroxy acids, cancerised field therapies, chemical peels, and laser and other light and infrared therapies.

For over 1000 years, many techniques have been used to treat the effects of time on the skin.[1] With an ageing population and a global market for antiageing products estimated at over $40 billion, public and scientific interest in therapies to maintain a youthful appearance has grown. Skin ageing is classified into two categories: intrinsic ageing and photoageing. Intrinsic skin ageing is influenced by genetics and results from the age-dependent deterioration of skin function and structure, such as epidermal atrophy and collagen reduction.[2,3] Photoageing is characterised by chronic exposure of the skin to sunlight, particularly ultraviolet (UV) radiation. Its manifestations include rhytids, lentigines, coarse texture, laxity, sallowness, neoplasias and telangiectasias, depending on skin types and ethnicity.[2] The features of intrinsic ageing and photoageing are compared in Table 1.[4,5]

A broad range of field therapies to target photoageing are available. These are defined as treatments that address the visible signs of photoageing and potentially subclinical photodamage. Field therapies for photoageing include topical therapies, cosmeceuticals, chemical peels and laser, light and other nonlaser modalities, with options for people of all skin phototypes. This article introduces clinicians to the general concepts of photoageing and some of the main field therapies available (summarised in Table 2).

Pathogenesis of photoageing

The term photoageing was first coined in 1986 and was used interchangeably with the term 'dermatoheliosis', erroneously implying a pathological condition of the sun.[4] Both UVA and UVB radiation are involved in the photoageing process. However, UVA has a significant role, as it penetrates more deeply into the dermis and reaches the earth's surface in 10 times greater quantity than UVB.[4]

Sun exposure is thought to be responsible for 80% of facial

KEY POINTS

- Photoageing caused by chronic exposure to ultraviolet radiation is responsible for about 80% of facial ageing and manifests as rhytids, lentigines, coarseness and neoplasia.
- A broad range of field therapies that target photoageing are available, with options for all skin phototypes.
- Alpha-hydroxy acids promote skin desquamation and cell growth and stimulate collagen production; they can decrease fine wrinkling and lighten solar lentigines.
- Topical retinoids increase epidermal cell turnover and restore the dermal extracellular matrix; they can improve dyschromia and fine and coarse wrinkling.
- The ablative resurfacing laser, traditionally regarded as the gold standard for managing photoageing, has considerable side effects and downtime.
- Fractional and nonablative rejuvenation and radiofrequency techniques allow regimens with shorter healing times and fewer side effects, suitable for a wider range of skin phototypes.

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TABLE 1. COMPARISON OF INTRINSIC AGEING AND PHOTOAGEING

Feature	Intrinsic ageing	Photoageing
Pathophysiology	• Age-related decline of functioning keratinocytes and fibroblasts • Intracellular and extracellular accumulation of by-products • Decreased function of sirtuins (signalling proteins involved in metabolic regulation) • Mitochondrial damage • Loss of telomeres	• Free radicals causing DNA damage • Oxidative stress leading to activation of the arachidonic acid pathway, resulting in inflammation • Mitochondrial damage • Protein oxidation • Telomere-based DNA damage responses
Histopathological changes	• Loose, short, thin, disorganised collagen • Epidermal atrophy • Loss of rete pegs • Flattening of the epidermal-dermal junction • Decreased melanocytes, Langerhans and mast cells	• Elastosis • Collagen fragmentation • Uneven epidermal thickness • Increased glycosaminoglycans and proteoglycans • Increased inflammatory markers (mast cells, eosinophils, mononuclear cells) • Melanogenesis
Clinical manifestations	• Fine lines • Increased skin laxity • Atrophy • Prominence of the vasculature[4]	**Fitzpatrick skin phototypes I and II[5]** • Epidermal atrophy • Focal depigmentation • Pseudoscars • Fewer wrinkles • Freckles • Naevi • Lentigomaligna • Melanoma • Actinic keratoses • Basal cell carcinoma • Squamous cell carcinoma **Fitzpatrick skin phototypes III to VI** • Tanning • Lentigines • Epidermal thickening[5] • In severe cases – accentuated ridging – deep furrows – leathery appearance – severe atrophy – open comedones – milia – cobblestone effect from elastosis – actinic purpura – epidermal and dermal thickening

ageing.[3] UV irradiation of the skin produces reactive oxygen species, which activate growth factors and receptor-initiated signalling to induce a transcription factor, activator protein 1 (AP-1). Increased AP-1 activity decreases synthesis of dermal collagen and keratinocyte proliferation.

UV irradiation also stimulates the expression of metalloproteinases, which degrade extracellular matrix proteins such as collagen, fibronectin, elastin and proteoglycans.[6] UV-induced collagen degradation leads to the accumulation of partially degraded collagen fragments in the dermis, reducing the structural integrity of the skin.[5] Further, continuous generation of reactive oxygen species injures the mitochondria, compromising their function and exacerbating collagen degradation and skin photoageing.[4,5] UV irradiation can also cause cellular protein oxidation, inhibiting proteasomal function and interfering with the effective degradation of defective proteins.

Telomeres are also susceptible to UV damage, triggering tumour suppressor protein p53 and other DNA damage response proteins to induce proliferative senescence or apoptosis. This may explain the features shared by photoageing and chronological ageing.[3,5]

Visible light and infrared radiation may also contribute to photoageing. Visible light is a substantial constituent of the solar spectrum but is suggested to contribute to less than 10% of total DNA damage caused by solar exposure, and infrared radiation generates reactive oxygen species in the skin. However, further research is needed on the role of visible light and infrared radiation in photoageing.[7]

Clinical manifestations of photoageing

The clinical manifestations of photoageing vary with skin type and ethnicity. Photoageing is more prominent in fair-skinned individuals and less discernible in those with Fitzpatrick skin phototypes IV and higher (Table 1).[6] Individuals with skin phototypes I and II show atrophic skin changes, with guttate hypomelanosis, lentigines and premalignant changes such as actinic keratoses and epidermal malignancies but fewer wrinkles (Figures 1a to c). Those with skin types III and IV tend to develop hypertrophic responses, such as deep wrinkling, coarseness, leathery appearance of the skin and lentigines.[5,8] They also tend to experience photoageing effects 10 to 20 years later than their type I and II counterparts, and the effects are

less severe because of the added photoprotection of darker skin.[4]

Photobiologic scoring of photoageing

Evaluating the level of photodamage in a patient is crucial for determining a treatment plan and assessing treatment response. Several scales have been developed to quantify the severity of photoageing. The Glogau scale is an established tool that grades photoageing as mild, moderate, advanced or severe. This scale relies predominantly on the extent of rhytids in its classification (Table 3).[4,9] Generally, patients with higher Glogau scores can receive more intensive treatments but have higher complication rates. The Glogau scale does not factor in skin type, which also influences complication rates.[4,9]

Other tools to quantify photoageing include the photonumeric nine-point scale of Griffiths and colleagues and a validated grading scale by Carruthers and Carruthers that rates forehead lines, brow positioning elemental folds and crows' feet.[5] The Wrinkle Severity Rating Scale and Global Aesthetic Improvement Scale are used in clinical research studies to quantify facial folds.[4]

Treatments for photoageing

Sunscreens

Sunscreens have a long history; ancient Greek athletes applied a mixture of oil and sand to protect their bodies from the sun when training for the Olympic games.[7] Regular use of broad-spectrum sunscreens, which block UVA and UVB, is the first line of defence in the prevention of photoageing. Sunscreens should be used in conjunction with other photoprotective measures, such as seeking shade when outdoors, wearing sun-protective clothing and avoiding exposure to both natural and artificial sources of UV light.[4]

Sunscreens provide temporary protection against UV radiation through organic filters such as avobenzone that absorb UV light or inorganic filters such as zinc oxide and titanium oxide that absorb, reflect and scatter UV light. Studies have shown that daily sunscreen application can prevent the development of actinic keratoses, basal cell carcinoma, squamous cell carcinoma and melanoma, lessen the signs of premature ageing and prevent exacerbations of photodermatoses such as polymorphous light eruption.[10]

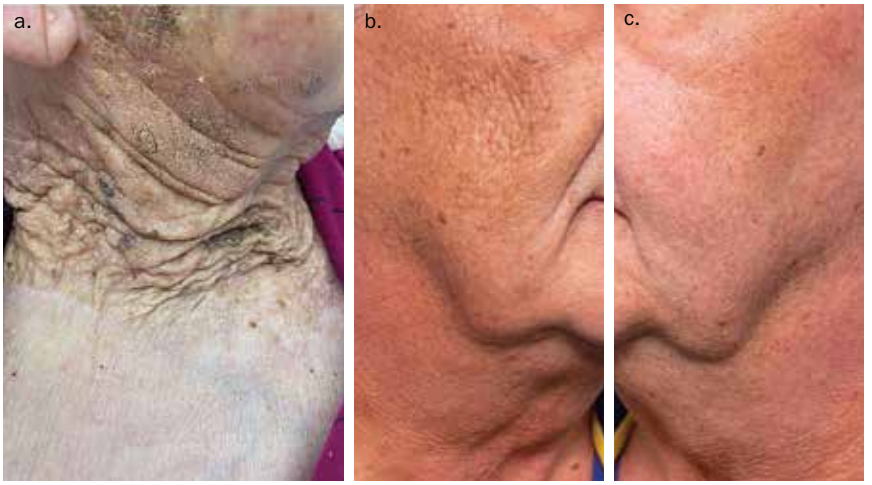
In Australia, it is recommended that sunscreen with a sun protection factor (SPF) of 30 should be applied 20 minutes before going outdoors. One teaspoon of sunscreen should be applied per limb, with a full-body application for an adult requiring at least 35 mL or around seven teaspoons.[11]

TABLE 2. FIELD THERAPIES FOR PHOTOAGEING

Field therapy	Indications	Considerations for skin phototypes IV to VI
Sunscreen	Primary prevention for: • photoageing • basal cell carcinoma • actinic keratoses • squamous cell carcinoma • melanoma	Nil
Topical retinoids	• Dyschromia • Fine and coarse wrinkling • Skin fragility	• Topical tretinoin can be used to treat dyspigmentation
Chemical peels	• Improve skin tone • Skin tightening • Acne vulgaris • Actinic or solar keratoses • Melasma and scarring	• Superficial peels only should be used • Chemical peels are used to treat mottled dyschromia, acne vulgaris, postinflammatory hyperpigmentation, melasma and pseudofolliculitis barbae
Ablative resurfacing with laser therapy	• Improve fine lines and skin texture	• Postinflammatory hyperpigmentation is common • Non-CO_2 fractional resurfacing is the preferred modality
Nonablative rejuvenation with laser, light and infrared therapy	• Infrared-emitting devices are suitable for those with mild facial or nonfacial photodamage • Intense pulse light therapy can treat photodamage, lentigines, hyperpigmentation and vascular lesions including telangiectasia	• Radiofrequency energy can be used to improve facial hyperpigmentation, telangiectasis and skin texture because of the minimal risk of postinflammatory hyperpigmentation
Field cancerisation treatments	• Actinic keratoses and subclinical lesions	–

Topical retinoids

Retinoids are a family of substances containing vitamin A (retinol and its natural and synthetic derivatives). Topical retinoids were first used in dermatology around 80 years ago to treat acne vulgaris, and their use has since expanded to treat other skin conditions, including photoageing.[12] Retinoids bind to nuclear retinoic acid receptors and exert their effects by modulating cellular differentiation to increase epidermal proliferation, compaction of the stratum corneum, and biosynthesis and deposition of glycosaminoglycans.



Figures 1a to c. Photoageing. a (left). Skin of a patient aged over 100 years, showing photoageing of the neck with erythema, brown pigmentation, dryness, roughness and wrinkles, compared with the sun-protected skin of the chest. b, c (centre and right). Asymmetrical photoageing in a man whose occupation involved driving a car about 100 km per week for more than 30 years. The right side of his face, which faced the side window (b), shows greater deflation, hyperpigmentation and solar comedones than the left side of his face, which faced the cabin (c).

Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

Retinoids can also inhibit dermal matrix degradation after sun exposure and block induction of AP-1 and AP-1-regulated metalloproteinases.[5]

Topical retinoids have been shown to improve dyschromia, fine and coarse wrinkling, and skin fragility and to exert an anti-inflammatory effect.[12] Additional short-term histological effects include improvement of atypia and dysplasia.[13]

Types of topical retinoids

Topical retinoids are classified by molecular structure as first-generation (retinol, tretinoin, retinaldehyde), second-generation (acitretin, etretinate), third-generation (adapalene, tazarotene) and fourth-generation (seletinoid G).

Tretinoin is the most researched compound for the treatment of intrinsic ageing or photoageing.[14] It is available on prescription in 0.025% and 0.05% strengths. Tretinoin 0.05% cream has proven long-term efficacy and safety (Figures 2a to c). Low-strength tretinoin (0.025%) is also quite effective while being more tolerable. The benefits of tretinoin are dose-dependent and increase with the duration of therapy for at least 10 to 12 months. Cessation of treatment results in some clinical deterioration.[15,16] Thus, most clinicians recommend initial treatment once daily at night for six to nine months, followed by a long-term maintenance, maybe at a lower concentration or reduced frequency (alternate days).[17]

Tazarotene 0.1% gel, available in the USA, is also effective in improving skin hydration and reducing skin texture and fine wrinkling. It may have a faster effect than 0.05% tretinoin.[18]

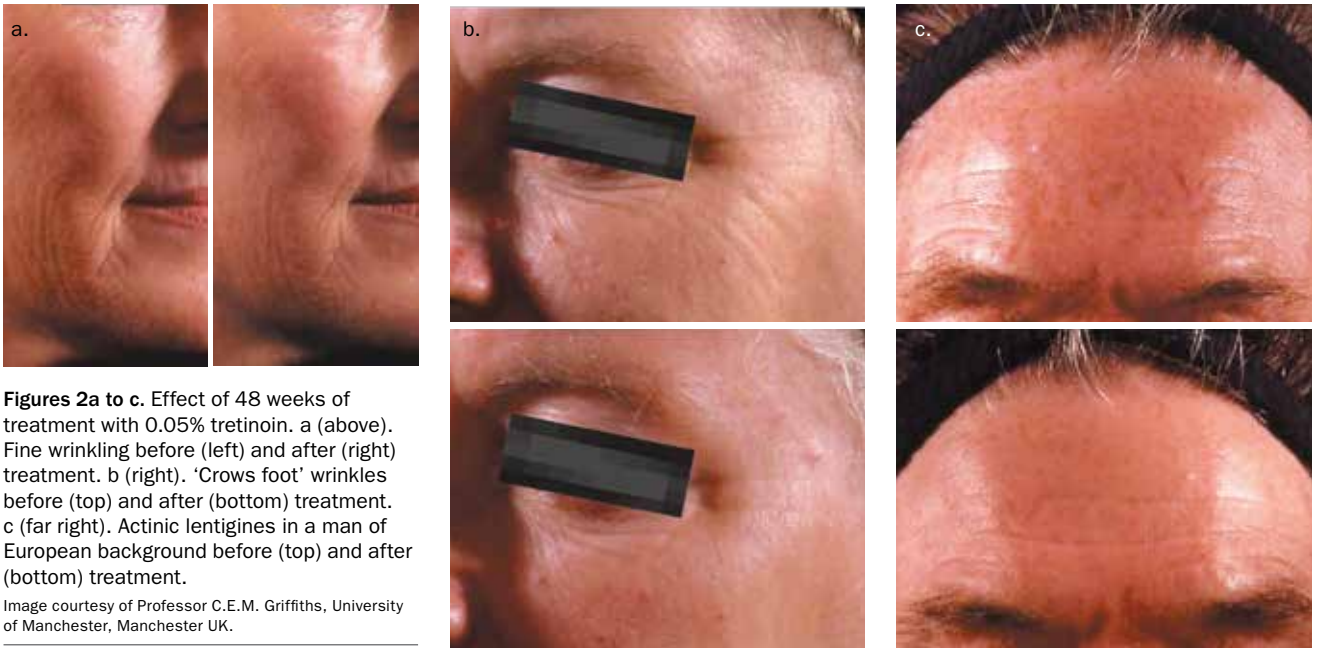
Retinols and retinaldehyde are available in several over-the-counter preparations. Retinol has been estimated to be 10 times less potent than tretinoin, and factoring this, studies comparing retinol and tretinoin have shown similar clinical benefits in photoaged skin.[12] Retinaldehyde has been shown to improve fine and deep wrinkles when compared with 0.05% tretinoin, with less irritation.[12]

Clinical use of topical retinoids

Importantly, the benefits of topical retinoids may be seen only after a couple of months of use, and diligent, concurrent use of sunscreen and moisturiser to prevent irritation is recommended.[19] Topical retinoids have photosensitising and irritating effects and hence should only be applied at night and washed off in the morning. Daily use of sunscreen with SPF 15 or higher before going outdoors and avoidance of strong sunlight if unprotected are recommended. Irritation can be minimised by the application of a

TABLE 3. GLOGAU SCALE FOR CLASSIFICATION OF PHOTOAGEING[4,9]

Glogau skin type	Photoageing classification	Age (years)	Skin characteristics
I	Mild	28 to 35	• No wrinkles • Early photoageing: mild pigment changes, no keratosis, minimal wrinkles, minimal or no make-up
II	Moderate	35 to 50	• Wrinkles in motion • Early to moderate photoageing: early brown spots visible, keratosis palpable but not visible, parallel smile lines appear, wears more foundation
III	Advanced	50 to 65	• Wrinkles at rest • Advanced photoageing: obvious discolouration, visible capillaries, visible keratosis, wears heavier make-up
IV	Severe	60 and over	• Only wrinkles • Severe photoageing: yellow/grey skin colour, prior skin malignancies, wrinkles throughout, no normal skin, cannot wear make-up because it cracks and cakes



Figures 2a to c. Effect of 48 weeks of treatment with 0.05% tretinoin. a (above). Fine wrinkling before (left) and after (right) treatment. b (right). 'Crows foot' wrinkles before (top) and after (bottom) treatment. c (far right). Actinic lentigines in a man of European background before (top) and after (bottom) treatment.

Image courtesy of Professor C.E.M. Griffiths, University of Manchester, Manchester UK.

moisturiser after topical retinoid therapy and by introducing slowly and increasing to a nightly application as tolerated. Clinicians should be aware that topical retinoids are teratogenic and should not be used by women who are planning to become pregnant or who are pregnant or breastfeeding.[20]

There are few data on the use of topical retinoids for photoageing in darker-skinned individuals. A small 40-week trial in people of Japanese or Chinese background found that once-daily application of 0.1% tretinoin cream significantly lightened hyperpigmentation in 90% of those in the treatment group, compared with 33% of those receiving a vehicle cream.[21] Hence, topical tretinoin may be indicated to treat dyspigmentation, a common manifestation of photoageing in individuals with darker skin pigmentation. However, in people with sensitive skin types, the exfoliative properties of retinoids can cause dryness and irritation, leading to postinflammatory responses that can worsen hyperpigmented lesions or patches.

Assessment of a patient's skin type, use of skincare and haircare products, cleansing techniques and history of irritation with dermal treatment can aid in deciding the best retinoid treatment regimen. Generally, the newer third- and fourth-generation retinoid formulations may be less irritating than older gel or cream formations, while offering the same level of efficacy.[22]

Topical alpha-hydroxy acids

Alpha-hydroxy acids (AHAs) are a class of organic acids commonly used in cosmetics and dermatology.[23] AHAs are found naturally in foods such as dairy products (lactic acid), fruit (malic acid and citric acid) and sugar cane (glycolic acid).[24] The ancient Egyptian queen Cleopatra was reported to have bathed in sour milk, which contains lactic acid, to smooth her skin and make her appear more youthful.[25,26]

The precise mechanism of action of AHAs is not fully defined. However, AHAs are hypothesised to affect the epidermis and dermis by reducing the pH, thereby inhibiting transferases and kinases, reducing calcium ion concentration and promoting desquamation and cell growth.[24] Studies have also shown that glycolic acid accelerates collagen synthesis and epidermal turnover while modulating matrix degradation and inhibiting melanin formation through antityrosinase activity.[27] The extent of the exfoliative effect of AHAs is determined by the concentration and pH of the product.

AHAs are often present at lower concentrations (4 to 20%) in nonprescription creams and gels for long-term application on aged skin and also in cleansers, moisturisers, toners, masks and age-spot removers. AHAs at higher concentrations (over 20%) are often used in chemical peels applied by dermatologists, as described below (*Chemical peels*).[28]

Research on the effectiveness of low-concentration AHAs is limited. However, a study of 8% glycolic acid or lactic acid applied daily over 22 weeks found that more than 70% of patients reported a noticeable improvement in the appearance and texture of photoaged skin.[25] Daily application of 12% lactic acid for three months was also shown to increase epidermal and dermal firmness and thickness.[25] The effect of AHAs on photoageing is not as well established as that of retinoids, and there is no evidence that high-cost creams with or without AHAs are more efficacious than low-cost creams.[24,29] Long-term effects of AHAs on the rate of exfoliation are unknown, although the skin may develop tolerance

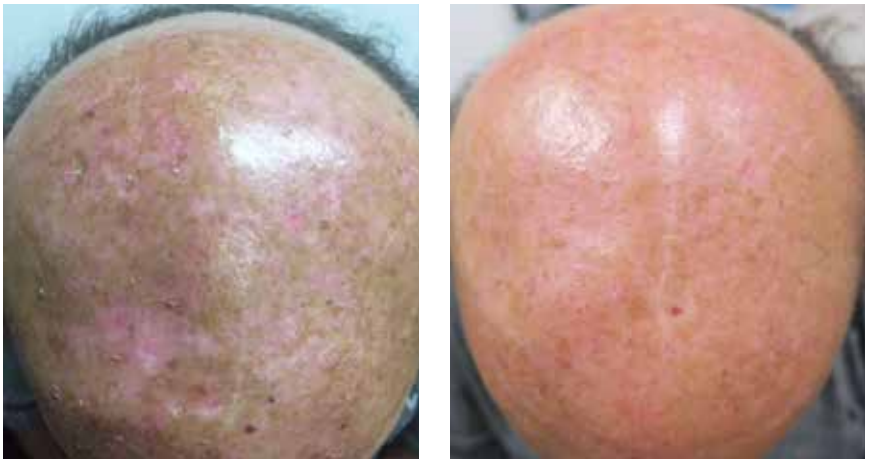
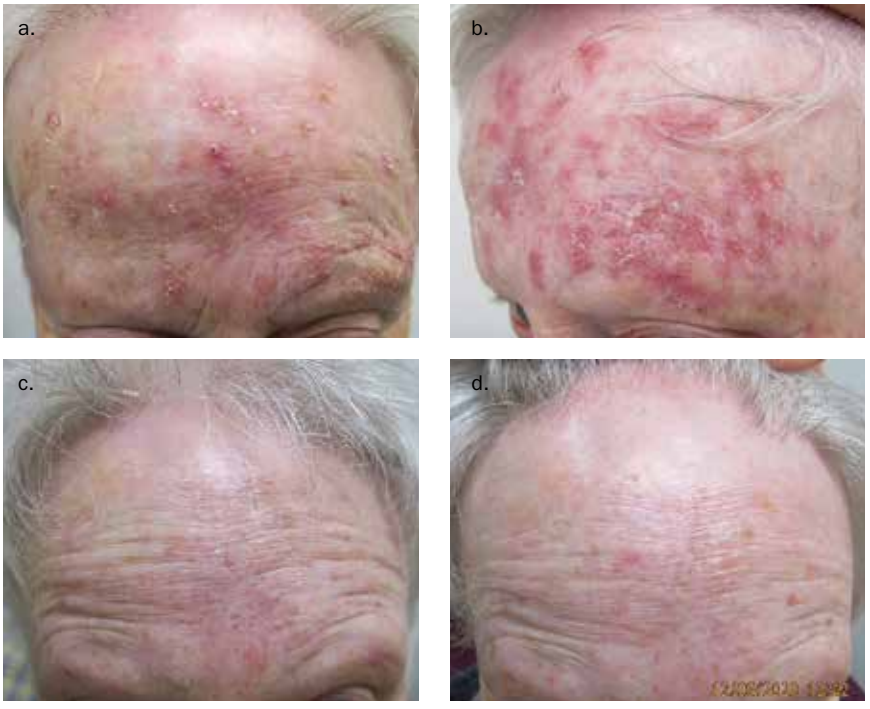


Figure 3. Effect of 5-fluorouracil treatment on severely photodamaged skin: before (left) and after (right) treatment.
Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.



Figures 4a to d. Stages of treatment of severely photodamaged skin with 5-flurouracil cream: before (a, top left), during (b, top right), six months after (c, bottom left) and three years after (d, bottom right) treatment.
Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

to the stimulatory effect of AHAs in cell shedding.[28]

Adverse reactions to AHAs depend on their pH and concentration, but daily application of a concentration of up to 20% is generally well tolerated in patients with normal skin. Patients should still be informed of the potential side effects of skin irritation, stinging, photosensitivity from exfoliation of the stratum corneum, pain and erythema.[23,24]

Research into AHAs led to the discovery of polyhydroxy acids. These include lactobionic acid, which has similar effects to AHAs with a better side-effect profile.[27]

Field cancerisation treatments

Precancerous changes and actinic keratosis are components of photoageing. Field treatments are available that aim to treat both visible and subclinical lesions, termed the 'cancerised field'.[30] These treatments include, but are not limited to, 5% fluorouracil cream, 5% fluorouracil chemowraps, 4% 5-fluorouracil cream, 5% topical imiquimod, 3% diclofenac in 2.5% hyaluronic acid gel, photodynamic therapy, dermabrasion and oral chemoprophylaxis agents (Figure 3 and Figures 4a to d).[31]

Chemical peels

First documented in ancient Egypt, superficial and medium-depth chemical 'peels' are safe, effective clinic-based procedures used to treat photoageing by wounding the skin with a caustic substance. Chemical peels cause partial or complete destruction of the epidermis or dermis, resulting in subsequent exfoliation, regeneration and remodelling of the layers, leading to improved skin tone and skin tightening.[1,4] Chemical peels can also be used to treat acne vulgaris, actinic or solar keratoses, melasma and scarring.[1] Patients should not be offered a chemical peel if they have an active infection, open wound, history of allergy to a peeling ingredient, recent isotretinoin therapy (unless being treated with a superficial chemical peel) or if they are pregnant.[1]

Types of chemical peel

Chemical peels are classified according to the depth of skin affected as superficial, medium or deep. Superficial peels target the epidermis and the epidermal-dermal interface and cause basal keratinocyte renewal and reactive inflammation that stimulates neocollagenesis.[32] Clinicians can use a superficial peel to treat mild photoageing. Examples of superficial peel agents include 10 to 30% salicylic acid, 20 to 70% glycolic acid, Jessner's solution and trichloroacetic acid at

a concentration less than 20% .

Medium-depth peels target the entire epidermis and papillary dermis, and even the upper reticular dermis, causing skin regeneration from the follicular epithelium. Medium-depth peels are used for moderate photoageing (Figures 5a to c).

Deep peels penetrate the midreticular dermis, causing intense collagen synthesis and protein coagulation, which is clinically observed as frosting.[32] They are suitable for severe photoageing and are best for skin phototypes I and II.[26] Deep peels are rarely used and should be performed only by experienced clinicians because of the high risk of side effects such as hypopigmentation, demarcation, scarring and (in the case of phenol) cardiac effects. Examples of deep chemical peeling agents include trichloroacetic acid at a concentration over 50% and the Baker-Gordon formula, containing phenol and croton oil.[1,4,32]

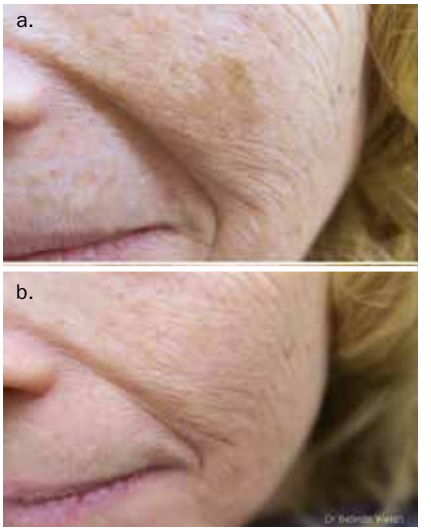
Chemical peels and darker skin

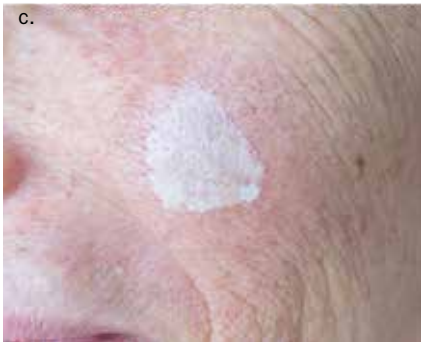
Special considerations apply to the use of chemical peels in people with Fitzpatrick skin phototypes IV to VI. In this group, chemical peels are not generally used to treat photoageing but rather for mottled dyschromia, acne vulgaris, postinflammatory hyperpigmentation, melasma and pseudofolliculitis barbae.

Superficial peels are well tolerated by those with darker skin. However, clinicians should avoid medium-depth and deep peels because of the high risk of disfiguring, long-term postinflammatory pigment changes or hypopigmentation from an unpredictable response of melanocytes to injury.[26] The risk of postinflammatory pigment changes can be reduced by meticulous procedure planning (such as starting with a low-potency peel and titrating up) and close monitoring after treatment. Treating prolonged erythema with emollients and topical corticosteroids can help to avoid dyschromia.[26]

Ablative skin resurfacing with laser

Ablative laser skin resurfacing is the process by which the epidermal and superficial dermal layers of the skin are removed to minimise the signs of photoageing. Ablative skin resurfacing is also used to treat scarring, actinic keratoses, seborrhoeic keratoses and facial wrinkles.[33]





Figures 5a to c. A solar lentigo before (a, top left) and after (b, bottom left) a chemical peel with 25% trichloroacetic acid. c (above). 'Frosting' from the peel treatment.

Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

Laser ablation for facial rejuvenation started with the continuous carbon dioxide (CO_2) laser in the 1980s. For a time, this was regarded as the gold standard for the treatment of photoageing. The CO_2 laser produces an invisible beam that emits energy at a wavelength of 10,600 nm, which is primarily absorbed by water, the most abundant chromophore in the skin. The delivered light energy contracts the skin immediately by denaturing collagen, which subsequently stimulates the production of new collagen. The CO_2 laser can markedly improve rhytids, dyspigmentation and skin laxity but best targets fine wrinkles around the eyes and mouth.[4,34] Nonetheless, because of the difficulties in controlling tissue-dwell time, CO_2 lasers were prone to excessive thermal diffusion and unintended tissue damage, leading to a high risk of char formation, pigment changes, fibrosis, scarring and prolonged recovery.[4,35]

The subsequent development of the erbium:yttrium aluminium garnet (Er:YAG) laser allowed greater precision and depth of cutaneous ablation, with a reduced side-effect profile.[35] Like CO_2 lasers, Er:YAG lasers act on water but energy absorption is 12 to 18 times greater, leading to complete ablation of tissue with little thermal damage.[36] Er:YAG lasers have less of a skin tightening effect than CO_2 lasers but may be preferred by dermatologists to treat dyschromia and fine wrinkles or areas with a high risk of scarring, such as periorbital skin. Er:YAG laser therapy has a shorter recovery period, less postoperative oedema and fewer side effects.[34,37]

Because of the high risk of side effects with ablative lasers, they should be used only by experienced clinicians and in people with Fitzpatrick skin type I (the latter because of the risk of relative hypopigmentation). Anaesthetic techniques such as eutectic mixture local anaesthetics (EMLA) cream, regional nerve blockade for cosmetic units and intravenous sedation or general anaesthesia for the full-face ablative laser are needed to ensure patient comfort during epidermal ablation and dermal heating.[38]

Fractionated laser and radiofrequency therapy

The prolonged postoperative recovery time and significant risk of side effects with traditional ablative laser therapy prompted the development of fractionated therapies in the 2000s. Fractional laser therapy uses narrow columns of laser light to create microscopic thermal zones surrounded by islands of healthy tissue, allowing rapid re-epithelisation and healing.[39]

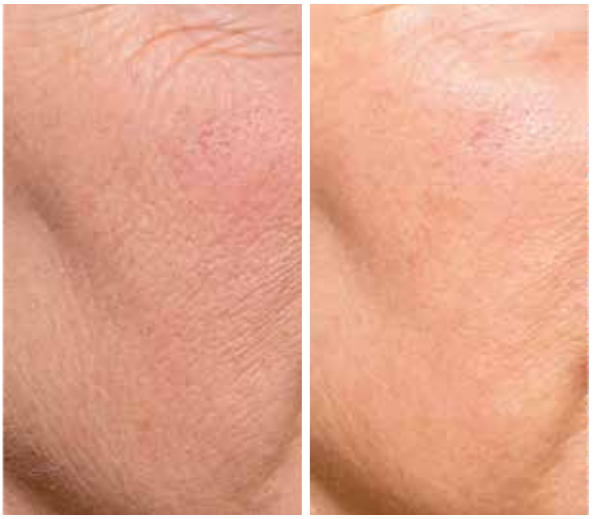


Figure 6. Photoageing before (far left) and after (left) one session of ablative fractional laser therapy with a fractionated CO_2 laser.

Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

Ablative and nonablative fractionated lasers

Fractional laser therapy can be ablative or nonablative. Ablative fractionated lasers are effective in treating dyspigmentation, skin laxity, skin rhytids and atrophic acne scarring, and their use is significantly safer than conventional ablative resurfacing (Figure 6). However, there is still a high risk of complications in the form of scarring, discolouration and skin infection. Ablative fractionated lasers include the 10,600 nm fractional CO_2 laser, 2940 nm fractional Er:YAG laser and the 2790 nm fractional erbium:yttrium scandium gallium garnet (Er:YSGG) laser.

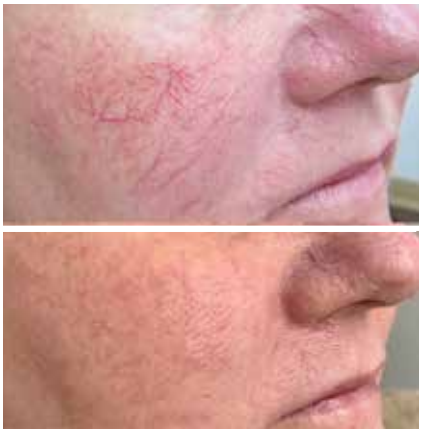


Figure 7. Actinic telangiectasia before (top) and after (bottom) treatment with a pulsed dye laser.

Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

Nonablative fractionated lasers combine the safety and gentleness of fractionated and nonablative technologies, delivering narrow beams of high-energy light at differing wavelengths to target tissue water, leaving the stratum corneum intact. Nonablative fractional laser therapy can improve skin texture, wrinkling, dyspigmentation and telangiectasia and can safely treat the neck, chest and extremities. Examples include the 1410 nm laser, 1440 Nd:YAG laser and 1540 nm pulsed laser.

Although ablative fractionated lasers can be more effective than nonablative fractionated devices at improving fine lines and skin texture, they typically produce more discomfort and have a longer recovery time. For these reasons, nonablative fractionated lasers have increased in popularity for the treatment of photoageing. These lasers are also effective in darker-skinned individiuals with reduced risk of pigment changes.

Skin tissue contraction after fractional resurfacing has been shown to persist for a minimum of one year after the procedure.[39] Operators may use topical anaesthetics alongside nerve blocks or intralesional anaesthesia for procedures involving broad regions, such as the central forehead.[33]

Fractionated radiofrequency devices

Fractionated radiofrequency devices deliver another type of fractionated therapy that uses deep dermal heating in an inverted-cone distribution. These devices are used for photoageing treatment, skin tightening and reduction of rhytids and scars. As radiofrequency energy does not target epidermal melanin, it can be used to treat all skin types (see below). Radiofrequency devices are safe and effective with no patient downtime.[40]

Facial resurfacing and darker skin

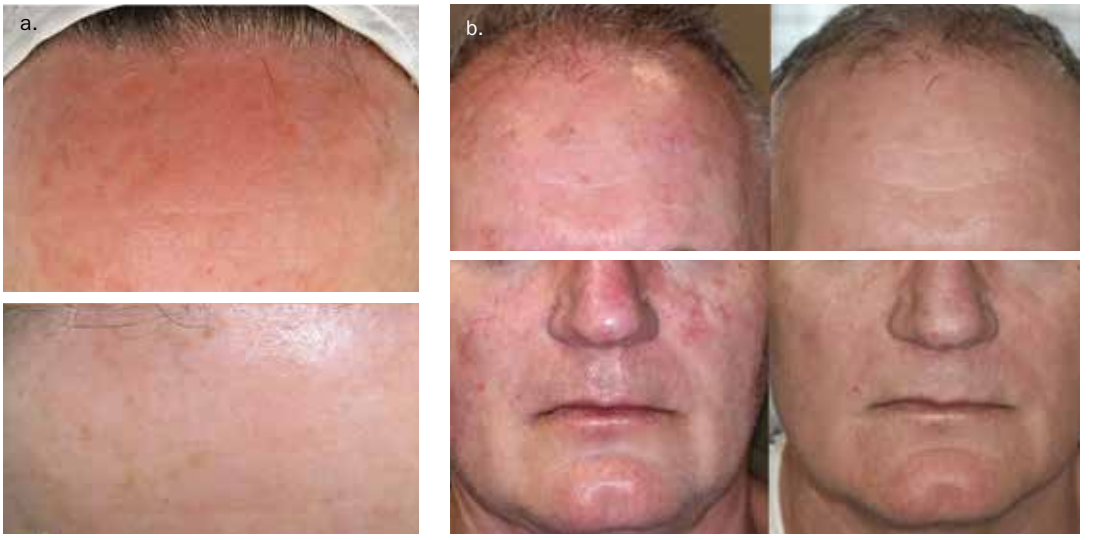
A common complication of facial resurfacing in patients with darker skin is postinflammatory hyperpigmentation. In some cases, hyperpigmentation can occur three to four weeks after treatment and persist up to six to nine months.[15] The rate of postinflammatory hyperpigmentation increases with the energy and density of the treatment but is often unpredictable. Hence, it is crucial to start with conservative settings in patients with skin of colour.

Non-CO_2 fractional resurfacing is the preferred modality for people with skin phototypes IV to VI, as CO_2 laser use carries a higher risk of laser-induced dyspigmentation.[33,34] Counselling and implementation of a pretreatment topical regimen consisting of sunscreen and prophylactic topical hydroquinone or topical retinoids are essential for all patients undergoing facial resurfacing. Strict sun avoidance before the procedure and for several weeks or months afterwards is crucial.

Treatment of delayed onset hyperpigmentation involves broad-spectrum sunscreen, topical bleaching agents such as hydroquinone or light glycolic acid peels. Other bleaching agents such as kojic acid and azelaic acid may also be helpful for long-term management of postinflammatory hyperpigmentation.[9]

Nonablative rejuvenation with laser, light and infrared therapy

The undesirable adverse effects and long recovery time after ablative therapies led to the development of nonablative laser, light and other energy-emitting devices. These devices were initially designed for managing vascular and pigmented abnormalities but have been adapted for skin rejuvenation.[5,41]



Figures 8a and b. Effect of one treatment session with a pulsed dye laser followed by CO_2 laser-assisted photodynamic therapy. a (far left). Before (top) and after (bottom) treatment. b. Before (left) and after (right) treatment.

Image courtesy of Dr Belinda Welsh, Complete Skin Specialists, Melbourne, Vic.

Nonablative treatments selectively damage the dermal tissues, leaving the epidermis intact, and are associated with less morbidity and downtime.[33,42]

Most nonablative systems emit light in the infrared range of the electromagnetic spectrum and target water molecules. Examples include the infrared nonablative 1320 nm Nd:Yag laser, 1450 nm diode laser and 1540 nm Er:glass laser. These are suitable for people with mild facial or nonfacial photodamage.[43,44] Most studies report clinical improvement in facial and nonfacial rhytids of 30 to 50% after a series of these nonablative laser treatments.[44]

Pulsed dye lasers are considered the treatment of choice for cutaneous vascular disorders. These lasers emit visible (yellow) light, which is selectively absorbed by oxyhaemoglobin and can treat facial telangiectasias, port-wine stains, haemangiomas and vascular growths (Figure 7). Off-label uses of pulsed dye lasers include treating rhytids, actinic keratosis and Bowen's disease (Figures 8a and b). Side effects include transient purpura, hyperpigmentation and atrophic scarring.[45]

Another type of nonablative device uses intense pulsed light (IPL). This is not a laser but a polychromatic flashlamp-based device used to treat vascular and pigmented lesions.[43,46] It emits light in the 500 to 1200 nm wavelength range and is useful in treating large regions and the decolletage area.[47] The indications for IPL therapy include photodamage, lentigines, hyperpigmentation and vascular lesions including telangiectasias. Long-term IPL treatments have been linked to youthful changes in gene expression and retardation of skin ageing. IPL devices are used mainly in patients with skin phototypes I to III and are generally avoided in darker- skinned patients because of the risk of epidermal injury and melanin chromophore competition.[47]

Special considerations for skin phototypes IV to VI

The development of the novel radiofrequency device to deliver energy in electrical current mode has added to the armamentarium of photoageing therapies for different skin types. Its main advantage is the minimal risk of postinflammatory hyperpigmentation in darker skin types. The radiofrequency device relies on the electric property of the target tissue, as the impedance of subcutaneous fat to electric currents generates heat. This leads to an immediate tightening effect from collagen contraction and long-term neocollagenesis.[36]

A comparative study examining the efficacy of radiofrequency, IPL and carboxy therapy in 60 patients (16 with skin phototype IV) resulted in a statistically significant decrease in Glogau score after intervention in the radiofrequency treatment group.[48] Radiofrequency energy can also be combined with optical energy such as IPL to improve facial hyperpigmentation, telangiectasias and skin texture.[49]

Conclusion

Many interventions are available for the management of photoageing. These include topical therapies, chemical peels and laser, light and other nonlaser treatments. The development of fractional and nonablative rejuvenation and radiofrequency techniques has allowed regimens with shorter healing times and reduced side effects that are suitable for a wider range of skin phototypes. The Glogau Scale for severity of photoageing is a useful tool in treatment planning. Clinicians should consider the patient's goals, severity of photoageing and skin phototype when referring patients for photoageing therapy. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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An introduction to field therapies for photoageing

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Rosacea

A thorny problem with a rosy outlook

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Rosacea is a common and often underdiagnosed chronic inflammatory centrofacial dermatosis, with a diverse clinical presentation. Symptoms can have profound impacts on the social and psychological wellbeing of affected patients. Optimising management requires an accurate diagnosis and tailored treatment to the presenting features of the individual patient.

Rosacea is an often underdiagnosed chronic inflammatory centrofacial dermatosis.[1] It is diverse in its clinical presentation and is characterised by exacerbations and remissions.[2] Symptoms and signs encompass flushing, erythema, papules and pustules. Ocular involvement can occur in up to 50% of patients with rosacea and symptoms can be nonspecific.[3] Phymas or enlargement and thickening of the facial skin, particularly the nose in men, is a diagnostic feature of rosacea (Figure 1).[4] Initially, symptoms and signs may be transient, but persistent erythema with telangiectasia can develop over time due to repeated vasodilation.[5]

Rosacea is estimated to affect up to 5.5% of the global population.[6] It can occur in all skin types; however, it predominantly affects people with fair skin, especially those of Celtic heritage.[7] Men and women are both affected, although women have a slightly higher prevalence and men develop phymatous changes more frequently.[8,9] Typically, symptoms will peak from 30 to 50 years of age.[10]

Rosacea symptoms are often distressing and can have profound impacts on the social and psychological wellbeing of affected patients. People with rosacea have

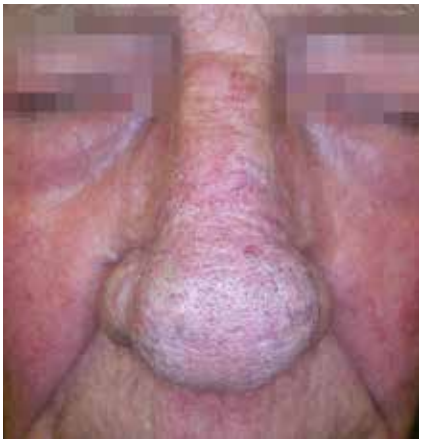

Figure 1. Rosacea complicated by phymatous changes.
Photo courtesy of A/Prof Alvin Chong.

KEY POINTS

- Rosacea is a common and often underdiagnosed inflammatory centrofacial dermatosis.
- Rosacea has a diverse clinical spectrum and includes symptoms of flushing, erythema, papules, pustules and, for some, skin thickening or ocular symptoms.
- Rosacea can have a profound impact on the social and psychological wellbeing of those affected.
- Early recognition and treatment can improve quality of life.
- Treatment options are diverse and should be tailored to the individual.

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1. DIFFERENTIAL DIAGNOSES OF ROSACEA[2,11,14]

- Seborrhoeic dermatitis
- Allergic/irritant contact dermatitis
- Photodamaged skin
- Periorificial dermatitis
- Acne
- Keratosis pilaris rubra
- Eczema
- Lupus erythematosus
- Steroid rosacea*
- 'Maskne' (acne mechanica)

* May occur after application of topical corticosteroids to the face.

2. DIAGNOSTIC CRITERIA FOR ROSACEA[2,9]

Primary diagnostic features
The following two features are independently diagnostic for rosacea:

- fixed centrofacial erythema: erythema in a characteristic centrofacial pattern that may periodically intensify (flushing)
- phymatous changes: patulous follicles, skin thickening or fibrosis, glandular hyperplasia and bulbous appearance of the nose (rhinophyma is the most common form)

Major features
In the absence of primary diagnostic features, the presence of two or more of the following major features can establish the diagnosis of rosacea:

- inflammatory papules and pustules
- flushing: frequent and typically prolonged
- telangiectasia: predominantly centrofacial in skin phototypes I to IV, rarely seen in darker phototypes
- ocular manifestations

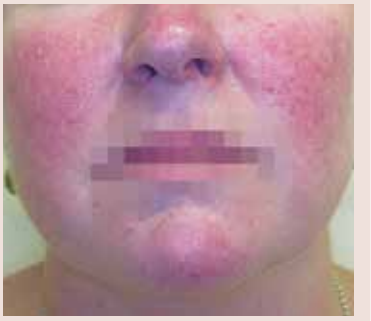
Minor features
The following minor features may also present with diagnostic or major features:

- burning and stinging sensation of the skin
- oedema: facial oedema
- dry appearance: central facial skin may be rough and scaly

3. A WOMAN WITH ERYTHEMATOTELANGIECTATIC ROSACEA

A 52-year-old woman presented with a several year history of periodic flushing and erythema to her cheeks, nose and chin. More recently, she had noticed the erythema was constantly present. On examination she was diagnosed with erythematotelangiectatic rosacea. Patient education focused on avoiding triggers and skin irritants in addition to the importance of photoprotection. She was effectively managed with vascular laser.

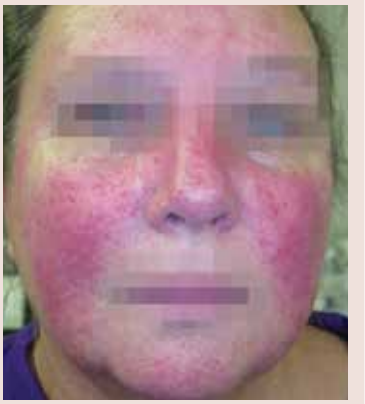
Photo courtesy of A/Prof Alvin Chong.



4. A WOMAN WITH ERYTHEMATOTELANGIECTATIC AND PAPULOPUSTULAR ROSACEA

A 55-year-old woman presented with a 10-year history of tender papules and pustules, periodic flushing and erythema to her cheeks, forehead, nose and chin. On examination, she had features of both erythematotelangiectatic rosacea and papulopustular rosacea. She was managed with 100 mg oral doxycycline daily for six months, along with daily application of topical ivermectin. Although she had a partial response to this regimen, she requires long-term oral isotretinoin to optimise control.

Photo courtesy of A/Prof Alvin Chong.



increased levels of embarrassment, social anxiety and depression and a decreased quality of life.[1] Appropriate treatment of symptoms and signs of rosacea results in an improved quality of life for affected patients.[1]

Pathophysiology

The pathophysiology of rosacea is yet to be fully elucidated but is known to be influenced by genetics and neurovascular dysregulation, in association with an abnormal cascading innate and adaptive immune response.[7,9]

Flushing and erythema develop from increased vascular reactivity, which contributes to increased blood vessel density near the skin surface.[11] Endogenous and exogenous triggers activate primary proinflammatory cytokines resulting in inflammation, which induces the characteristic histopathological features of rosacea. These triggers include sun exposure, heat and noxious cold, spicy food, smoking, exercise and alcohol.[12] Microbes such as the *Demodex* mite are thought to be an additional trigger for this inflammatory cascade.[13] In women during menopause, hot flashes may also trigger rosacea flares. Exposure to increased sunlight in the summertime may be a trigger for some people, whereas for others winter months will trigger symptoms through temperature fluctuations, cold temperature, icy winds and dry heat through heating systems.

Investigations

Rosacea is a clinical diagnosis and, as such, there are no histological or serological

markers. Histology, patch testing and serology should be considered for cases if there is diagnostic uncertainty, such as the need to exclude allergic contact dermatitis or lupus erythematosus.

Diagnosis

Erythematous facial dermatoses can pose significant diagnostic challenges. Differential diagnoses that need to be considered are outlined in Box 1.[2,11,14] It is important to remember that rosacea can coexist with other conditions (e.g. rosacea and photodamage or rosacea and perioral dermatitis) so it is possible to have more than one condition contributing to the presenting features.

Rosacea was previously classified into four subtypes (erythematotelangiectatic, papulopustular, phymatous, ocular) with one variant (granulomatous). In recent years, our understanding of rosacea has evolved. A new classification system has been developed based on diagnostic criteria, including major and minor features (Box 2).[9] The primary diagnostic features, which are independently diagnostic for rosacea, focus on persistent centrofacial erythema with periods of increased intensity and phymatous changes. In the absence of diagnostic features, a diagnosis of rosacea can be made if there are at least two major features, encompassing flushing (transient erythema), inflammatory papules and pustules, centrofacial telangiectasia and ocular manifestations. Minor features might also present with diagnostic or major features and encompass burning, stinging, oedema or dry sensation of the skin.[2]

Ocular symptoms are common and may include burning, itching, watering, grittiness, photosensitivity, lid margin or conjunctival erythema with or without recurrent stye and chalazion formation.

Comorbidities

Rosacea can often occur with other dermatological conditions, including extrinsic photoaging, telangiectasias, seborrhoeic dermatitis, acne, irritant contact dermatitis and keratosis pilaris. More recently, it has often been associated with 'maskne', or acne mechanica, from mask wearing in the context of the pandemic.[14] Maskne can be differentiated from rosacea as it will usually onset within six weeks of starting regular facial mask wear and will typically be distributed over the lower half of the face (underneath where the mask is worn). Maskne, unlike rosacea, will also typically present with comedones.[15]

There is also emerging evidence linking rosacea with other organ systems and

5. AN ELDERLY MAN WITH PAPULOPUSTULAR ROSACEA

A 75-year-old man presented with a 30-year history of tender facial papules, pustules and nodules with some background erythema. Examination showed severe papulopustular rosacea, particularly to the cheeks. He requires extensive periods of 100 mg daily oral doxycycline to maintain control.

Photo courtesy of A/Prof Alvin Chong.

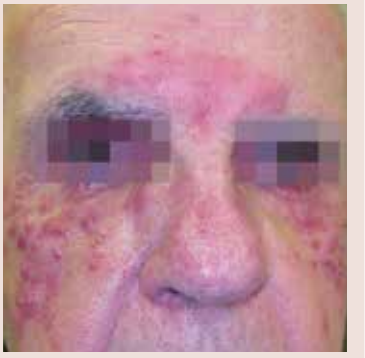


TABLE. COMMONLY USED TOPICAL THERAPIES AVAILABLE IN AUSTRALIA FOR ROSACEA

Topical medication	Application	Notes
Metronidazole	Twice daily for up to 3 to 4 months	• Targets inflammatory papulopustules • Available as 0.75% cream and gel formulations • Has a long history of safety and moderate efficacy • Mild stinging and burning can occur on application. Burning and stinging may be worsened with either gel or cream formulations, which may improve with change of formulation • Pregnancy category B2
Azelaic acid	Once daily	• Targets inflammatory papulopustules • Available as 15% gel and foam or 20% cream formulations • Similar efficacy to metronidazole • Pregnancy category B
Ivermectin	Once daily for up to 12 weeks	• Targets inflammatory papulopustules • Available as 1% cream • Reported to be more efficacious than 0.75% metronidazole cream[20] • Pregnancy category B3
Brimonidine tartrate	Once daily	• Used to manage moderate to severe facial erythema • Available as 0.33% gel • Has a rapid onset (in as little as 30 minutes) of noticeable reduction in erythema after the first application, lasting up to 12 hours • May be associated with a rebound erythema • Pregnancy category B3

comorbidities. Comorbidities include gastrointestinal, cardiovascular, respiratory and neurological disorders. Associations have also been found with several autoimmune diseases such as coeliac disease, rheumatoid arthritis, multiple sclerosis and diabetes mellitus.[16]

Treatment

Treatments should be tailored to the presenting features of the individual and the degree of distress caused by the condition (see the case studies in Boxes 3, 4 and 5). Optimising treatment begins with appropriate patient education. Education should highlight that rosacea is a treatable but not curable condition. Although the exact aetiology is unknown, it is caused by a combination of an overactive immune system, alongside heredity and environmental factors. Education should also emphasise the important role of reducing irritation through photoprotection and gentle skin cleansing as well as the avoidance of exacerbating factors and triggers.[5]

Skin care is important to maintain the epidermal barrier but ideally the cleansing and moisturising routine will be simple and contain a soap-free cleanser.[17] Scrubs and abrasive cleansers should be avoided, along with alpha and beta hydroxy acids such as salicylic or glycolic acid. Cosmetic products should be free from fragrance, colours and essential oils.[18] Patients should also be advised to avoid touching the face when possible throughout the day.[19]

Finding evidence-based and reliable patient information can be challenging, especially with the rise of social media. Although there is no Australian rosacea society, patients may find the US National Rosacea Society (rosacea.org) helpful for further information.

Topical agents

Topical agents are first-line therapy for the treatment of mild to moderate rosacea. They are typically used for their anti-inflammatory effects (such as metronidazole, ivermectin or azelaic acid) or their vasoconstrictive effects (such as brimonidine). Commonly used topical agents are outlined in the Table.[20] Typically, patients are reviewed after six weeks on topical treatment to assess for response.

Systemic agents

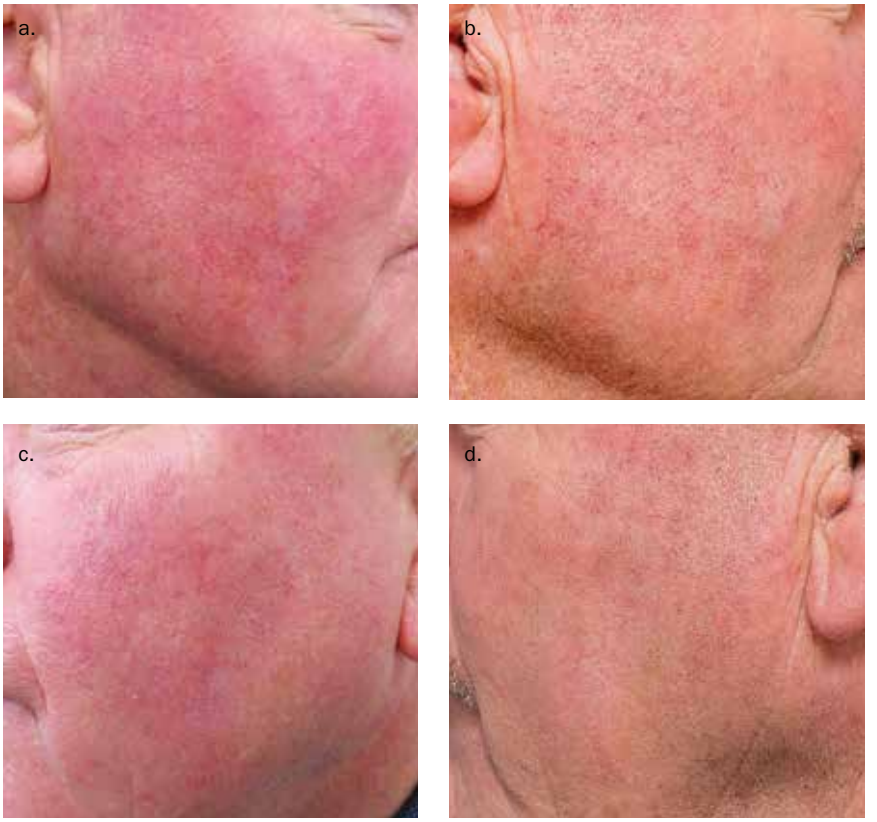
Oral antibiotics play a key role in the management of moderate to severe rosacea. Tetracyclines, such as doxycycline and minocycline, have been the long-term mainstay of papulopustular rosacea, but also have efficacy in ocular rosacea. The primary mode of action is anti-inflammatory. Typically, a patient is started on 50 to 100 mg doxycycline or 50 to 100 mg minocycline daily for six to eight weeks and then reviewed, with a view to ongoing treatment. If a patient fails to respond to doxycycline then referral to a dermatologist should be considered. Patients should not take doxycycline for longer than six months at

a time. Additionally, if they respond but papules and pustules rebound on cessation, requiring repeat courses, then referral to a dermatologist is also required. Adverse reactions of doxycycline may include photosensitivity, candida vaginitis and oesophagitis.[11] Treatment with minocycline should be limited to six months or less, due to the risks of iatrogenic hepatitis, drug-induced systemic lupus erythematosus and skin pigmentation changes. Erythromycin, although not always as effective, may also be trialled and has the benefit of being safe for use in pregnancy and breastfeeding.[21]

Off-label, low-dose oral isotretinoin, as prescribed by dermatologists, has good evidence of efficacy in people with rosacea, and has particular efficacy in the treatment of papulopustular rosacea variants.[22,23] Isotretinoin is thought to act through its downregulation of local cutaneous immunity, but its effect on lipid metabolism may also play a role.[5]

Laser and light devices

Laser and light devices are particularly valuable in the treatment of rosacea-associated erythema and telangiectasia. They can also remodel and rebuild dermal collagen, assisting in improving overall skin quality. Numerous different laser and light therapies are available, including pulsed dye laser (Figure 2), potassium titanyl phosphate laser, long-pulsed-neodymium-yttrium-aluminium garnet laser, intense pulsed light and nonablative and ablative lasers. The choice of laser or light devices should be tailored to the specific presentation of the patient.



Figures 2a to d. Erythematotelangiectatic rosacea responding to pulsed dye laser over four treatments. a (top left). The right side of face before laser treatment and b (top right) after four laser treatments. c (bottom left). The left side of face before laser treatment and d (bottom right) after four laser treatments.

Photos courtesy of Dr Belinda Welsh.

Management of specific features

Specific presentations of rosacea may require tailored management. Phymatous changes can be managed through oral isotretinoin, fully ablative carbon dioxide laser resurfacing or surgical excision.[24]

First-line therapies for ocular rosacea are eye hygiene measures and artificial tears. Often, patients will also benefit from use of systemic antibiotics such as tetracyclines. Early referral for ophthalmological care should be considered for moderate to severe cases.[24]

Treatment options for problematic flushing include beta-adrenergic blockers, such as propranolol or carvedilol. Monitoring for side effects such as bronchospasm, bradycardia and hypotension is important. Alpha-adrenergic receptor agonists, such as clonidine, may also be used but may be associated with systemic side effects.[5] Recently described emerging treatments include off-label use of botulinum toxin.[25]

Conclusion

Rosacea is an extremely common chronic centrofacial dermatosis with diagnostic features of erythema and flushing and tissue fibrosis (phymas). Its impact on the psychological wellbeing of patients should not be underestimated. Although our understanding of the pathophysiology of rosacea remains incomplete, current management strategies are very successful in controlling the signs and symptoms. Optimising management requires accurate diagnosis and tailored treatment to the unique circumstances of each patient and their presenting features. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: Dr Willems and Associate Professor Chong: None. Dr Welsh has received honoraria for a presentation on rosacea for the Candela Academy and from Galderma for media work for Rosacea Awareness Month.

Rosacea

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Pruritic papules in a 10-month-old boy

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Test your diagnostic skills in our regular dermatology quiz. What has caused this itchy skin eruption in a young child?

Case presentation

A 10-month-old boy presents with a six-week history of a pruritic eruption (Figure). He has been otherwise well, with no antecedent fevers, rhinorrhoea, cough, dyspnoea, anorexia or diarrhoea. His past medical history is otherwise normal and his immunisation record is up to date. Aside from cradle cap, he has had no other dermatological issues.

No other members of his family or any close contacts at his daycare centre have had a skin eruption of similar appearance. There is no family history of atopic dermatitis or psoriasis. His parents deny any antecedent trauma or insect bites but noticed that the onset of the rash coincided with a family holiday. They have two dogs, which live in their house.

On examination, diffusely scattered, excoriated papules and pustules are observed on the child's face, arms, legs and trunk. He is well and interactive. There is no involvement of mucosal surfaces, dermographism or lymphadenopathy. The lesions do not urticate.

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Differential diagnoses

Conditions to consider among the differential diagnoses for a child with a persistent, diffuse maculopapular and pustular eruption include the following.

- **Sweet syndrome.** Also known as acute febrile neutrophilic dermatosis, this idiopathic condition is characterised by peripheral neutrophilia, increased inflammatory markers (C-reactive protein [CRP], leukocytosis), fever and acute onset of a skin rash. Paediatric Sweet syndrome is rare, with fewer than 100 cases reported in the literature.[1] Known associations include non-specific respiratory or gastrointestinal tract infection, autoimmune disease (e.g. systemic lupus erythematosus), immunodeficiency (e.g. HIV infection, primary immunodeficiency), drugs (e.g. granulocyte-colony stimulating factor, all-trans retinoic acid) and malignancy (e.g. myelodysplastic syndrome, juvenile myelomonocytic leukaemia).[2] Paediatric Sweet syndrome presents with acute onset of tender, erythematous papules and plaques involving the trunk and head that may appear vesiculated; mucosal involvement is rare.[1,2] In addition to fever, other accompanying symptoms include conjunctivitis, arthralgia and arthritis. Visceral involvement resulting in hepatitis, pericarditis, encephalitis and myositis has been reported as extracutaneous manifestations of Sweet syndrome.[2] Blood test results reflect a leukocytosis, neutrophilia and raised inflammatory markers (erythrocyte sedimentation rate [ESR], CRP). There is variability of cutaneous manifestations of paediatric Sweet syndrome, but biopsy is diagnostic and demonstrates interstitial and perivascular dermal neutrophilic infiltrate with associated leukocytoclasia and nuclear dust without fibrinoid necrosis.[1]
- **Pityriasis lichenoides et varioliformis acuta (PLEVA).** This idiopathic inflammatory dermatosis is characterised by acute onset of a maculopapular eruption at varied stages of development involving the trunk and flexural aspect of the upper and lower limbs.[3] Males are slightly more affected than females. Most cases occur in the second and third decades of life, although PLEVA is also seen in paediatric populations. Despite the occasional generalised distribution of the erythematous maculopapular rash, PLEVA is usually asymptomatic, with an absence of associated constitutional signs or symptoms.[3] Biopsy is diagnostic and demonstrates a diffuse and perivascular lymphocytic (CD8+ T-cells) and histiocytic dermal infiltrate with associated disruption of the dermoepidermal junction.[3]
- **Wells syndrome.** Also known as eosinophilic cellulitis, this rare idiopathic dermatosis is characterised

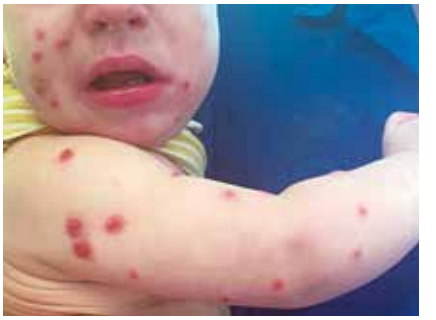

Figure. Crusted erythematous papules and pustules on the face and arm (case patient).

by acute onset of erythematous bullae and plaques over 48 to 72 hours that last up to eight weeks and then spontaneously resolve.[4] Constitutional signs such as fever and lymphadenopathy are uncommon.[4] Associations with Wells syndrome include arthropod bites, infections, drugs (e.g. penicillin, danazol), haemoproliferative disorders and malignancy (e.g. nasopharyngeal carcinoma).[4] A full blood count shows a leukocytosis and eosinophilia in half of patients, with elevated ESR and IgE levels. Biopsy demonstrates 'flame figures' (degenerated collagen bundles due to eosinophil major basic protein), which are indicative of, but not exclusive to, Wells syndrome.[4]

- **Papular acral located syndrome (PALS).** Also known as Gianotti-Crosti syndrome, this is a common dermatosis in the paediatric population. Associated infections are most often enteroviruses but many others have been reported, including cytomegalovirus, Epstein-Barr virus and *Mycoplasma pneumoniae*.[5] PALS presents with an acute, symmetrical eruption consisting of monomorphic papules and vesicles favouring the extensor surfaces of the upper and lower limbs, face and buttocks that remain for approximately 10 days; there is usually sparing of the mucosal surfaces.[5] Children are usually well but may exhibit a prodrome of malaise, fever, diarrhoea and lymphadenopathy. Full blood count results are variable, showing a lymphopenia or lymphocytosis.[5] The diagnosis of PALS is made on a clinical basis, although biopsy demonstrates spongiosis, lymphocyte and Langerhans cell-rich vesicles, and dermal infiltrate with perivascular lymphocytes.[5]
- **Papular urticaria.** This is the correct diagnosis. Papular urticaria is a dermatosis induced by hypersensitivity to insect bites or stings.[6] The pathogenesis is attributed to both immediate (initial) and delayed (late) type hypersensitivity reactions to arthropod antigens.[6] Papular urticaria mostly affects children between the ages of 2 and 10 years and is responsible for approximately 5% of paediatric visits to dermatology clinics.[6] Groups of erythematous, intensely pruritic papules appear on exposed areas, although the pattern of the eruption varies with the causative arthropod and can be generalised.[7] The onset of papular urticaria is seasonal – it more commonly appears during the spring and summer months and is related to mosquito exposure. Household pets can harbour fleas and may be a reservoir for the ectoparasite; the presence of similar pruritic papules in other household members should raise suspicion of scabies infestation or bedbugs (*Cimex lectularius*).[6,7] Biopsy shows dermal oedema, perivascular eosinophils, mast cells and lymphocytes.[6] Papular urticaria is sometimes referred to as insect bite-induced hypersensitivity.

Diagnosis and management

The diagnosis of papular urticaria is mostly clinical and requires a targeted history to discern environmental exposures that coincided with the onset of the skin eruption. Although initial exposures to arthropods induce an immediate hypersensitivity reaction (type I), lesion persistence and/or recurrence is due to ongoing reactivation of delayed-type hypersensitivity reactions propagated by repeated exposure to arthropod antigens, which may take up to six weeks to resolve (provided that the inciting arthropod exposure is removed).[6] The lesions resolve spontaneously when the child has become desensitised to the inciting arthropod antigen and/or the exposure is removed from the environment.

The treatment of papular urticaria is mostly symptom relief, with antihistamines and high-potency topical corticosteroids to treat intense pruritus. Infection control with a topical antibiotic such as mupirocin is helpful because these lesions often become superinfected as a result of scratching.

Prevention is crucial to prevent further exposure to arthropod antigens. Children should wear clothing with long sleeves and insect repellent while outdoors, particularly after dusk. Stagnant water that could encourage mosquito propagation should be removed from the garden and surrounds. Household pets should be treated for flea infestations, and household pesticide fumigation may be required for prolonged cases.

Outcome

In this patient, a skin biopsy was performed to exclude sinister diagnoses such as paediatric Sweet syndrome. A punch biopsy showed a predominantly eosinophilic cellulitis involving the dermis (superficial more so than deep). There were also scattered 'flame figures' to the superficial dermis. There was no evidence of vasculitis or malignancy. He commenced treatment with potent topical corticosteroids for symptomatic lesions and oral antihistamines for persistent itch, which subsequently improved. The source of the reaction was assumed to be fleas, and the family were encouraged to treat the dogs and eradicate their residence of arthropod infestation. The child's skin eruption subsequently resolved over the following months. MT

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COMPETING INTERESTS: None.

Diffuse linear streaks on the trunk and limbs

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Test your diagnostic skills in our regular dermatology quiz. What has caused this rash of maculopapular linear streaks?

Case presentation

A 65-year-old man presents with a two-day history of a mildly itchy rash (Figures 1a and b). He has been otherwise well and denies any fevers, night sweats or unintentional weight loss. The patient does not have any other medical issues or take regular medications. He has not recently travelled or started any new medications.

On examination, there is a symmetrical maculopapular rash involving the patient's trunk and his upper and lower limbs. The macules and papules are erythematous and have a distinct linear 'flagellate' appearance.

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Differential diagnoses

The morphology of the eruption is consistent with a flagellate dermatosis. The term flagellate describes a distribution that is patterned in linear streaks, as though the patient has been whipped. Flagellate rashes are often erythematous at first, evolving to become pigmented with time, and are rare. There are several known causes, some of which are serious. Conditions to consider among the differential diagnoses include the following.

- **Bleomycin toxicity.** Bleomycin, which is derived from *Streptomyces verticillus,* has antineoplastic and antibiotic properties and is used to treat Hodgkin's lymphoma and germ cell tumours.[1] Bleomycin hinders the incorporation of thymidine into DNA and is inactivated by bleomycin hydrolase in most organs – except for the lungs and the skin, where this enzyme is absent.[2] Thus, bleomycin toxicity is usually observed in the lungs, causing pulmonary fibrosis, and the skin, causing multiple mucocutaneous reactions such as flagellate dermatitis.[1,2] Bleomycin-induced flagellate dermatitis presents with linear, hyperpigmented and erythematous pruritic flagellate streaks on the trunk, which can appear within one day and up to nine weeks following bleomycin administration.[1] The pathogenesis of bleomycin-induced flagellate dermatitis is not known and can occur with a total dose as low as 15 mg.[2] Biopsy features are nonspecific and include spongiosis, perivascular eosinophilia, acantholysis, basal vacuolisation, dyskeratosis and melanin incontinence.[1,2]

Figures 1a and b. Case patient. a (top). Linear erythematous maculopapular streaks on the forearm. b (above). The streaks were also observed on the thighs and trunk.

- **Adult-onset Still's disease (AOSD).** This systemic idiopathic inflammatory disease presents with arthralgia and has a characteristic salmon-pink maculopapular erythematous eruption involving the upper and lower limbs that coincides with fever.[3] AOSD requires prompt attention because the complications include aseptic pericarditis, pleuritis and

haemophagocytic lymphohistiocytosis.[3] Despite being the most commonly observed cutaneous manifestation of AOSD, the classic salmon-pink rash is only one of many morphologies. An atypical presentation is linear erythematous and hyperpigmented flagellate streaks of papules and plaques that may bear surface crusting and involve the trunk and limbs.[3] Biopsy of these flagellate lesions shows hyperkeratosis, scattered neutrophilic dermal infiltrate, dermal mucin and dyskeratosis.[3]

- **Dermatomyositis (DM).** This inflammatory condition presents with progressive symmetrical myopathy that usually involves proximal muscles and skin.[4] Pathognomonic cutaneous changes include hyperkeratotic violaceous papules and plaques on the extensor surfaces of the upper and lower limbs (Gottron's papules) and a periorbital violaceous, maculopapular rash involving the eyelids (heliotrope rash).[4] An uncommon morphological manifestation of DM is a pruritic, flagellate erythema consisting of linear, violaceous streaks that mainly involve the truncal skin.[5] This type of flagellate erythema is associated with idiopathic DM, and has not been reported in paraneoplastic, juvenile or amyopathic DM.[5] Skin biopsy features of DM are nonspecific and often difficult to distinguish from systemic lupus erythematosus; histopathological changes include perivascular inflammation, increased deposition of dermal mucin, telangiectasias and vacuolar change at the dermoepidermal junction.[6]
- **Shiitake mushroom dermatitis.** This is the correct diagnosis. First described in 1977, the consumption of shiitake mushrooms *(Lentinula edodes)* can cause a characteristic flagellate dermatosis.[7,8] It presents with pruritic, linear streaks of erythematous papules and vesicles commonly affecting the trunk, limbs and posterior neck within one to three days of consuming the mushrooms.[8,9] When the case patient was questioned about his diet, he described eating shiitake mushrooms two days prior to the onset of the rash. The aetiology is thought to stem from the thermolabile polysaccharide toxin lentinan, a known immunomodulator capable of inducing interleukin-1 release and vasodilatation. However, despite initial reports relating to inadequately cooked shiitake mushrooms, flagellate dermatitis also occurs in patients who have consumed thoroughly cooked shiitake mushrooms.[9] The mechanism by which lentinan results in a flagellate dermatitis is unknown. The histopathological features of shiitake mushroom dermatitis are nonspecific and include spongiosis, a focal lymphocytic interface reaction and a perivascular lymphocytic infiltrate.[9]

Diagnosis

In this patient, the diagnosis of shiitake mushroom dermatitis was made from a combination of a clinical history confirming shiitake mushroom consumption and a physical examination demonstrating the typical skin reaction. The absence of a history of medication use and hyperpigmentation excluded bleomycin-induced flagellate dermatitis. A full blood count showed normal white cell count and neutrophils, while a C-reactive protein level was within normal limits. The lack of constitutional symptoms concerning for DM (muscle weakness, photosensitive rash) or AOSD (fever, night sweats, arthralgia) made a systemic inflammatory process less likely. Skin biopsies were performed, which showed a patchy mild interface reaction with patchy vacuolar change and a perivascular lymphocytic infiltrate in the superficial dermis, consistent with shiitake mushroom dermatitis. Immunofluorescence testing returned negative results for IgA, IgG, IgM, C3 and fibrinogen.

Management and outcome

The patient was reassured that the rash was not indicative of a sinister process and he was advised not to consume shiitake mushrooms again. His pruritus resolved with regular application of topical betamethasone dipropionate 0.05% ointment and moisturiser with oral antihistamines as required. He was reviewed two weeks later and his rash had resolved. MT

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