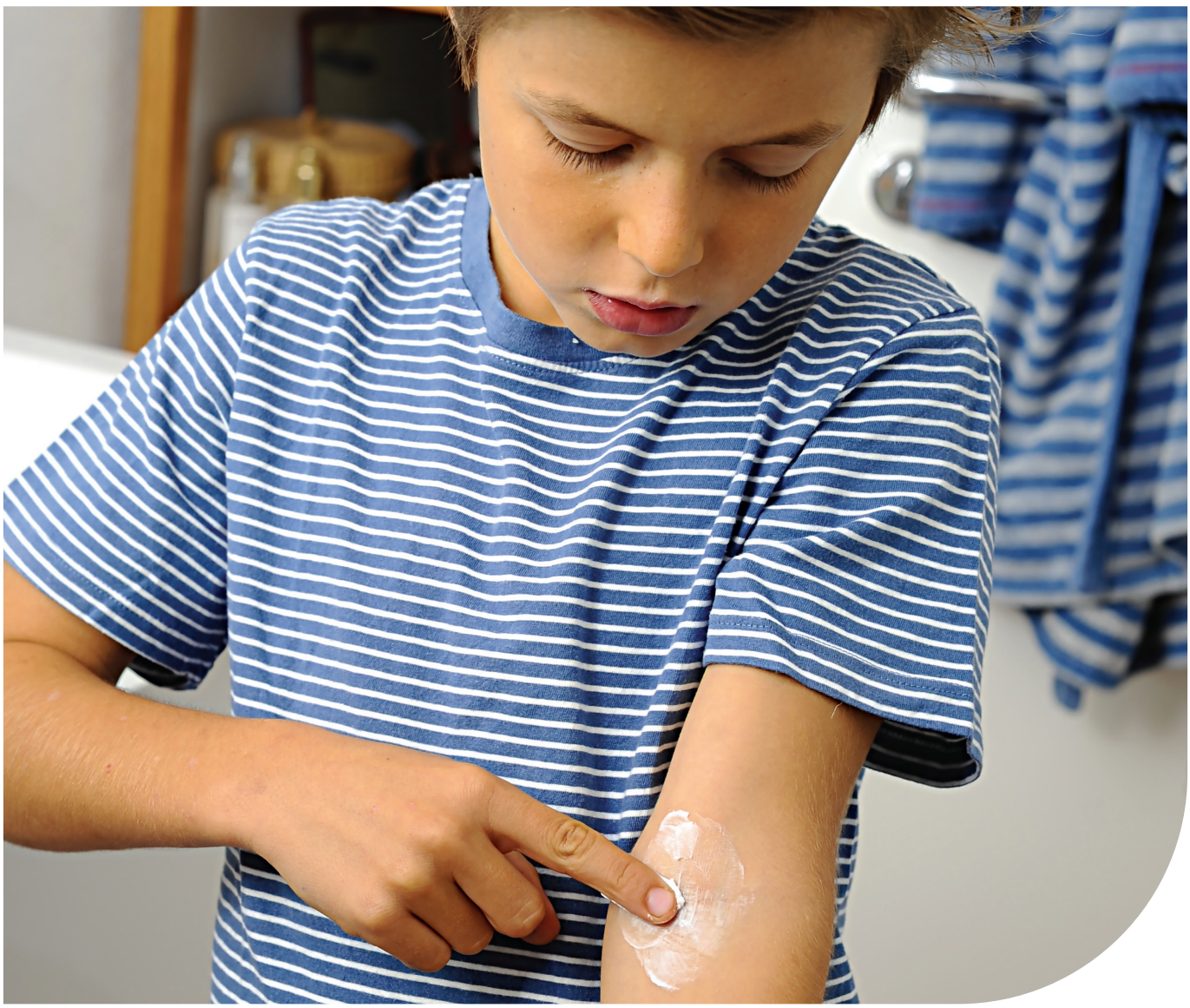
JUNE 2021 VOL 5 NO 1

A MEDICINE TODAY PUBLICATION

Dermatology Collection

PEER REVIEWED UPDATES FOR MEDICAL PRACTITIONERS



Reprints in Dermatology

Common skin problems in children. Managing atopic dermatitis

Common skin problems in children. Rashes other than atopic dermatitis

Treating acne. How to minimise physical and emotional scarring

Therapies for psoriasis. Beyond lesion control

Recurrent painful intertriginous nodules

A sudden outbreak of facial papules and pustules

A rapidly progressing, blistering eruption in a febrile patient

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A MEDICINE TODAY PUBLICATION

Dermatology Collection

PEER REVIEWED UPDATES FOR MEDICAL PRACTITIONERS

FOREWORD FROM THE EDITOR-IN-CHIEF, DERMATOLOGY COLLECTION

This issue considers some of the most common skin disorders seen in general practice as well as some less common presentations.

Accurate and family-focused advice from GPs is key to successful management of atopic dermatitis, the most common chronic skin disease in children, as well as management of other dermatosis in prepubertal children, including nappy rash, neonatal acne and psoriasis.

GPs have a frontline role in managing acne in patients from prepubescence to middle age and in addressing its psychological impact. Many recent developments have occurred in acne treatment.

Treatment of psoriasis has been revolutionised with increased understanding of the immunological mechanisms underlying the condition and expansion in the range of targeted therapies available. Although biologic therapies are prescribed by specialists, it is important for the wider medical community to understand their role.

Finally, test your diagnostic skills in three dermatology quizzes. What are the differential diagnoses and causes of the lesions in these case presentations?

I hope you enjoy reading this informative collection of dermatology articles.

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

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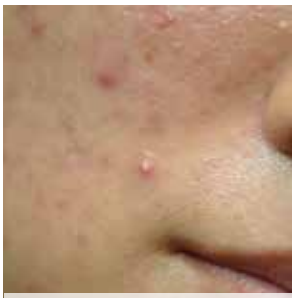

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Common skin problems in children

Managing atopic dermatitis

GAYLE FISCHER OAM, MB BS, FACD, MD

Atopic dermatitis is the most prevalent chronic skin disease seen in children, particularly before puberty. Accurate, family-focused advice from the GP is key to treatment success and maintaining remission.

KEY POINTS

- Atopic dermatitis (AD) is common and the range of severity large, ranging from trivial to life ruining.
- Diagnostic criteria for AD have been established.
- About 50% of patients with AD have an abnormality of filaggrin, an epidermal protein involved in the protective skin barrier.
- Itch, which results in sleep deprivation, can disrupt the lives of children with AD and significantly affect their families.
- Environmental modification is an essential part of management; however, house dust mite reduction measures are only effective among a subgroup of patients and are controversial.
- Topical therapy with emollients that restore the skin barrier is key.
- Topical corticosteroids are gold standard therapy.
- Corticosteroid phobia continues to be a significant barrier to effective treatment.
- Allergy testing is often requested by parents, but it does not change management in most cases and is probably carried out more than is necessary.
- When a child fails to respond to treatment, consider noncompliance, infection, allergy or combination with another dermatosis, most often psoriasis.
- The prognosis for AD is good, with most children recovering by the end of primary school.

Worldwide, atopic dermatitis (AD) is the most common condition seen in paediatric dermatology practice. The prevalence of atopy in the Australian population is about 20% and most patients with the condition are children.

AD is a genetic condition with complex genetic susceptibility moderated by environmental factors. Most affected children have a first-degree family member with an atopic condition, not necessarily dermatitis, and about 40% have a deficiency of the epidermal protein filaggrin, which is involved in the normal skin barrier. Additionally, atopic immune dysregulation related to the T-helper 2 (Th2) cytokine cluster can occur. Children with severe AD commonly have raised total immunoglobulin (Ig) E levels.

Various scoring methods are used to determine severity of AD, for instance the Eczema Area and Severity Index (EASI). These are most useful in a research setting. Assessing severity in a clinical setting can be done pragmatically, not only by noting the extent and clinical severity but also by assessing the impact on quality of life of the child, burden of treatment on the family and degree to which sleep is disturbed.

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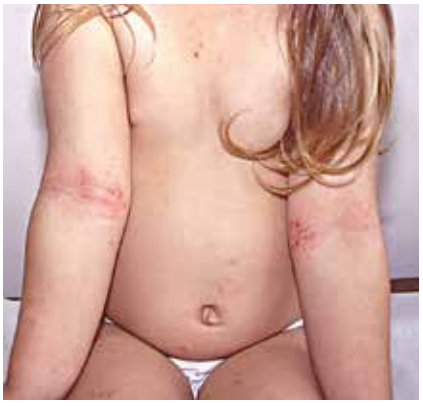

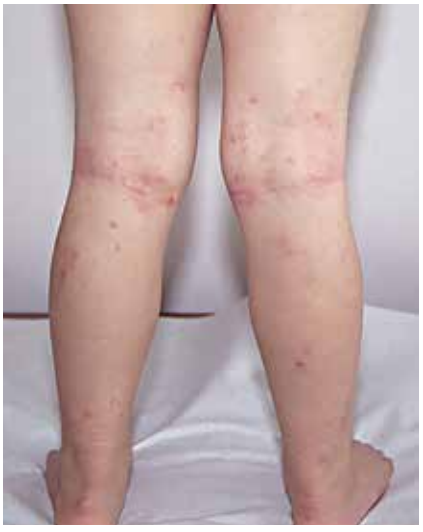

Figures 1a and b. Atopic dermatitis on the cubital fossae (a, above) and popliteal fossae (b, right).

Clinical features

The onset of AD most often occurs in the first year of life between the ages of 3 and 12 months. Clinical criteria for AD established by Rajka and Hanifin and the UK Working party include three or more of itch, typical flexural distribution, patchy, excoriated erythema and personal history of atopy or atopy in a family member.[1] Commonly there is also skin dryness. In children the rash is most often found on the face, cubital fossae and popliteal fossae (Figures 1a and b). The distribution and severity are highly variable, ranging from mild dryness and a minor rash on the arms and legs to total body involvement (Figure 2).

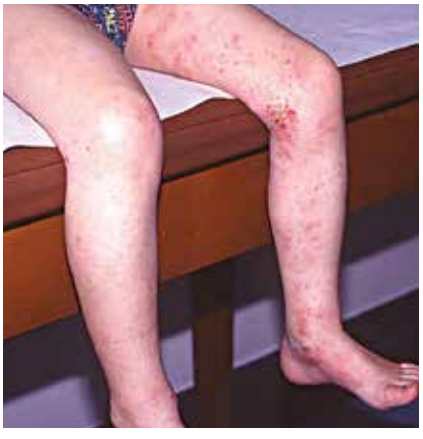

Figure 2. Atopic dermatitis on the legs.

The itching of AD may be very disruptive, particularly during sleep. Severely affected children may wake up many times during the night, and parents often comment that the child's sheets are streaked with blood from excoriations in the morning. Interestingly, small children often forget about the itchiness during waking hours until their clothes are removed, when they can literally go into a frenzy of scratching all over. Constant scratching often leads to areas of thickening of the skin. This is termed lichenification when it occurs in plaques and prurigo when it occurs in discrete nodules. Lichenification complicates AD, making it more challenging to treat.

Cutaneous infections

Cutaneous infections are very common, not only because of constant scratching and disruption of the epidermal barrier, but because of inherent immunological and cutaneous abnormalities in these patients that increase susceptibility. The most common bacterial pathogen is *Staphylococcus aureus*, which causes areas of weeping, crusting and folliculitis (Figure 3). Chronic *S. aureus* carriage exacerbates eczema and is a much more common cause of treatment resistance than allergy.

In some cases, children with AD are also prone to relatively severe infections with herpes simplex virus. In contrast to most children, who may only ever suffer from stomatitis or herpes labialis, widespread or generalised infection with systemic upset may occur. Atopic children are probably not more prone than others to molluscum contagiosum, but the presence of this viral infection certainly exacerbates AD.

Environmental irritants and allergens

Children with AD are sensitive to environmental irritants and allergens, and this can include their topical therapy. It is well known that sand, wool, nylon, grass, soap and bubble bath cause irritation. Temperature changes and overheating are also problematic. Sometimes, even labels and rough seams in clothing can be a problem. Allergy to latex can be a little thought of trap for the unwary if caregivers are wearing gloves. It is common for these children to complain that their topical treatments sting and for their parents to comment that they cause erythema. This does not always indicate true allergy and may only be a problem when skin is excoriated and inflamed. The antiseptic triclosan in some bath oils can cause a cutaneous reaction that simulates a chemical burn. Although many patients with AD have raised IgE levels or positive skin prick test results to house dust mite, its role in causality and

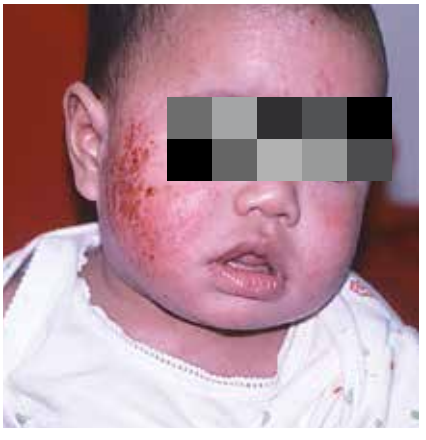

Figure 3. Atopic dermatitis infected with *Staphylococcus aureus*.

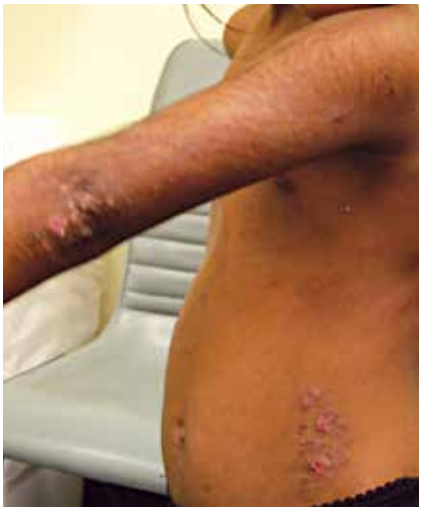

Figure 4. Mixed atopic dermatitis and psoriasis showing lichenification.

management is controversial and probably overvalued. Contact with grass and other airborne allergens such as animal danders, moulds and pollens can exacerbate AD.

Food allergy and intolerance

Food allergy, which is immunologically mediated, and food intolerance, caused by direct histamine release, are not common exacerbating factors in AD but they can be very relevant in some patients. It is common for parents to request allergy testing. Often they have good reason to do so, having observed their child's reactions to certain foods – particularly cow's and soy milk, peanuts, eggs, shellfish and high salicylate foods such as tomatoes and fresh fruits. However, misinformation on the internet leads many to believe that AD is an allergy in itself and to hold high hopes that if they can discover and eliminate the allergen(s) that a cure will result. This is rarely the case.

Dermatitis and psoriasis

The coexistence of dermatitis and psoriasis is not uncommon when AD seems more difficult than usual to control or never completely responds to topical corticosteroids (Figure 4). Both are common skin conditions. Psoriasis in young children is much more subtle than that in adults, and the classic thickened plaques rarely occur. When AD and psoriasis occur together a clinical picture termed 'psoriasiform dermatitis' applies.[2] These children have features of both; however, their condition is usually much more treatment resistant than children with AD only and requires specific psoriasis therapy.

Parents should be asked about the family history, and signs of psoriasis in the child and parents looked for – for example, scaling of scalp and postauricular skin, or cracking under the earlobe and nail pits. Scaling, lichenification and papules on the dorsal surface of the knees and elbows in combination with dermatitis on the ventral surface is common and rarely looks like a typical psoriatic plaque seen in an adult.

Dermatitis and symptomatic dermographism

When children with apparently mild or well-suppressed eczema experience itch out of proportion to their clinical signs, they may have coexistent symptomatic dermographism. Dermographism is a form of chronic inducible urticaria. In this condition, histamine is easily released from mast cells in skin as a result of minor friction such as scratching or overheating. It can uncommonly be associated with allergy. Dermographism is easy to diagnose simply by firmly stroking the skin. This will result rapidly in a red wheal which takes 10 to 20 minutes to resolve (Figure 5). Although in general antihistamines are unhelpful in treating AD other than acting as night-time sedatives, they are useful in this subgroup.

Psychological problems and other pressures

Psychological problems are more often seen in children who are severely affected with AD, and the impact on quality of life should never be underestimated. An Australian study has shown that severe AD is as impactful as other severe paediatric conditions such as diabetes and epilepsy.[3]

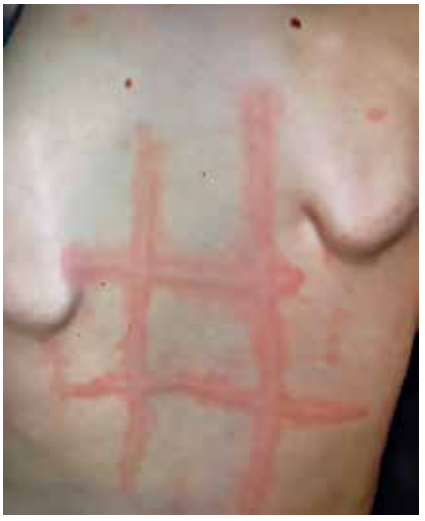

Figure 5. Red wheal produced by firmly stroking the skin of a child with dermographism.

The most common problem is exhaustion from not sleeping well, leading to behavioural problems and poor concentration at school. However, the management of AD can come to dominate the child's and parents' lives, and it is common for any child with a chronic condition to become weary of the daily routine of treatment and to complain, fight, abscond and resist. Many parents are also exhausted, and, in the worst cases, outright rejection of the child by the parents may ensue.

Cost can also become a factor, as many of the required treatments, particularly emollients and bath oils, are not listed on the PBS. In addition, many parents are confused by conflicting information on the safety of treatments, particularly corticosteroids, and almost paralysed by the fear of long-term effects of treating their children.

Management

The management of children with AD is not simple, particularly in severe cases. The following factors need to be considered:

- compliance and counselling
- environmental modification

Figure 6. Patients with severe nonresponsive dermatitis may need dressings. Hospitalisation is often required for such patients.

- control of skin dryness
- medical management of the dermatitis
- control of infection
- management of the dermatitis plus psoriasis combination
- in some cases, investigation and management of allergy.

Compliance and counselling

It cannot be stressed too strongly that AD is a chronic genetic condition. The patient's parents or carers must understand the need for both continuous suppressive therapy at times of activity and ongoing preventive environmental modification in times of remission (see Practice Points and the Parent and Carer Handout). Further, they must understand that AD is rarely entirely caused by allergy and that management of allergy alone rarely delivers good outcomes. Treatment often fails because therapy is ceased as soon as the dermatitis clears, in the belief that a 'cure' has been achieved. When the inevitable relapse occurs, parents may then believe that treatment has been a failure and subsequently abandon further therapy.

Treatment also often fails because parents are apprehensive about using topical corticosteroids. Parents need to be reassured that, when used correctly, topical corticosteroids have an excellent safety record. An Australian study has demonstrated that appropriate use of topical corticosteroids in mild to moderate eczema can maintain an EASI score of 0, without side effects.[4] To encourage compliance, parents need education about the nature of AD, that it tends to become less severe with each passing year, the safety of the medication and the relative unimportance of allergy in aetiology and management.

It is often little things that make a big difference, such as:

- devising a simple regimen that fits in with the family lifestyle
- minimising cost with the use of authority prescriptions
- providing clear written instructions
- recommending that the parents talk to the child's teachers about dust, sand and grass exposure at school. Small children are often expected to sit on the bare floor during school hours and are exposed to grass during sport and recess.

Regular follow up is always important to keep reassuring and reaffirming that parents are doing the right thing, modifying treatment according to response and complications, and praising positive results. There are so many negative influences on these families that it becomes imperative to keep repeating that of all the treatments available, by and large Western medicine still works best and is safe.

Environmental modification

Environmental modification is an essential part of AD management, and one that parents readily accept, in theory at least. It is always important when telling parents what to take out of the child's environment that you suggest what they should put in instead. Soap, shampoo and bubble bath do need to be eliminated. There are numerous soap substitutes that can be used (Box 1). Skin contact with woollen or acrylic clothes, blankets and toys should also be avoided, substituting pure cotton or at least 70% cotton blends.

When dust and other aeroallergens such as animal dander, pollen, grasses and moulds are a genuine problem, children often have an accentuation of their rash in exposed areas such as the periocular area or the thighs where their skin contacts dust on the floor when sitting cross-legged at school. There is a history of exacerbation on exposure, and these children are more likely to have asthma and hayfever.[5] Dust is difficult to minimise; however, using mattress and pillow covers, washing bedding and other fabric that comes in contact with the child's skin in hot water, eliminating dust-catching objects (e.g. fluffy toys) and vacuuming thoroughly can help. If the child has to sit on the floor at school, a washable bathmat should be used. Before taking steps to reduce aeroallergens it is important to confirm with allergy testing that there genuinely is a very significant reaction present.

1. EXAMPLES OF BATH OILS AND SOAP SUBSTITUTES

Bath oils

- QV bath oil (liquid paraffin)
- Dermaveen shower and bath oil (colloidal oatmeal, light liquid paraffin)
- Alpha Keri bath oil (light liquid paraffin, lanolin oil)
- Hamilton Skin Therapy bath and shower oil (light liquid paraffin)

Soap substitutes

- QV wash (glycerin), bar (glycerin, petrolatum, dimethicone, paraffin) and kids balm (liquid paraffin, dimethicone)
- Dermaveen cleansing bar (colloidal oatmeal)
- Cetaphil gentle cleansing bar (glycerin, petrolatum, titanium dioxide)
- Hamilton Skin Therapy gentle wash (glycerol)

Many households, preschools and primary kindergartens have a sandpit. Sand is a major problem for children with AD. It is easy to get rid of the sandpit at home, but parents need to talk to carers about trying to keep the child out of sand elsewhere. Sand tends to accumulate in socks and shoes and is mostly a problem for hands and feet.

In summer, or year-round for the child who is swimming training, chlorinated pools can be a problem. It can be helpful to apply a greasy emollient before swimming and to shower and apply emollient immediately afterwards.

Control of skin dryness

Dispersible bath oil should be used daily in the bath. It is a common belief that baths should be taken infrequently and kept cool, but a normal daily bath helps to reduce bacteria and airborne allergens and irritants on skin without causing dryness as long as such an additive is used (Box 1).

After bathing, an emollient should be applied over the whole body. The frequency of use will depend on the child's degree of skin dryness. For mild cases, application of emollient after bathing is sufficient. For more severe xerosis, application two or three times daily is often necessary. Emollients are easiest to apply when the skin is still damp after bathing.

Numerous emollients are available (Box 2), and the choice depends on the severity of the AD (greasier emollients are used for more severe xerosis), the climate (a less greasy product is needed in hot, humid weather) and personal preference. Cost can also be a factor and, as large amounts are required, compliance is more likely if this is minimised. Simple generic preparations, such as emulsifying ointment BP mixed with water, are as effective as proprietary compounds. Generally, greasier emollients available in tubs tend to be better moisturisers than thinner lotion preparations in pump packs. The adverse effects of some emollients can limit their use. The ubiquitous product sorbolene cream can cause stinging in some children that can lead to noncompliance and loss of confidence in treatment. It is helpful to keep samples of various emollients in the office for patients to try before purchase to determine if there is a problem. Useful over-the-counter emollient preparations include, for example, QV cream, Cetaphil moisturising cream, Dermaveen moisturising lotion, and Dermeze, Epaderm and DermaDrate products (the latter brand is useful for severe xerosis, but may sting).

ATOPIC DERMATITIS: PRACTICE POINTS

- Corticosteroid phobia has reached epidemic proportions in the community. It is essential to be positive and reassuring about the long safety record of topical corticosteroids otherwise parents may be too scared to use them.
- Recommend preparations that do not sting. Sorbolene cream is often the culprit of stinging, but, generally, ointments are less likely to cause this problem. Avoid recommending urea-containing products.
- Remember to make sure parents understand the nature of chronicity. Extra time given at the first consultation will be well worth it.
- The cost of managing atopic dermatitis can be considerable. Minimise cost with authority scripts and encourage parents to buy moisturisers and bath oils in bulk.
- Parents often ask for allergy testing. Although this is not necessary for every child, it is often best to acquiesce: parents are often right.
- Devise a regimen for your patient that is simple to understand and execute: remember this has to be a daily routine and children and parents will tire of it.
- It is not necessary for children to bath infrequently in cool water: this is a myth. Advise parents to add bath oil to the bath, and all will be well.
- Complex regimens and rigid restrictions on the number of days on and off topical corticosteroids do not work for many patients and result in poor control.
- Review regularly. Parents need reassurance and affirmation in the face of enormous pressure that the Western medicine approach to atopic dermatitis is dangerous. The fact is, it still works the best.
- Beware the dermatitis/psoriasis combination as a cause for nonresponsiveness to treatment.
- Parents are very keen to try new noncorticosteroid medications. Inform them that these are still immunosuppressant with, so far, only a relatively short period of follow-up safety data compared with topical corticosteroids. Their child should use sunscreen while using them.

Medical management of dermatitis

Topical corticosteroids, which have been available for many years and for which we have long-term follow up information, remain the treatment of choice for mild to moderate AD. If used correctly, they are very safe and effective. Despite these facts, fear of their use is widespread in the community and is termed corticosteroid phobia. Social media have only added to the distrust of these medications and fear of corticosteroids is as prevalent and troubling now as it was 25 years ago.[6] Thus it is important that doctors prescribing them are positive and reassuring about their usefulness. It is important to keep in mind that many other people, including the pharmacist, baby health nurse, naturopath, friends and relatives – all possibly more trusted by the patient than their doctor – may be denouncing them as dangerous.

The main fears with topical corticosteroids are that they will 'thin the skin' and 'depress the immune system'. Both are theoretically true if potent preparations are overused or applied under plastic occlusion. However, when used as recommended below, this is highly unlikely.

Topical corticosteroids should be applied daily to any areas of active dermatitis, titrating the strength of the

2. EXAMPLES OF EMOLLIENTS

Very greasy
White/yellow soft paraffin, wool alcohols (e.g. Epaderm)

Greasy
Emulsifying ointment (e.g. Dermeze)

Moderately greasy
Sorbolene cream with glycerine 10%, aqueous cream (e.g. QV cream)

preparation and the frequency of application to the severity of the dermatitis. An emollient is applied to the entire skin before the corticosteroid is applied. Patients should have a range of topical preparations. If there is an inadequate response to a milder preparation after three days, a stronger one should be used.

Generally, the use of corticosteroids in children does not differ significantly from that in adults; however, the issues discussed in Box 3 are important to consider.

Other topical anti-inflammatory medications

There are two topical calcineurin inhibitors: pimecrolimus, which is available commercially as a 1% cream; and tacrolimus, which is available through compounding chemists as a 0.1% and 0.03% cream or ointment. Of the two preparations, tacrolimus is the more effective. These products are certainly no more effective, are more expensive and are much more likely to be irritating than topical corticosteroids. A recent meta-analysis has not shown that they are superior.[7]

Pimecrolimus has been evaluated in children and is indicated for the treatment of AD in children over 3 months of age. It is used twice daily. Its main advantage over topical corticosteroids is its lack of atrophogenic properties, particularly in thin skin such as the face in children who are unresponsive to mild corticosteroid preparations or who need to use them continuously.

Pimecrolimus is available on the PBS only with an authority prescription and only for the treatment of facial and periocular AD where there are contraindications to the use of topical corticosteroids. It is significantly more expensive than topical corticosteroids. Compared with topical corticosteroids, its very long-term safety is not as well known, although we have up to 20 years of follow up with calcineurin inhibitors so far. Because of the immunosuppressive properties of these agents, there has been concern that in the long term we may see skin cancer as a result of their use, particularly in sunny climates like Australia. It is wise, therefore, to use a sunscreen on exposed skin being treated. Only time will tell how safe the use of these compounds on young children really is.

Parents of children with AD are sometimes keen to avoid the use of topical corticosteroids by substituting pimecrolimus. Most do not realise that it is an immunosuppressant with its own hazards.

Another new anti-inflammatory product is the topical phosphodiesterase-4 inhibitor crisaborole. It is indicated only for mild to moderate AD, is not PBS listed and is significantly more expensive than topical corticosteroids. Its role in treatment is similar to the calcineurin inhibitors and it may well appeal to parents with exaggerated fears of topical corticosteroids.

Oral immunosuppressive therapy

Most children with AD can be very successfully managed with topical therapy. However, for very severely affected children systemic immunosuppression is required. Any child for whom topical corticosteroids are needed in such large amounts that there could be a genuine chance of side effects is a candidate for such treatment.

Oral corticosteroids are contraindicated because severe rebound is usually experienced on withdrawal, and repeated courses destabilise the dermatitis and can result in erythroderma. This situation is completely different from treating acute exacerbations of asthma.

Oral ciclosporin may be initiated by a dermatologist or clinical immunologist for the treatment of very severe AD in children.

3. USING TOPICAL CORTICOSTEROIDS IN CHILDREN: IMPORTANT ISSUES

- Hydrocortisone 1% is the only corticosteroid that should be used on the flexures. This is also usually true of the face, although more potent corticosteroids may be used on the face for short periods
- The relative potencies of topical corticosteroids are not related to the percent concentration but to the molecules themselves. This has to be learned
- The potency of the medication is titrated to the severity of the rash. Potent preparations may be safely used in children if they are indicated on severity grounds
- Children have poor tolerance of preparations that sting. Ointments are therefore preferable to creams as they are less likely to produce stinging
- In severe, nonresponsive dermatitis, corticosteroids may be used under wet dressings (Figure 6); however, plastic film occlusion should not be used because of the risk of inducing skin atrophy and striae. Patients needing wet dressings often require hospitalisation
- The corticosteroid should be used until the skin has normalised, then ceased until there is evidence of recurrence. It is not necessary to give patients strict guidelines about the number of days on and off corticosteroid treatment as this varies with every patient. Use should be matched to response
- Breaks from therapy, even if brief, reduce the risk of adverse effects
- Children who do not respond to the corticosteroid, and those who flare rapidly after stopping, frequently have coexistent psoriasis and should be referred to a dermatologist. Very rarely they may have an immune deficiency or a rare genodermatosis

Treatment must be very carefully monitored, and this means numerous blood tests and blood pressure readings for the child. This is a huge step for most parents, although certainly it can be sanity-saving in children

Figure 7. Impetiginised dermatitis.

with severe, life-disrupting AD. It is used when all conservative measures have failed to control the dermatitis and the patient's quality of life is severely affected.

Other medications that may be used in children include azathioprine and methotrexate, which is particularly useful when there is coexisting psoriasis. Newer systemic biologic agents that will become available in future include the injectable interleukin (IL)-4/IL-13 receptor inhibitor dupilumab and the Janus kinase (JAK) inhibitors, which are oral medications. Both can be highly effective and are relatively low in side effects.

Control of infection

The most common infections seen in children with AD are:

- impetigo (Figure 7) – most often due to *S. aureus*; occasionally due to a mixed infection of *S. aureus* and *Streptococcus pyogenes*, or *S. pyogenes* alone
- herpes simplex (Figure 8)
- molluscum contagiosum (Figure 9).

Any of the above infections often exacerbate AD, and control of infection is essential before the dermatitis can be treated effectively. A bacterial swab of involved skin is a useful, inexpensive test that confirms infection and determines antibiotic sensitivities. Community acquired methicillin-resistant *S. aureus* is becoming more common and often requires treatment with clindamycin. If herpes simplex is suspected clinically by the presence of grouped vesicles or erosions, viral swabs should be taken. This is always an acute, and sometimes also recurrent, event. When the infection is widespread, treatment with aciclovir or valaciclovir is needed and specialist referral recommended.

Molluscum contagiosum infection, although by no means confined to children with dermatitis, does often make the dermatitis refractory to treatment. The best way to eradicate the lesions is to remove them physically; however, this is often easier said than done. It can be difficult to change the course of the infection and one may have to accept that until the lesions resolve spontaneously, more aggressive treatment of the dermatitis may be necessary.

In many cases, the child's skin is chronically colonised by *S. aureus*. This can result in exacerbation of the dermatitis, difficulty in controlling it, and crusting and folliculitis. When any of these are encountered, cutaneous and nasal bacterial swabs should be taken to confirm the infection and determine the sensitivities of the *S. aureus*. This situation requires more than one course, and at times repeated courses, of oral antibiotics. Adding bleach to the bath water has been shown to be very effective in controlling chronic bacterial skin infection.[8] A topical antibiotic such as mupirocin 2% ointment should be kept on hand to apply to crusted areas twice daily for a week. It is more effective if the crusts are removed by soaking under a wet cloth or in the bath. If nasal carriage is detected, mupirocin 2% nasal ointment should also be used twice daily for seven days.

Dicloxacillin or flucloxacillin are the treatments of choice for obvious secondary infection, but cefalexin or roxithromycin are useful for patients who are allergic to penicillin. Many strains of *S. aureus* are resistant to erythromycin. In some children in whom chronic infection makes AD impossible to control, long-term oral antibiotic treatment may be useful. However, before embarking on this, specialist referral is recommended.

Figure 8. Herpes simplex complicating atopic dermatitis.

Treating the dermatitis/psoriasis combination

Patients with a combination of dermatitis and psoriasis need treatment for both conditions. Therefore, in addition to the usual management of AD, tar creams and shampoos or topical calcipotriol may be needed. It is important that the parent understands which areas of the rash are AD and which are psoriasis. Managing this situation can be difficult, and referral

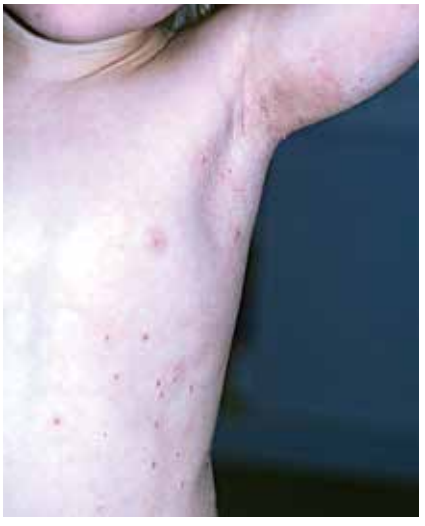

Figure 9. Molluscum contagiosum and atopic dermatitis.

to a dermatologist is recommended; this often happens anyway because the 'dermatitis' does not respond to treatment.

Investigation and management of allergy

Most parents of children with AD want to know why they have it, and the answer, 'It's genetic', is not enough. As a result, many will request allergy testing. The thought that they may find a substance that if avoided will end the problem is very attractive and also gives them something tangible that they can control without the use of drugs. Further, parents who think their child has an inherited health problem often feel unnecessarily guilty and one response to this is denial of the diagnosis.

In an ideal world, a child should be considered for allergy assessment if:

- the dermatitis is severe or difficult to control
- parents report exacerbations in relation to particular foods or infant formula
- there is an urticarial component
- the distribution is on exposed areas, particularly the periocular area or other parts of the face, indicating the role of an aeroallergen such as house dust mite.

In practice, however, many unnecessary allergy tests are conducted because of parental pressure, and children are sometimes put on very restrictive diets on thin evidence. Parents may also embark on expensive measures such as pulling up carpets and removing all the curtains, only to find that these make little difference. Allergy testing may be carried out by either skin prick testing (SPT) atopic patch testing (APT) or radioallergosorbent testing (RAST). The latter is a blood test and is readily available for a wide range of allergens. Allergy testing has many pitfalls, and results need to be considered in conjunction with the clinical presentation. Not all food reactions are detectable with these tests, particularly when salicylates and other food additives are involved. Referral is strongly recommended before any major action, either dietary or environmental, is put into practice.

Prognosis

Generally, the prognosis of AD is good, with most children substantially improving by the time they start school and remitting by the end of primary school. A minority still suffer from the condition as teenagers, but it continues into adult life in only a few. Treatment resistance is often due to noncompliance, but infection, allergy or the onset of a new skin condition such as psoriasis should be considered.

Certain environmental situations may bring out the tendency for AD later - for example, an occupation or hobby where there is heavy aeroallergen or irritant exposure, or an outdoor sport in a patient who is allergic to grass. Certain geographical areas suit some patients better than others, no doubt related to humidity and aeroallergen levels.

Until remission occurs, parents need to maintain all environmental modification precautions and ensure treatment is given regularly. It is important in young children, and even in many teenagers, never to leave treatment up to the child. It is a bit like teeth cleaning: unless the parent nags, it often does not happen.

Conclusion

AD is a common paediatric presentation in primary care and GPs maintain key long-term relationships with both the child and their parent or carer. Educating parents and carers about the safety of gold standard therapy and the importance of day-to-day skin maintenance measures and environmental modifications is central to treatment success and maintaining remission. The GP's assistance in negotiating many of the associated considerations, such as minimising the cost of treatment and suggesting simple solutions for when the child is at school, make the world of difference to the wellbeing of children with AD. MT

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COMPETING INTERESTS: None.

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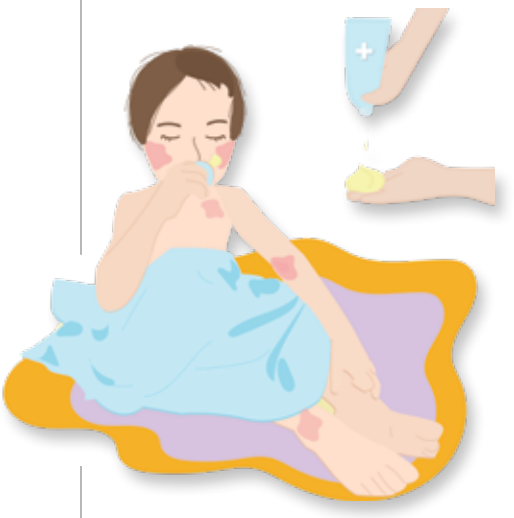
Helping your child with atopic dermatitis: what you should do every day

Prepared by Professor Gayle Fischer, Professor of Dermatology at Sydney Medical School – Northern, The University of Sydney, Royal North Shore Hospital, Sydney, NSW.

This handout provides some information about treatments for children with atopic dermatitis



What your child should avoid

- Soap, bubble bath and shampoo
- Woollen, nylon or furry clothes and items, including wool blankets, toys, bunny rugs, car seat covers, clothes you are wearing when carrying your child
- Sandpits and sand at the beach
- Chlorinated water
- Perfumed products
- Overheating – for example, wearing tight nylon clothes, using electric blankets, participating in activities like aerobics or athletics
- Known, proven allergens

How you and your child can do this

- Use a soap substitute instead of soap and shampoo, and use a bath oil in the bath
- Keep products used on the skin simple and nonperfumed; experimentation can result in irritation of the skin
- Wear loose cotton or cotton-blend clothes
- Do not put more clothes on your child than you would wear yourself, and avoid sudden temperature changes
- Remove the sandpit at home, speak to the teacher at preschool about avoiding sand, and immediately wipe off any sand that gets on your child
- Rinse off chlorinated water immediately and apply moisturiser
- If your child has a proven dust allergy use a dust cover for your child's mattress and pillow; remove fluffy toys from the bedroom, hot wash bedding and clothes and vacuum regularly

What you should do each day

- Apply a bland, greasy moisturiser all over your child twice a day: after the bath and before getting dressed in the morning are the best times
- Always use bath oil in the child's bath
- Check daily to see which parts of the skin have dermatitis: use your child's cortisone creams and ointments on these areas at the strength recommended by your doctor

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Using cortisone creams

Many people will tell you that cortisone creams and ointments, which are usually preferable to other products, are very dangerous and should not be used on children.

It is true that cortisone (also called corticosteroid) is a potent and effective medication; however, it is completely untrue that it is too dangerous to use in atopic dermatitis.

The truth is that cortisone creams are very safe when used correctly. Inadequate use of these creams is one of the main reasons that parents find it difficult to control their children's dermatitis.

You should use your cortisone creams on your child as soon as you see a patch of dermatitis. Waiting until the dermatitis gets really bad before using them only results in having to use more. The earlier you start, the better you will control the situation. When the dermatitis is better, stop using the creams.

What about Elidel?

Elidel (which is also called pimecrolimus) is a nonsteroid product for the treatment of dermatitis. It is called an 'immunosuppressive' drug, which means that it dampens down the body's immune, or defence, system. Its strength is equivalent to a weak-to-moderate strength cortisone cream.

Elidel does not thin the skin. Its main side effect is stinging or burning. We have no information about the very long-term safety of this product. Until we know more, it is wise to use a sunscreen on any exposed areas being treated, as there are concerns about a possible link with skin cancer.

Elidel is not a highly effective treatment for dermatitis and is less effective than all topical corticosteroids other than 1% hydrocortisone. It is in general most useful on the face and eyelids.

Specific instructions

Problems your child might encounter

- **Stinging.** Particularly when dermatitis is severe, creams may sting. Sorbolene cream often causes stinging. If this happens, talk to your doctor about changing to another product.
- **Night waking.** This usually stops when the dermatitis is better, as it is the result of itching. Some sedating antihistamines, such as alimemazine (trimeprazine) tartrate, taken at bedtime will often help.
- **Infection.** If dermatitis becomes crusty or weeping or exudes pus, get in touch with your doctor. Your child may need antibiotics.
- **No improvement.** Sometimes dermatitis just becomes difficult to treat and does not respond to the usual medicines. Contact your doctor in this case. MT

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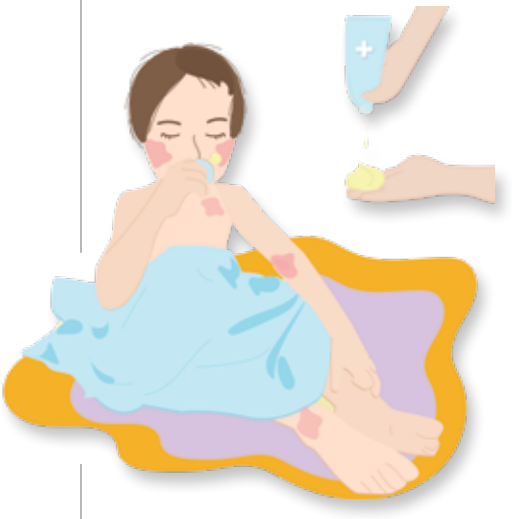

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Common skin problems in children

Rashes other than atopic dermatitis

GAYLE FISCHER OAM, MB BS, FACD, MD

In addition to atopic dermatitis, numerous other endogenous and exogenous dermatoses are seen in prepubertal children including nappy rash, psoriasis, neonatal acne and allergic rashes. Many of these childhood dermatoses will clear over time with environmental modification or no intervention, but some may require treatment.

KEY POINTS

- Most cases of nappy rash are due to irritation and maceration, but *Candida albicans* infection, seborrhoeic dermatitis and psoriasis are other common causes.
- Not all babies with seborrhoeic dermatitis recover; one-third will develop psoriasis and another third, atopic dermatitis.
- The early signs of psoriasis in children include cradle cap, nappy rash, and post- and infra-auricular scaling and fissuring.
- Childhood-onset psoriasis, ichthyosis vulgaris and keratosis pilaris are often confused with atopic dermatitis.
- Urticaria is the only childhood skin condition that is effectively treated with antihistamines.
- Hypersensitivity to insect bites and plant contact dermatitis are common in children and preventative measures are often the best treatment.

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The earliest dermatoses seen in infants other than atopic dermatitis are nappy rash, seborrhoeic dermatitis and neonatal acne. In preschool-aged children, florid insect bite reactions may be a problem. Skin conditions that are often confused with atopic dermatitis are childhood-onset psoriasis and the keratinisation disorders, ichthyosis vulgaris and keratosis pilaris. The most common allergic skin conditions in children, other than insect bite reactions, are virally induced urticaria and contact allergy to plants.

Early dermatoses

Nappy rash

Nappy rash is the term used to describe any rash occurring in the area under the nappy. It has become less common, probably due to the use of highly absorbent disposable nappies.

A simple irritant dermatitis is the most common cause of nappy rash, but there are many other causes, including *Candida albicans* infection (Figure 1), seborrhoeic dermatitis and psoriasis (Figure 2). There are also some very rare causes, such as zinc deficiency and Langerhans cell histiocytosis, and thus any infants with a severe, nonresponsive rash, particularly with lesions in areas other than under the nappy, should be referred to a dermatologist. Nappy rash can be mild or it can become so inflammatory that ulceration occurs. Rarely, it may become papular or nodular and result in lesions that can appear alarming. This condition is called pseudoverrucous papules and nodules (PPN).[1]

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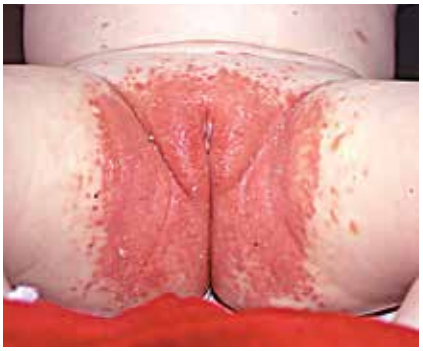


Figure 1. Nappy rash caused by *Candida albicans* infection.

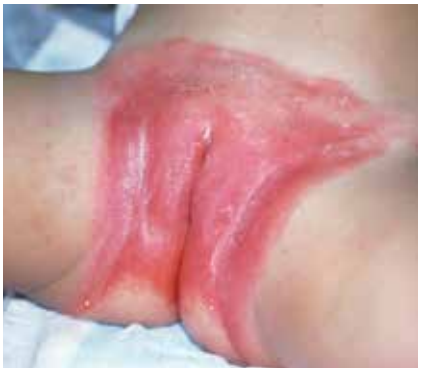


Figure 2. Nappy rash caused by psoriasis.

Figure 3. Generalised seborrhoeic dermatitis.

Generally, a simple irritant rash does not involve the flexures, whereas endogenous dermatoses and infections do. Irritant nappy rash results from loss of barrier function of the epidermis due to maceration from urine and irritation from faecal enzymes. Sometimes topical products, including soap and over-the-counter treatments, aggravate the rash. In many cases of nappy rash, the affected area is colonised with *C. albicans*.

Management

Generally, management for all forms of nappy rash is the same, even when the rash is very severe. Treatment involves environmental modification and specific medical management. Highly absorbent disposable nappies are preferable to cloth nappies. If cloth nappies are used, parents should be advised to change them every two hours and avoid using plastic overpants and nappy liners. As with any sort of dermatitis, a soap substitute should be used instead of soap and a dispersible bath oil used in every bath. At each nappy change, a damp cloth and bland emollient should be used instead of commercial wipes, and further emollient applied. Zinc and castor oil preparations are popular as a nappy rash treatment, but any greasy emollient is effective.

In many cases, environmental modification alone is inadequate and the medical treatment of choice is 1% hydrocortisone cream used in conjunction with a topical antifungal such as nystatin or an imidazole (clotrimazole or miconazole). There are several combined products, such as clotrimazole plus hydrocortisone, which are convenient and not much more expensive. The treatment should be used three times daily until the rash has resolved. Generally, hydrocortisone 1% is the only corticosteroid that should be used in the nappy area.

Inadequate response to treatment may be due to:

- noncompliance with treatment
- irritancy or allergy from topical therapy
- bacterial or viral infection
- psoriasis
- an underlying rare condition.

Pustules, erosions, vesicles, ulcers or areas of weeping may indicate a bacterial or viral infection, particularly in infants in whom there has been an inadequate response to therapy. A bacterial, and possibly a viral, swab should be taken and treatment started according to culture and sensitivity results. *C. albicans* will grow from a bacterial swab.

In the very rare instance of a herpetic infection, no specific treatment is needed, as the lesions will heal spontaneously within two weeks. If the infection is severe with ulceration or urinary retention, the infant may need to be admitted to hospital for intravenous aciclovir.

Seborrhoeic dermatitis

Seborrhoeic dermatitis is the term used to describe a clinical presentation that may occur in three common infantile dermatoses: idiopathic seborrhoeic dermatitis, atopic dermatitis and psoriasis. The eruption is seen most often before 2 months of age. Initially, the face, scalp, neck, axillae and nappy areas are involved, but the rash may generalise (Figure 3). The lesions are well defined and have a greasy scale. Characteristically, babies with seborrhoeic dermatitis are well and not itchy.

The rash in classic, idiopathic seborrhoeic dermatitis is self-limiting, clearing spontaneously in a few weeks or sooner if treated. However, both atopic dermatitis and infantile psoriasis may also present in this way, and in these cases, the rash recurs. In about one-third of cases, seborrhoeic dermatitis will remit completely and the babies will have no further problems with their skin; in the other two-thirds, psoriasis or atopic dermatitis will develop. Infection with either *C. albicans* or *Staphylococcus aureus* is common; it should be suspected if crusting, weeping or pustulation are present and actively treated.

Very rarely, Langerhans cell histiocytosis (an increase in Langerhans cells in the skin) may simulate seborrhoeic dermatitis. The cause for this is unknown. In small children it may cause death as the infiltrate may also involve internal organs. The condition is differentiated from seborrhoeic dermatitis by the

DIFFERENTIATING CHILDHOOD PSORIASIS FROM ECZEMA

A diagnosis of classic paediatric psoriasis requires any of the following:

- palmoplantar disease
- guttate disease
- pustular psoriasis
- nail pits
- napkin psoriasis
- well-demarcated psoriatic plaques on elbows, knees or lower back

A diagnosis of atopic eczema can be made in children with itchy skin and three or more of the following:

- visible flexural dermatitis in the skin creases (such as the bends of the elbows or behind the knees)

  OR visible dermatitis on the cheeks and/or extensor areas in children aged ≤18 months
- history of flexural dermatitis

  OR visible dermatitis on the cheeks and/or extensor areas in children aged ≤18 months
- history of dry skin in the last 12 months
- history of asthma or allergic rhinitis

  OR history of atopic disease in a first-degree relative of a child aged <4 years
- onset of signs and symptoms in children aged <2 years (do not use this criterion if the child is aged <4 years)

Adapted from Forward E. Clin Exp Dermatol 2021; 4: 65-73.[4]

presence of purpura and erosions as well as treatment resistance.

Management

Management of seborrhoeic dermatitis is essentially the same as that for atopic dermatitis.[2] Scalp scaling responds to treatment with liquor picis carbonis (LPC, or coal tar solution) 2% and salicylic acid 2% in a moisturising base, and the nappy area is treated with a combination of 1% hydrocortisone and an anticandidal cream, such as nystatin or an imidazole. It is a good idea to follow up the infant to ensure that this is not the first presentation of a chronic dermatosis such as atopic dermatitis or infantile psoriasis.

Childhood acne

Acne is usually thought of as a condition seen in teenagers, but it may also occur in babies and prepubertal children. Because acne is an androgen-dependent condition occurring in genetically predisposed patients, it may be seen in children at times when there is a high enough androgen level to permit expression of the tendency. Neonatal acne is the term used to describe acne occurring in the first two years of life. The acne is often predominantly comedonal and its onset is soon after birth. It is more common in boys, varies in severity and often needs no treatment, but it can be severe enough to cause scarring. Parents should be warned that neonatal acne may, and often does, recur at puberty. Children with early onset acne usually go on to suffer from teenage acne.

Acne is also seen in prepubertal children after the age of 8 years, when the androgens secreted at adrenarche stimulate sebaceous glands in predisposed individuals. It is not usually necessary to investigate for androgen excess unless there are other concerning signs such as excess facial hair. Acne presenting for the first time after 12 months of age and before the age of 8 years raises the possibility of androgen excess. Such patients should be referred to a dermatologist or an endocrinologist.

Management

Neonatal acne is self-limiting and usually remits by 12 months of age, but it may persist to 24 months. If treatment is needed, topical therapy usually used for mild teenage acne is appropriate. This includes topical tretinoin 0.025% cream once daily and erythromycin 2% gel once daily. Rarely, neonatal acne may be nodulocystic and can be treated with oral isotretinoin to prevent permanent scarring. In this case referral to a paediatric dermatologist is required.[3] For prepubertal children with acne, topical therapy is also often adequate. Oral antibiotic therapy is usually not required, but in severe cases, oral erythromycin may be used (tetracycline is contraindicated in this age group because it may stain teeth).

Other childhood rashes

Psoriasis

Although psoriasis is less common in children than in adults, up to 30% of cases have their onset in childhood and in about 5% the onset is before the age of 2 years. The average age of diagnosis in childhood cases is about 8 years.

There are surprisingly few meaningful studies on the incidence, prognosis and nature of childhood psoriasis. We know little about how likely it is to remit compared with the disease in adults, and this is largely because there is no definitive definition for childhood psoriasis. In many studies, the diagnosis is usually clinical and, therefore, open to interpretation. A recent publication has sought to clarify how to differentiate childhood psoriasis from eczema (Box).[4]

The earliest sign that a child is destined to suffer from psoriasis is often cradle cap or persistent nappy rash that typically involves the flexures and has a well-defined edge. The term 'napkin psoriasis' refers to a psoriatic nappy rash associated with cradle cap, plaques on the trunk and axilla and often a facial rash, particularly on the cheeks.

In children, psoriasis may present with the typical plaques seen in adults (Figure 4a); however, these are usually smaller, thinner and less scaly. Acute guttate psoriasis with eruption of small lesions after a streptococcal throat infection is a frequent presentation. Common presenting sites include the scalp, retroauricular folds, face, flexures and genital areas. Scalp scaling and a persistent retroauricular rash or infra-auricular fissuring are common and often subtle signs. Acral psoriasis with nail dystrophy (Figure 4b) and erythema and scaling of the fingertips may occur, and may involve only one or a few digits. However, the

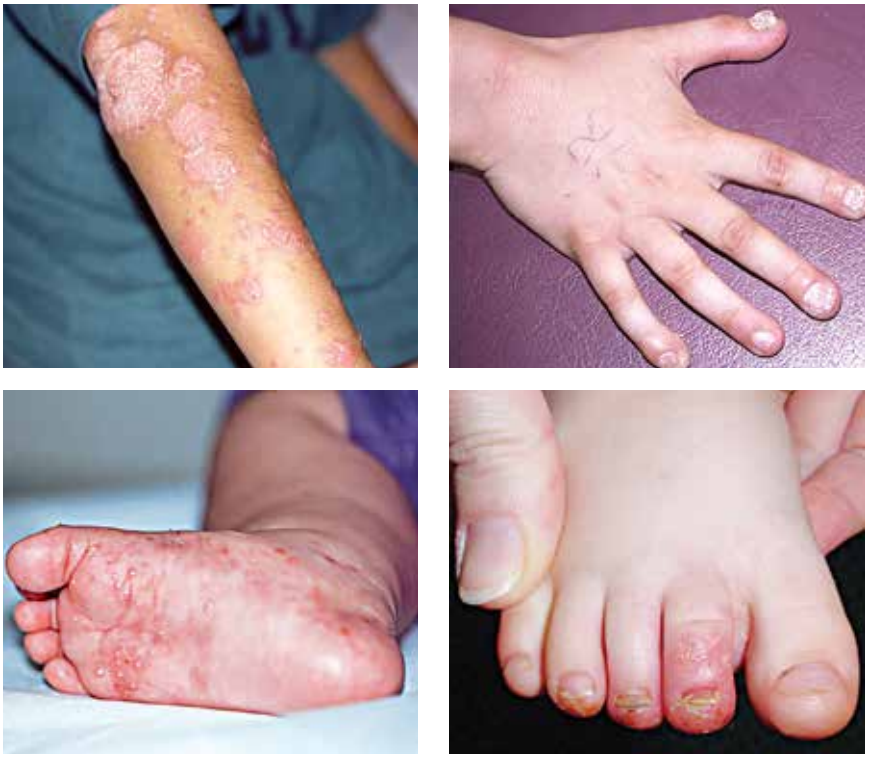
most common nail change is pitting, and is a useful diagnostic clue. Unusual presentations include persistent rashes on the palms and soles (Figure 4c), intertrigo of the hands and feet (Figure 4d), follicular eruptions, persistent angular cheilitis and blepharitis.

Rarely, acute pustular psoriasis may occur in children, with sudden onset of widespread erythema studded with sheets of pustules and associated fever and systemic toxicity. Children with this condition should be admitted to hospital and monitored for systemic infection and evidence of dehydration. Mild topical corticosteroids, wet dressings and oral antibiotics are used for treatment. Recovery may take several weeks.

In some children, psoriasis and atopic dermatitis occur together. This is not surprising, considering how common each is, and recent evidence suggests they may be linked genetically in some patients. When this occurs, typically there are eczematous lesions in the cubital and popliteal fossae, but also psoriatic plaques on the dorsal surface of the elbows, knees and other typical areas such as the scalp. Parents will often relate that the dermatitis component clears easily and promptly with topical corticosteroid, while other lesions are resistant to treatment. Concurrent psoriasis is one of the most common reasons for 'nonresponsiveness' in treating atopic dermatitis.

In children a common precipitant of psoriasis is streptococcal throat infections. Stress and trauma may also play a part, as they do in adults.

Psoriasis is an unpredictable, recurrent or chronic condition. It is seldom severe in children, and psoriatic arthritis is very uncommon.



Figures 4a to d. Typical presentations of psoriasis in children include plaques (a, top left), similar to adults, and psoriatic nail dystrophy (b, top right), often confused with onychomycosis. Unusual presentations include psoriatic rash on the hands and soles of the feet (c, above left) and intertrigo of the feet (d, above right).

Management

Management of psoriasis in children may vary depending on the site, nature and severity at different stages. It is important that treatment is individualised. Almost all of the topical therapies used for adult psoriasis may be used in children.

Generally, topical coal tar preparations are safer in the long term and usually more effective than topical corticosteroids for treating psoriasis in children. There are drawbacks, however, and irritancy, cost and poor patient acceptance because of their odour may limit their use. Tars are usually started at a strength of 4% LPC on the body and limbs. This may be increased up to 10% LPC with the addition of salicylic acid to reduce scale, but this is not often required. Weak tars, usually no more than 2% LPC, may be used on the face and flexures. Tar treatment needs to be carefully monitored but when tolerated and used persistently is very rewarding. Topical corticosteroids may be used in conjunction with tars, particularly where the rash is itchy.

Calcipotriol combined with betamethasone dipropionate has good patient acceptance because of its lack of odour and can be more effective than topical corticosteroid monotherapy. It is usually well tolerated. It is too potent to use on the face and flexures in children but is useful on the trunk and limbs.

Topical pimecrolimus may also be useful for psoriasis affecting the eyelids but in general is too weak to be effective. Narrow band UVB phototherapy, oral retinoids, methotrexate and ciclosporin A may be used in very severe cases of childhood psoriasis, but this situation rarely arises and if it does, the patient needs to be referred to a paediatric dermatologist.

When an attack of psoriasis has been precipitated by a streptococcal infection, the infection should be treated with oral antibiotics. Eradication of streptococci will not always improve the psoriasis. In some patients, psoriasis is exacerbated by chronic or recurrent streptococcal

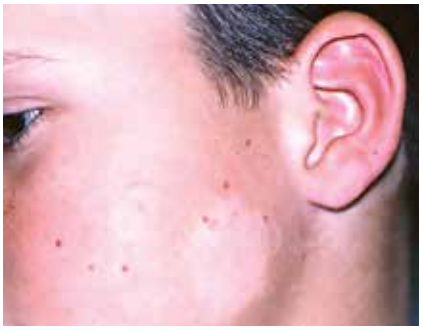


Figure 5. Hypopigmented patches of pityriasis alba.

infections, particularly of the ear, nose and throat. In these patients there may be a role for prophylactic antibiotics and some benefit from tonsillectomy.

Response to psoriasis treatment is typically slow, much more so than to atopic dermatitis treatment. This is because psoriasis is a hyperproliferative rather than an inflammatory condition. The normal turnover time of the epidermis is about six weeks, and this is usually the minimum time needed to obtain a good response from any treatment aimed at treating the rash. Unless patients are warned of this, many will give up long before their treatment has had a chance to become effective (see the Patient and Carer Handout). Once the rash has cleared, preventative treatment with tar ointments can be effective at maintaining remission, and topical corticosteroids should be restarted at the first sign of any new lesions.

Treatment of psoriasis can be complex, and if a patient's response is particularly slow, referral to a dermatologist is recommended.

Pityriasis alba

Pityriasis alba is a common mild form of dermatitis in which postinflammatory hypopigmentation is marked. Patients present with poorly defined hypopigmented scaly patches on the face (Figure 5). It is most obvious in summer, when the skin is tanned, and in dark-skinned children, and it is more common in children with atopy. Usually, symptoms are minimal.

Pityriasis alba must be differentiated from pityriasis versicolor, a fungal skin condition that, in children, typically occurs on the face (Figure 6). Vitiligo should also be considered as a differential diagnosis but is not scaly and has a very sharp border, with obvious depigmentation rather than hypopigmentation.

Management

It is often not necessary to treat pityriasis alba, as it is more a cosmetic than symptomatic problem. Avoidance of skin irritants such as soap and shampoo and use of a soap substitute as well as an emollient twice daily are often all that is needed.

Hydrocortisone ointment 1% twice daily will settle irritation and scaling but will not restore pigmentation. This requires graduated sun exposure to the pale areas while using a sunscreen daily to avoid excess tanning of the skin that is not affected. As this is quite difficult to do, it is often better to ignore the condition, which improves with age.

Ichthyosis

Ichthyosis is a genetically determined skin condition. It presents at or soon after birth and persists throughout life. Affected patients have chronically dry, scaly skin.

Ichthyosis is often confused with atopic dermatitis, but it lacks the itch and inflammatory component (unless there is concomitant atopic dermatitis). There are many forms, dominantly inherited ichthyosis vulgaris, X-linked and a number of recessively inherited forms. Most are quite rare; ichthyosis vulgaris is the most common. In patients with ichthyosis vulgaris, the skin surface is dry and scaly. This may be obvious only on the lower legs. Additionally, these children have 'hyperlinear' palms and soles; in other words, the normal lines seen on these surfaces are accentuated. In the more severe X-linked ichthyosis, seen only in boys, the lower legs may exhibit a 'crazy-paving' appearance (Figure 7) and the whole skin may be dry, particularly early in life. All forms of ichthyosis are more troublesome in dry, cool weather. The recessive ichthyosis skin dryness is of a degree that will not be confused with eczema and patients' very abnormal skin is usually obvious from birth, when most present as 'collodion babies' with an appearance of being encased in plastic wrap as neonates.

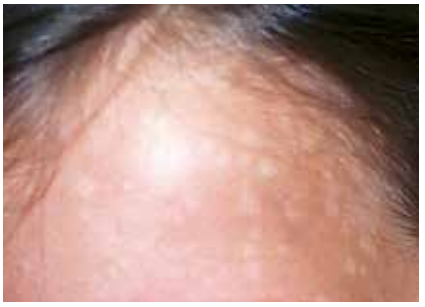


Figure 6. Pityriasis versicolor, which can occur on the face in children and should be differentiated from pityriasis alba.

Management

Treatment of ichthyosis consists of avoidance of products that dry the skin, such as soap, shampoo and bubble bath. A dispersible bath oil and moisturiser need to be used daily and can make the skin appear relatively normal. Generally, greasier preparations are more useful, particularly in winter. Excess scale may be removed with a preparation containing a keratolytic such as urea 10%, salicylic acid 2 to 6%, lactic acid 10% or propylene glycol 10 to 20%. Urea cream containing sodium pyrrolidone carboxylate is particularly useful. However, keratolytics may cause stinging and may be poorly tolerated by children. Topical corticosteroids are not required in the treatment of ichthyosis unless there is also atopic dermatitis.

Keratosis pilaris

Present in about 50% of the population, keratosis pilaris is a very common, dominantly inherited condition. It comprises very small keratotic papules found

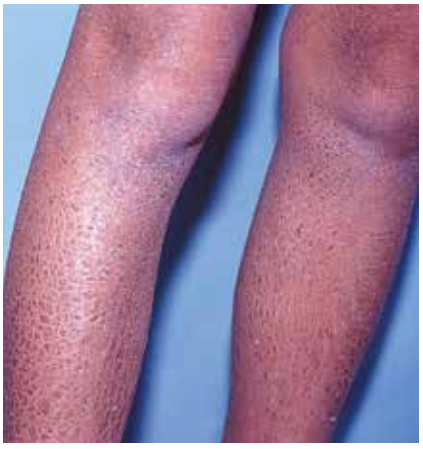


Figure 7. 'Crazy paving' appearance of ichthyosis vulgaris.

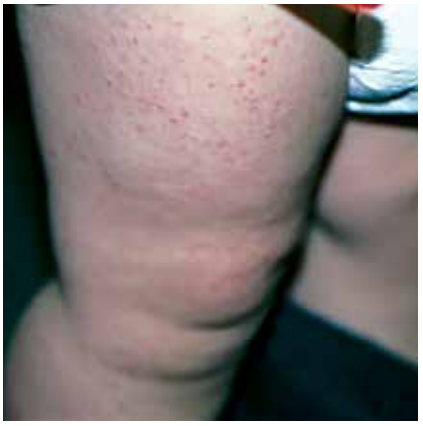


Figure 8. Keratosis pilaris, which occurs predominantly on the lateral thighs and upper outer arms.

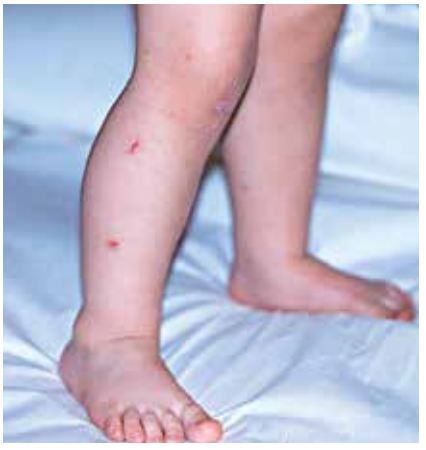


Figure 9. Lesions of papular urticaria occurring on exposed skin surfaces.

predominantly on the upper outer arms and lateral thighs (Figure 8). It is often also found on the cheeks in young children. Rarely, it generalises and is then termed follicular ichthyosis. Sometimes the lesions appear pustular but are usually sterile.

Keratosis pilaris is asymptomatic. Some parents see it as a cosmetic problem and a few are truly distressed by it. Occasionally, it may appear erythematous, which can be a cosmetic problem, particularly if it is on the face. Sometimes it is confused with dermatitis and inappropriately treated with corticosteroids.

The prognosis of this condition is good. The facial papules disappear around puberty, and although the lesions elsewhere may be most prominent in the second decade, they become less obvious with advancing age.

Management

Keratosis pilaris is a normal variant. It is difficult to treat effectively and is best ignored. If treatment is desired, keratolytics such as urea, salicylic acid or glycolic acid can be used overnight in combination with an abrasive therapy (e.g. an abrasive sponge or facial scrub) in the shower in the morning. Care should be taken when using these topical preparations in children as they may sting or cause redness, irritation or dryness.

If facial redness is a problem, keratosis pilaris can be treated with vascular laser, although the results are variable. This treatment is uncomfortable and expensive, requiring a general anaesthetic in most children. It may be best, therefore, to wait until patients are old enough to make the decision for treatment themselves. Unless very highly motivated, most patients tire of topical treatment eventually and accept the condition.

Common allergic rashes

Papular urticaria

The term papular urticaria is used to describe hypersensitivity to insect bites, usually from mosquitoes and fleas. It is a misleading term, as it bears no relation to ordinary urticaria and the condition is not helped by antihistamines.

Seen in young children aged between 2 and 6 years, papular urticaria usually occurs in spring and summer. The lesions most often occur on exposed surfaces (Figure 9), although fleabites usually occur under clothes. Individual lesions are intensely itchy papules, blisters and crusts. Scratching leads to excoriation, infection and ulceration that may result in scarring and hypopigmentation. The prognosis of this condition is good, with most children becoming hyposensitive to the bites after two to four years. In children of any age, grass ticks can also produce very persistent itchy papular rashes.

Management

The best approach in regard to papular urticaria is prevention with insect repellent, protective clothing and insect control, using insecticide, screens and treatment of pets. These strategies must be maintained throughout spring and summer. If infection occurs, it can usually be treated with topical antibiotic ointment and itch can be relieved with topical corticosteroid. It is best to use a potent corticosteroid and to cover the lesions with a dressing to prevent excoriation. In areas where grass ticks occur, avoidance of playing outside is the best prevention.

Urticaria

Urticaria (hives) is most often a benign, self-limiting, condition in children (Figure 10). The most common precipitant is a preceding or current viral illness but foods and medications can be less often involved. Intestinal giardiasis may cause urticaria and, occasionally, urticaria may be a complication of scabies and fungal infections. Extensive systemic investigations are rarely indicated for children with this condition.

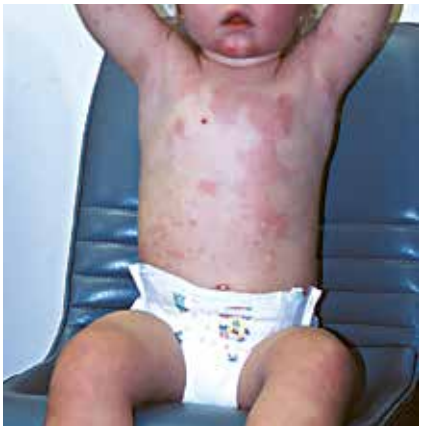


Figure 10. Urticaria, which is often precipitated by a viral illness, foods or medications.

Management

The best approach to urticaria management is simply to treat children empirically with an oral nonsedating antihistamine such as cetirizine or loratadine for two weeks or until the rash has resolved, and then gradually withdraw it. If the rash recurs, the antihistamine can be restarted and an attempt made to withdraw it every two weeks. If urticaria persists for more than six weeks, it is worth excluding giardiasis, and an elimination diet may be considered. In children, this is best done with the help of a dietitian with an interest in food allergy.

Antihistamines have been linked to sudden infant death syndrome in children under 2 years of age and should only be used in children younger than 12 months if the rash is very distressing; in this case only a nonsedating preparation should be used.

Plant dermatitis

Acute contact dermatitis from touching allergenic substances is not common in children as they have much less contact with potential allergens than adults. However, children are more prone than adults to have contact with plant allergens, which may occur while they are playing outside.

Although the rhus tree (*Toxicodendrom succedaneum*) was once a well-known culprit of plant dermatitis, this has now been declared a noxious weed, and many of these trees have been removed. They are still found in some gardens, however, and have a potent allergen that cross-reacts with the allergens in the ubiquitous plant genus grevillea. Grevillea is currently the most common plant allergen for children.

Grevillea Robyn Gordon, an attractive hardy plant with red flowers, used to be quite ubiquitous but has been removed from public places because of the problem of allergy. Other grevillea varieties such as Superb, Ned Kelly and the silky oak tree are close relatives, and the allergens of these all cross-react with each other.

Allergic contact dermatitis presents with an intensely itchy and often blistering rash. It may cause significant oedema on the face and around the genital area. It often has a streaky, asymmetrical pattern, reflecting where the plant brushed against the skin (Figure 11). Often contact has been very brief and is not remembered by the child.

Management

If untreated, lesions of plant dermatitis tend to keep appearing for several days and may take weeks to resolve. They respond well and rapidly to a short course of oral prednisone, starting with 0.5 mg/kg/day until settled then reducing the dosage over two weeks. An attempt should be made to identify the cause. This can be confirmed by applying a tiny bit of the plant to the skin, which will rapidly reproduce the rash. Take care when doing this as there is a risk of a severe reaction. Do not occlude the plant, and leave it on the skin for only five minutes.

Conclusion

Not all childhood skin conditions are atopic dermatitis, even though this is by far the most common problem. Nappy rash is rarely atopic and is more likely to indicate simple irritation, seborrhoeic dermatitis, *C. albicans* infection or psoriasis. Several endogenous dermatoses that can present in childhood are often confused with atopic dermatitis, including psoriasis, ichthyosis vulgaris and keratosis pilaris. Psoriasis is the most important of these, and many patients with 'treatment resistant atopic dermatitis' presenting to paediatric dermatologists turn out to have psoriasis. Pityriasis alba is a very common and harmless childhood facial depigmenting dermatosis that is most often confused with pityriasis versicolor and vitiligo, both of which are much less common. Acne may occur in babies, most often boys, and is not a cause for concern. The most common allergic rashes in children include florid reactions to insect bites, contact dermatitis from plants and urticarial reactions to viral illnesses. MT

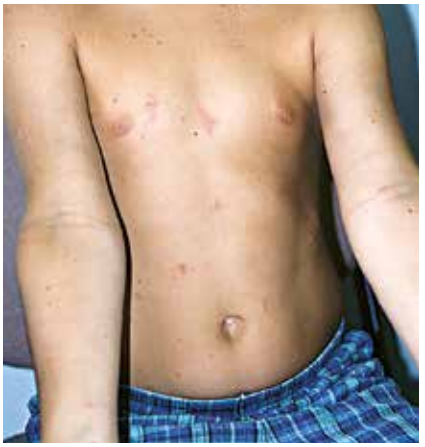


Figure 11. Plant contact dermatitis.

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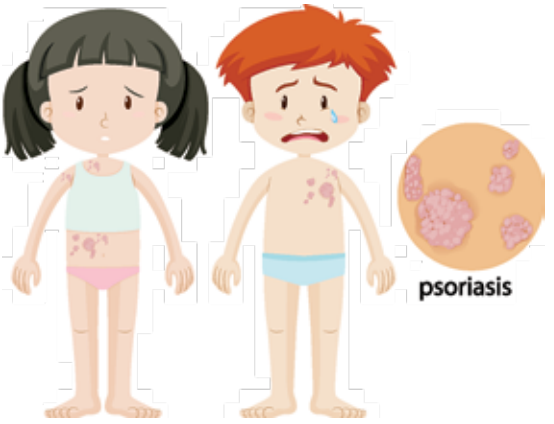
COMPETING INTERESTS: None.

Frequently asked questions about psoriasis

This handout provides some information about psoriasis in children

Prepared by Professor Gayle Fischer, Professor of Dermatology at Sydney Medical School – Northern, The University of Sydney, Royal North Shore Hospital, Sydney, NSW.

Q. What is psoriasis?
A. Psoriasis is a very common inherited condition where areas of the skin look red and scaly and are often itchy. It is a skin condition, and although in adults it may be associated with arthritis, this is very rare in children.



Q. Can other people catch psoriasis from my child?
A. No, psoriasis is not an infectious disease. It cannot be caught, it is not cancer, and it is rarely dangerous. However, children can inherit from their parents the genetic tendency to have psoriasis.

Q. Is there a cure for psoriasis?
A. At present there is no cure for psoriasis, and beware anyone who claims to have one. This is because we still don't have any way to alter our genetics. However, we know a great deal more about this than we did 10 years ago.

Q. Is psoriasis caused by something in my child's diet?
A. We don't believe that diet has any effect on psoriasis. This is a medical point of view, and natural therapists will disagree. However, eating a healthy diet improves your child's general health, and this is always good for psoriasis.

Q. What will make psoriasis worse?
A. Stress, illness, lack of sleep and injury, especially to your child's skin, may make psoriasis worse. Infection with a type of bacteria called Streptococcus, which causes tonsillitis, will also often result in the psoriasis getting worse.

Q. What treatment is available?
A. Psoriasis in your child can be controlled with a bit of time and effort from you and help from your doctor; however, you have to be committed. There are many ways to treat the psoriasis. It often takes at least six weeks of treatment to achieve a good result. Remember, everyone is different and an individual treatment needs to be prescribed for your child. Your doctor will recommend the best and safest treatment. MT

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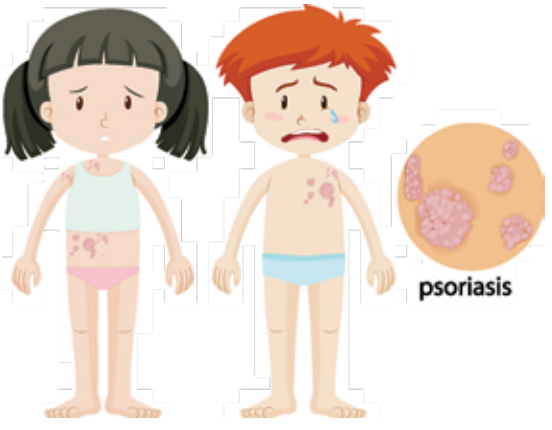

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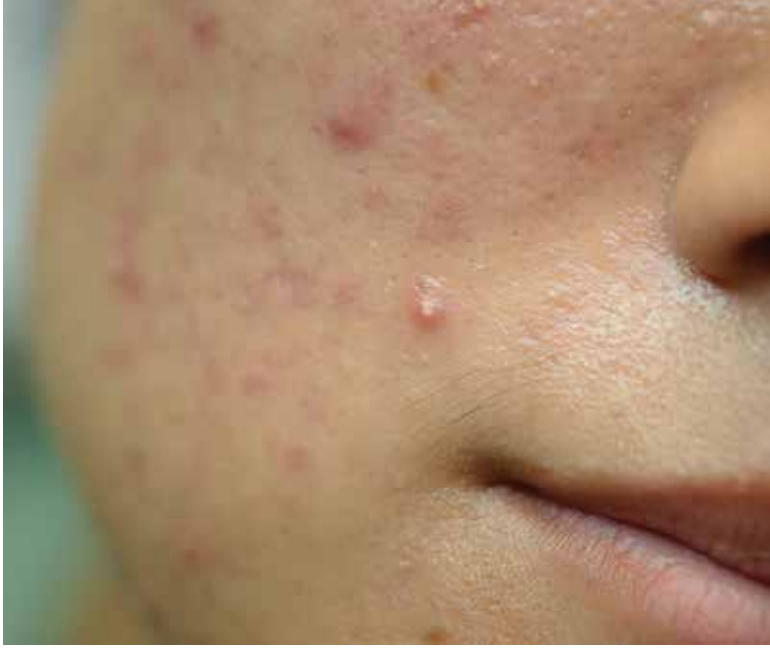
Treating acne

How to minimise physical and emotional scarring



JO-ANN SEE MB BS, FACD
PHILIP TONG MB BS(Hons), PhD, FACD

Acne is a common skin condition associated with significant physical and psychological morbidity that affects people from prepubescence to middle age. Treatment should be individualised according to the patient's history, severity of disease and contraindications. The psychological impact of acne should be acknowledged and considered when developing a treatment plan.

KEY POINTS

- Acne is not just an adolescent condition; it is also common in prepubertal children and middle-aged adults.
- There is psychological harm associated with having acne and this may not correlate with disease severity.
- GPs play an important role in helping to dispel common myths surrounding the causes of acne.
- Taking an accurate history, identifying patient concerns and evaluating psychological impact are key to successful acne management.
- GPs should set guidelines for treatment, have a plan to review treatment outcomes and establish realistic expectations with their patients.
- Treatments should be individualised according to the patient's history, acne severity and contraindications, and patients referred when necessary.
- Acne scarring can be avoided through early intervention.

GPs are at the frontline for managing acne in patients from prepubescence to middle age. Year by year, there are more acne treatments available and the minefield of information, especially on the internet and social media, can make management confusing. This article guides the reader to consider treatment options for acne to help address patients' needs and concerns.

Since the last published article on acne in *Medicine Today* in 2015,[1] there have been many developments in acne treatment – new products, new procedures and promising new medications currently on trial. There is even a new name for *Propionibacterium acnes*, the bacterium linked to acne, which is now called *Cutibacterium acnes*.

Epidemiology – is acne really that common?

Acne is a common skin condition that is associated with significant physical and psychological morbidity. International studies have shown about 85% of people between the ages of 12 and 24 years experience at least minor acne.[2] It is particularly commonplace in teenagers in Australia, with a prevalence of 93.3% among those aged 16 to 18 years.[3] Although commonly thought of as a teenage disease, acne can start in prepubertal children and may coincide with an earlier onset of puberty.[4] Acne can also be considered a chronic disease.[5,6] It may extend from adolescence, through the 20s, and even to middle age. The prevalence has been noted to be 64% in those aged 20 to 29 years and 43% in the 30- to 39-year age group.[3]

Patient concerns

Acne can cause significant psychological harm and can affect quality of life.[7,8] Many studies link patients who have more severe acne and acne of a longer duration with a greater likelihood of

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Dr Tong is a Dermatologist in private practice at Central Sydney Dermatology and Visiting Medical Officer at St Vincent's Hospital, Sydney, NSW. He is a member of the All About Acne group (www.acne.org.au).

KEY QUESTIONS TO ASK A PATIENT PRESENTING WITH ACNE

- **How long have you had acne?** Ask the patient when their acne started. Was it as a teenager, in their 20s or later? The patient may have late-onset adult acne or a long period of acne, which may cause concern as there is an increased risk of scarring. The patient may be refractory to previous treatment or perhaps non-adherent
- **Do you have a family history of acne?** Asking about a family history of acne may point to a hormonal basis or a background history of scarring
- **Are you taking any medications or supplements?** Antiepileptics, steroids or supplements can trigger acne (e.g. whey in bodybuilding supplements)
- **Which acne treatments have you used and for how long?** Some patients do not persevere with a treatment long enough for it to be effective. It is important to know what they have used, if they experienced any side effects with treatment, and the reason for not wanting to continue treatment
- **Are you experiencing any psychological impact from having acne?** Perhaps ask about any issues of self-esteem or anxiety and if acne prevents the patient from socialising or has changed their lifestyle

low self-esteem and quality of life.[9] People with acne can also experience lack of self-confidence, anxiety and depression. In the Global Skin Disease Study, acne ranked highly as a skin disease associated with significant disease burden.[10,11] A recent Delphi survey showed that patients with acne reported:

- being self-conscious
- feeling unattractive to themselves and others
- feeling uncomfortable in their own skin
- not wanting pictures taken
- feeling envious of people with clear skin
- that time and effort was spent concealing scarring.[12]

Although previously considered a teenage concern, a recent meta-analysis found the prevalence of depression was higher among adults with acne (aged 20 years) compared with their adolescent counterparts (aged 12 to 19 years).[13]

Due to the chronicity of the condition, many patients can become disheartened and disillusioned with treatments offered to them. They often seek alternative measures, some of which have very little scientific basis. Many patients are now consulting social media platforms such as YouTube and Instagram, and social media influencers for advice – the advice given is not always in keeping with recommended acne guidelines.[14]

Patient concerns should be identified and addressed so that an individual management plan can be tailored to each patient. Patients with acne often question and are concerned about the possible side effects of acne medications such as oral antibiotics and oral isotretinoin. There is also increasing global concern about the use of antibiotics and increasing antibiotic resistance of bacteria. This may lead to patients not wanting to adopt antibiotic treatment strategies. It is recommended that antibiotic courses be limited to three to six months, and that topical and oral antibiotics are not prescribed simultaneously. Patients are also concerned about the possibility of acne scarring and it is important for the clinician to realise that early effective management can lessen the risk of this.[15]

The GP consultation

The GP is at the forefront of acne management, with presentations of chronic acne seen by Australian GPs at a frequency of 0.4 of every 100 consultations.[16] Acne is diagnosed clinically by patient history and physical examination, which evaluates the type and severity of the acne and if there is any psychological impact. Laboratory investigations may be considered if there is a possibility of underlying hormonal factors, such as polycystic ovary syndrome, as a baseline for oral medications such as isotretinoin, or monitoring in the setting of spironolactone. Key questions to ask patients presenting with acne can be found in the Box.

Although consultation time may be limited, it can be worthwhile asking patients what they think the cause of their acne is. The four main factors contributing to acne are:

- increased sebum
- hyperkeratinisation of the pilosebaceous duct
- colonisation by *C. acnes* (formerly known as *P. acnes*)
- immune activation and release of inflammatory mediators.

There are many myths around the factors that influence acne that should be dispelled. These include:

- acne is caused by poor hygiene
- only teenagers get acne
- popping pimples makes them go away faster
- acne scarring can be easily fixed
- acne always goes away on its own - it may eventually burn out after days, weeks, months, or years but, unfortunately, the longer a patient has acne, the greater the risk for permanent scarring.

Diet is a controversial triggering factor, with the common misconception that an unhealthy diet is always the cause of acne in every person. Recent evidence suggests that in a select group of patients, high sugar intake, high dairy intake and a high glycaemic index diet may contribute to the development of acne, thought to be mediated by mammalian target of rapamycin complex 1 (mTORC1) signalling (Figure 1).[17]

It is important to set realistic expectations for treatment success and to offer patients a review to see if management needs to be altered.

The physical examination

Acne severity can be quickly assessed by looking at the patient's face and torso. There is no standard method of acne grading, it can be simply classified as:

- mild – noninflammatory or inflammatory comedones (blackheads or whiteheads; Figure 2a)

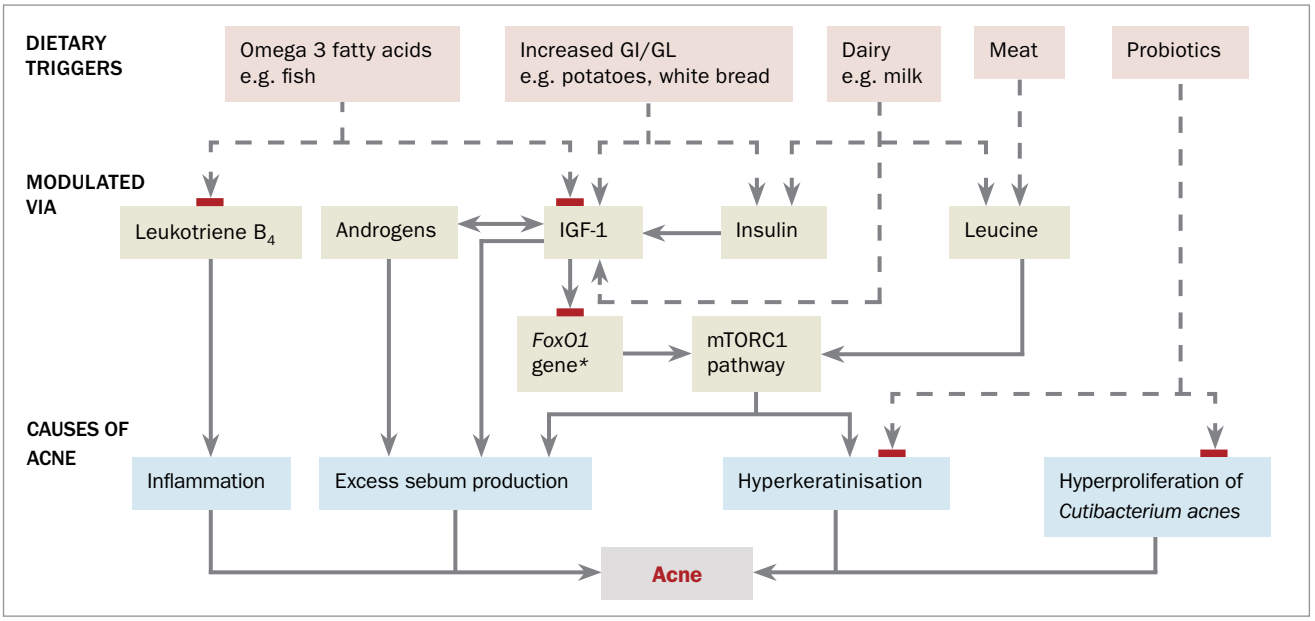

Figure 1. Proposed dietary triggers for acne.[17] Acne pathogenesis can be linked to four key factors: excess sebum, hyperproliferation of *Cutibacterium acnes*, hyperkeratinisation of pilosebaceous follicles and inflammatory mediators. A working hypothesis is that this is mediated via mTORC1 through a number of dietary influences. Dietary triggers such as meat, dairy and high GI foods can exacerbate acne by increasing the production of key mediators, whereas probiotics and omega 3 fatty acids may inhibit pathways that cause acne. Dietary triggers are labelled in pink, signalling molecules in beige and acne causes in blue. Pathways indicated with a broken line are currently under investigation.

Abbreviations: GI = glycaemic index; GL = glycaemic load; IGF-1 = insulin-like growth factor 1; mTORC1 = mammalian target of rapamycin complex 1.
Adapted from Baldwin H, Tan J. Am J Clin Dermatol 2020.[17]
* The *FoxO1* gene plays an important role in regulating gluconeogenesis and glycogenolysis.

- moderate – with inflammatory papules and pustules (Figure 2b)
- severe – with deeper inflammatory nodules and cysts (Figure 2c).

Many patients, especially those with darker skin (Fitzpatrick III or higher), may have postinflammatory redness or hyperpigmentation as inflammatory lesions resolve, which are often mistaken as active acne lesions or scarring.

Patients with severe acne with deep nodules and cysts that has not responded to treatment, and those with uncommon forms of acne such as acne conglobata and acne fulminans, may require urgent referral to a dermatologist for prescription of oral or intralesional corticosteroids or oral isotretinoin. Patients who have a psychological impact may require counselling with a psychologist or psychiatrist as well as referral for consideration of oral isotretinoin therapy.

Acne in adults can look the same as teenage acne. Both rosacea and perioral dermatitis can occur at the same time as adult acne but the clinical hallmark of acne is the comedone.

Investigations

Most patients with acne do not need laboratory investigations. Consider hormonal acne in patients who have symptoms of hyperandrogenism in the context of polycystic ovary syndrome; a hormonal assay should be performed in the luteal phase of the menstrual cycle after the patient has stopped taking the oral contraceptive pill for at least one month. Tests for women with suspected hormonal acne include measurement of serum dehydroepiandrosterone sulfate, total testosterone, free testosterone and sex hormone binding globulin levels and the luteinising hormone/follicle stimulating hormone ratio.[8] Patients with hormonal acne who are also insulin resistant may be at risk of developing diabetes and cardiovascular disease later in life.

If patients are having baseline investigations for oral isotretinoin, it may be helpful to order the following tests: liver function tests, creatine kinase (in athletic patients) and fasting lipids. Beta human chorionic gonadotropin should be added as a pregnancy screen in female patients. In healthy individuals, less frequent ongoing monitoring may be safe for those who are receiving typical doses of isotretinoin.[18]

Treatment options

Acne treatments are tailored to each patient according to severity, as shown in the Table. Clinicians must always bear in mind that acne can fluctuate from time to time; therefore, taking an accurate patient history and developing a flexible treatment plan that accommodates fluctuations in acne severity are an important part of management.

Patients often expect advice regarding skincare and the choice of skincare can be

Figures 2a to c. Representative clinical images of acne severity. a (left). Mild acne with blackheads. b (middle). Moderate acne with inflamed pustules. c (right). Severe acne with inflamed nodules.

paramount to the success of treatment. There are many inexpensive skincare ranges that offer acne cleansers and moisturisers that aim to be gentle to the skin and not be occlusive. The use of an appropriate cleanser and moisturiser can also minimise the irritancy of many topical acne treatments as well as dry skin often associated with oral isotretinoin use.

Patients may also expect advice on diet and, as mentioned previously, it is important to dispel acne myths and consider offering patients an acne educational resource such as the All About Acne website (www.acne.org.au).

Mild acne

When seeing a patient for the first time, be mindful that they may have already been to a chemist or beautician for advice. They may have fixed ideas about what is causing their acne and, even in patients with mild disease, acne can have significant psychological impact that does not necessarily correlate with their acne severity.[14]

Acne cleansers can be beneficial for all types of acne and are available at pharmacies and supermarkets. Cleansers usually contain salicylic acid, glycolic acid, azelaic acid or benzoyl peroxide. Cleansing twice daily is ideal to remove excess sebum, keratinous debris, make up and pollution. Micellar water can also be used on sensitive skin. Non-prescription leave-on acne treatments can be used once or twice a day and may contain benzoyl peroxide, salicylic acid, glycolic acid or azelaic acid.

Benzoyl peroxide reduces pilosebaceous duct colonisation by *C. acnes*, as well as decreasing sebum and comedone formation. Gradual introduction and starting with a low concentration are recommended to minimise potential skin irritation. It is the active ingredient in acne facial washes or leave-on creams and has also been incorporated into the fixed-dose combination prescription products clindamycin phosphate/benzoyl peroxide and adapalene/benzoyl peroxide combinations.

Alpha hydroxy acids such as glycolic acid (and others such as lactic, citric and mandelic acid) and the beta hydroxy acid, salicylic acid, decrease altered follicular keratinisation in blocked oil glands and improve skin appearance by exfoliation.

Azelaic acid works by inhibiting *C. acnes* growth and improving abnormal pilosebaceous follicular keratinisation. It has fewer irritant side-effects compared with benzoyl peroxide.

Prescription first-line therapy for mild acne usually consists of a topical fixed dose combination. The combination products tend to be more effective, work faster and target more areas of acne pathogenesis than monotherapy. They are applied at night to a cool dry face and are not used as spot treatments. Patients should be followed up eight to 12 weeks after starting treatment to assess its effectiveness and determine whether a change should be made. Therapies include:

- clindamycin phosphate 1% plus benzoyl peroxide 5% (not listed on the PBS)
- adapalene 0.1% or 0.3% plus benzoyl peroxide 2.5%, note that there are two strengths (currently listed onthe PBS)
- clindamycin phosphate 1% plus tretinoin 0.025%, the newest combination (not listed on the PBS).

Moderate acne

Patients with moderate acne have more lesions, characterised by papules and pustules, and usually require oral treatment, including an oral rather than topical antibiotic. Women with unresponsive acne may benefit from the oral contraceptive pill, cyproterone acetate or spironolactone.

Oral antibiotics

Oral antibiotics have been prescribed for decades as an acne treatment. They work by suppressing *C. acnes* growth and have anti-inflammatory action. Due to the growing concern over antibiotic resistance, use with topical benzoyl peroxide, topical retinoid and/or a probiotic is recommended. Oral antibiotics should not be used simultaneously with a topical antibiotic and the duration of usage should be limited to three to six months.

Doxycycline is probably the most prescribed oral antibiotic, at an average daily dosage of 100 mg daily; however, doses can range from 50 to 200 mg daily. Doxycycline should be taken with water, not milk, and should not be taken before lying down or at bedtime because of the risk of oesophageal irritation. It is not recommended for children under 12 years of age due to the

TABLE. RECOMMENDED THERAPIES FOR ACNE

	Acne severity			
	Mild		Moderate	Severe
Lesion type	**Noninflamed comedones (blackheads and whiteheads)**	**Papules/pustules**	**↑ Papules/pustules + nodules**	**Papules/pustules + nodules + nodulocystic lesions + psychological harm**
First-line therapy	BPO *or* topical retinoid	BPO *or* FDC*	FDC* + oral antibiotic	FDC* + oral antibiotic *or* oral isotretinoin
Alternative therapies	Azelaic acid *or* glycolic acid *or* salicylic acid ± manual expression†	Consider alternative antimicrobial agent *or* alternative topical retinoid	Consider alternative FDC *or* change antibiotic *or* combined oral contraceptive ± antiandrogen in female patients Biophotonic/light/IPL	
Therapies for pregnant patients	Azelaic acid + glycolic acid + salicylic acid ± topical antibiotic Topical niacinamide	Azelaic acid + glycolic acid + salicylic acid ± topical antibiotic Topical niacinamide	Oral erythromycin Antibiotic *or* azithromycin	

Abbreviations: BPO = benzoyl peroxide; FDC = fixed dosed combination; IPL = intense pulsed light.
* Examples of FDC include adapalene/BPO, clindamycin/BPO, clindamycin/tretinoin.
† Manual removal of comedones using a comedone extractor or similar instrument.

risk of tooth discolouration, or in women who are pregnant or breastfeeding.

Minocycline at a dosage of 100 mg daily is also prescribed. However, there are rare safety issues associated with its use including minocycline-induced hepatitis, drug-induced lupus-like hypersensitivity syndrome and hyperpigmentation.

Erythromycin 500 mg twice daily is also effective but *C. acnes* resistance and gastrointestinal side effects are more common. It is used in children and pregnant women, in whom tetracycline is contraindicated.

Other antibiotics such as trimethoprim can also be used as third-line therapy at a dosage of 200 to 300 mg twice daily. Although not commonly used, azithromycin has been considered as effective as doxycycline in some trials.[19] The dosage of 500 mg once daily for three days per week or in cycles of 10 days for 12 weeks are the most commonly used regimens.[20]

Hormonal therapy

The most commonly prescribed antiandrogen hormonal therapies for moderate acne are the oral contraceptive pill, cyproterone acetate and spironolactone. These can be prescribed as monotherapy, or as oral contraceptive/spironolactone or oral contraceptive/cyproterone acetate combinations. These therapies can be effective in women with acne, especially those who show resistance to other therapies, and can even be effective when serum androgen levels are normal. They work by decreasing ovarian and adrenal androgen production and also inhibit the local activity of androgen nuclear receptors on sebocytes and keratinocytes.[21] Before prescribing an oral contraceptive, it is important to check for any contraindications.

Women over the age of 25 years may have higher rates of treatment failure.[17] Suspect hormonal acne in women who fail multiple courses of systemic antibiotic medications or if there is a recurrence of acne shortly after treatment with isotretinoin.[22,23]

Patients may not see an improvement in their symptoms until after three months of taking an oral contraceptive for acne and the best response rate may not be seen until after six to nine months of treatment. Acne has been shown to improve in 50 to 90% of cases.[16] Many patients may experience a flare of their hormonal acne when their long-term oral contraceptives are ceased. Some patients may also have a worsening of their acne when contraceptive implants are used.[24]

Cyproterone acetate reduces sebum production and is usually given in combination with the oral contraceptive pill at a dosage of 12.5 to 50 mg daily during the first 10 to 15 days of the menstrual cycle. It can also be prescribed on its own at a dose of 50 to 100 mg daily from day 1 or 5 of the menstrual cycle and stopped before ovulation on day 14. An improvement is usually seen within three months.

Spironolactone is a safe and effective treatment requiring no monitoring in a young fit and healthy female.[25] Treatment can be started with a low dose such as 25 to 50 mg twice daily and then increased to 200 mg daily if the patient has no significant adverse events such as breast tenderness, 'breakthrough' bleeding or headache.

Improvement in acne may take up to three months. Spironolactone is contraindicated in pregnancy because of the risk of feminisation of the male fetus.

Severe acne

For patients with widespread and inflammatory deep lesions, oral antibiotics, often in conjunction with a topical retinoid, are the treatment of choice. Consider referral to a dermatologist for oral isotretinoin in the following situations:

- patients with severe acne that is unresponsive to treatment
- patients at risk of scarring
- patients with psychological distress as a result of their acne.

When referring for isotretinoin, some baseline investigations can be done, as mentioned previously. The daily dose and duration of treatment depends on the patient's weight, response to treatment and any side effects experienced. There is no standardised isotretinoin dose, and many dermatologists tend to start patients on a low daily dose and then gradually increase it as tolerated.[26] Female patients should be counselled on the need for contraception, as isotretinoin is teratogenic. All patients should be advised to report any mood changes to their GP or specialist and more regular review may be required. In the rare event of psychological distress or a psychiatric disorder resulting from isotretinoin use, consider referral to a psychologist or psychiatrist.[27]

Acne medication and pregnancy

Topical and oral retinoids are contraindicated during pregnancy because of the risk of birth defects, and tetracycline antibiotics should not be given due to the risk of deposition and staining of the infant's teeth. Treatment options for pregnant women include topical non-tetracycline antibiotics, azelaic acid, topical niacinamide and topical alpha hydroxy acids such as glycolic acid (Table).[28]

Adjuvant therapies

The following therapies may improve patients' appearance and be helpful additions to the overall treatment plan. They may also be helpful in treating acne scarring. These treatments include comedo extraction, electrocauterisation, chemical peels, microdermabrasion, intralesional corticosteroids, laser treatment, photodynamic therapy and phototherapy (Table).

Biophotonic light therapy is a non-invasive treatment, used especially for inflammatory acne, whereby a gel is applied to the affected area (either face or trunk) and fluorescent light energy applied to stimulate the skin's repair mechanisms.

Surgical techniques including punch excision, subcision and trichloroacetic acid cross hatching and filler may be used for acne scarring.

Complementary and alternative therapies

Many patients look to 'more natural' herbal and alternative treatments. There are limited data on the efficacy and safety of such products, and the specific ingredients, their concentrations and production processes are not well regulated. These alternative therapies include tea tree oil, niacinamide, ayurvedic compounds, antioxidant agents, zinc, probiotic treatments and many types of naturally occurring oils. Dietary modification, biofeedback-assisted relaxation, cognitive imagery and acupuncture have also been tried as alternative therapies to treat acne.

We must remember that patients will often seek treatment advice from non-medical sources and that even when seen by their own doctor, they may not adhere to the medication or attend follow-up appointments. The initial consultation should aim to establish trust between GP and patient and to emphasise the importance of review to see if treatment is working.

Novel treatments

New therapies for acne continue to be developed. Last year, a new fixed dose combination for acne treatment was launched (1% clindamycin phosphate/tretinoin 0.025%), and recently, trifarotene 0.005%, the newest fourth-generation retinoid cream, has been released to treat both facial and truncal acne. The newest agents include minocycline foam (currently available in the US) and a topical androgen clascoterone.[29,30] These new treatments are not available in Australia at the time of writing.

The role of cannabinoid signalling in skin maintenance and regeneration has prompted investigation of cannabinoids as potential therapeutic targets in acne treatment and includes the topical agent BTX1503, which demonstrated mixed results in a recent phase 2 clinical trial.[31,32]

Many of these therapies are in various stages of testing, and show promise for future treatments.

Conclusion

Patients with acne need to be assessed for severity of disease as well as for its psychological impact. Listening to patients' concerns and individualising treatment will help to strengthen the doctor–patient relationship. In a world of 'fake news' and so-called experts, healthcare professionals need to rely on their medical expertise and scientific background to offer patients effective treatment. MT

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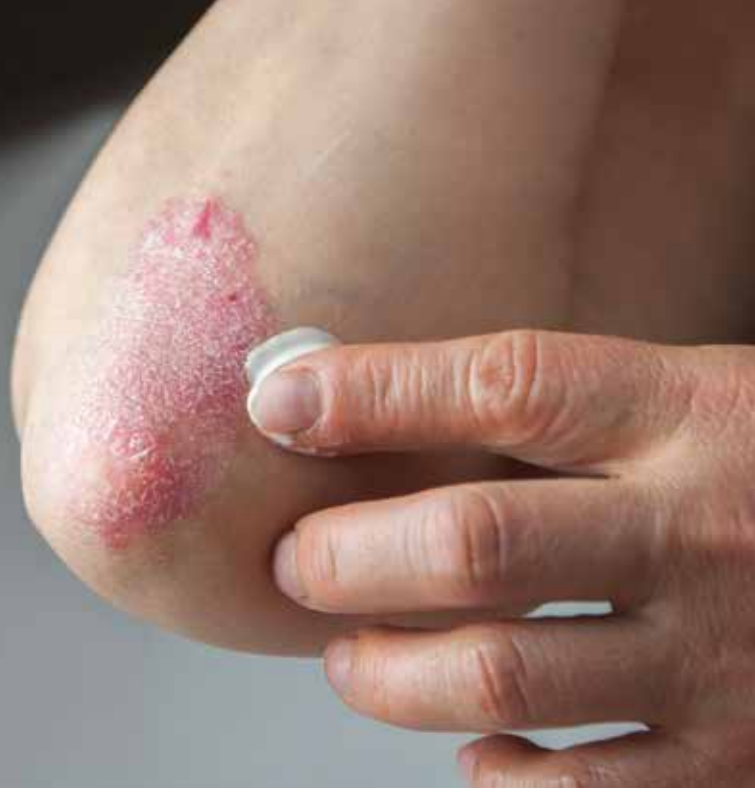

Therapies for psoriasis

Beyond lesion control

THEONE PAPPS MB BS; STEPHEN SHUMACK OAM, FACD

Conventional therapies for psoriasis that aim to decrease skin turnover have not met the needs of all patients. Novel biologic therapies that target the underlying immune mechanisms of psoriasis can be effective and well tolerated. They include the cytokine modulators infliximab, adalimumab, etanercept, ustekinumab, guselkumab, tildrakizumab, risankizumab, secukinumab and ixekizumab, and the enzyme inhibitor apremilast.

Psoriasis is a common condition, affecting 2 to 4% of the population, in which alterations in immune regulation manifest as skin disease.[1] Psoriasis also causes morbidity through associated systemic diseases and can have a major impact on patients, decreasing quality of life.[2] It is recognised that psoriasis is linked to psoriatic arthritis, inflammatory bowel disease, vascular inflammation and cardiac disease.[3] Long-term therapy for psoriasis also has social and quality of life implications and an economic impact on the healthcare system.

In recent decades, insight into the immunological mechanisms underlying psoriasis has increased, and the range of therapies has expanded to include novel biologic treatments that specifically target these mechanisms. These changes have revolutionised the treatment of psoriasis, decreasing morbidity and impact on the healthcare system.

KEY POINTS

- Psoriasis is a common disease involving chronic inflammation of the skin, nails or joints that often decreases quality of life.
- Traditional management aims to decrease skin turnover and control disease, rather than cure; options include topical medications, phototherapy and, for patients with resistant or widespread disease, systemic acitretin, methotrexate or ciclosporin.
- Moderate-to-severe psoriasis or involvement of special sites such as the scalp, genitals, palms or soles warrants specialist referral.
- Recent improved understanding of the immune mechanisms underlying psoriasis has led to novel biologic therapies that specifically target cytokines and enzymes involved in its pathophysiology.
- Targeted therapies for psoriasis include inhibitors of tumour necrosis factor-alpha (infliximab, adalimumab, etanercept), interleukin-23 (ustekinumab, guselkumab, tildrakizumab, risankizumab), interleukin-17 (secukinumab, ixekizumab), phosphodiesterase 4 (apremilast) and janus kinase (deucravacitinib and tofacitinib, which are not currently approved in Australia).
- Targeted therapies are effective, well tolerated and may have a better long-term safety profile than conventional systemic therapies.

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TREATMENTS FOR PSORIASIS AND MODE OF ADMINISTRATION

Conventional therapies

- Patient education and avoidance of triggers
- Corticosteroids (topical)
- Coal tar, with or without salicylic acid (topical)
- Vitamin D derivatives
  - calcipotriol (topical)
  - calcipotriol plus betamethasone (topical)
- Vitamin A derivatives
  - retinol (topical)
  - tazarotene (topical)
  - acitretin (oral)
- Dithranol (topical)
- Phototherapy
  - narrow-band ultraviolet B
  - psoralen plus ultraviolet A
- Immunosuppressants
  - methotrexate (oral or parenteral)
  - ciclosporin (oral)

Novel targeted therapies

- Anti-tumour necrosis factor-alpha
  - infliximab (IV infusion)
  - adalimumab (SC injection)
  - etanercept (SC injection)
- Anti-interleukin-23
  - ustekinumab (SC injection)
  - guselkumab (SC injection)
  - tildrakizumab (SC injection)
  - risankizumab (SC injection)
- Anti-interleukin-17
  - secukinumab (SC injection)
  - ixekizumab (SC injection)
- Janus kinase inhibitors
  - tofacitinib (oral)*
  - deucravacitinib*
- Phosphodiesterase-4 inhibitors
  - apremilast (oral)

Abbreviation: SC = subcutaneous.
* Not approved in Australia for treatment of psoriasis.

This article reviews the pathophysiology of psoriasis and conventional and novel treatments available for management of patients with psoriasis in Australia. Current treatments for psoriasis are summarised in the Box.

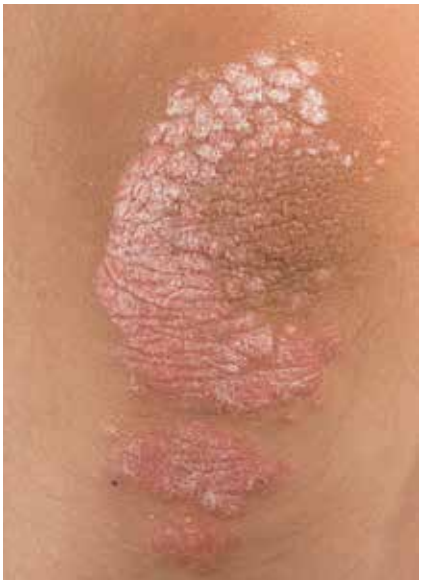

Figure 1. Chronic plaque psoriasis lesion.

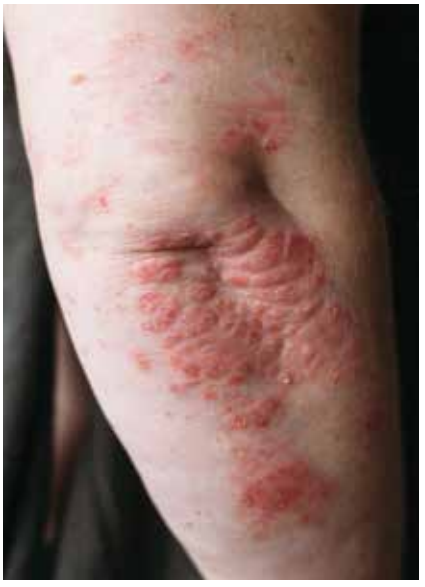

Figure 2. Psoriasis plaque on the elbow.

Clinical features

The main types of psoriasis are plaque-type psoriasis, guttate psoriasis, inverse psoriasis, localised pustular psoriasis and generalised pustular psoriasis.[4] Plaque-type psoriasis is the most common of these, and pustular or erythrodermic types are the least common.[5]

Pathologically, psoriasis is characterised by:

- parakeratosis – hyperproliferative epidermis and premature maturation of keratinocytes with retention of cell nuclei in the stratum corneum
- acanthosis – thickened epidermis due to an increased mitotic rate of basal keratinocytes
- dermal inflammatory infiltrate.[6]

Clinically, psoriasis manifests as raised, well-demarcated, erythematous and scaly plaques that typically affect extensor surfaces (Figures 1 and 2). Visible areas and special sites such as the scalp, genitals, palms and soles can pose a therapeutic challenge and have a high impact on quality of life. Psoriasis can also cause psoriatic nail dystrophy, which is often unsightly and can lead to psychological distress, pain and functional impairment.[2] Recognised comorbidities with psoriasis include psoriatic arthritis, metabolic syndrome and depression. Part of the GP's role is to recognise and manage comorbidities to improve patient outcomes.

Pathophysiology

The pathophysiology of psoriasis is underpinned by a complex interplay between environmental and genetic factors that act as disease initiating triggers. Environmental triggers include stress, bacterial products, drugs, trauma and smoking. Genetic studies have identified an association of psoriasis with several specific chromosomal loci, including psoriasis susceptibility locus 1 (PSORS1), and also with variants in the genes encoding the interleukin-23 (IL-23) and interleukin-12 (IL-12) receptors. Activation of a dysregulated immune system and the interplay between the immune system, skin epithelium and connective tissue shape and maintain the inflammatory disease process.[3]

Over the past two decades, it has been recognised that the immune process in psoriasis results from the functional role of dendritic cells, T cells and cytokines (Figure 3).[7] After an initial trigger, plasmacytoid dendritic cells become activated and secrete interferon-alpha, activating

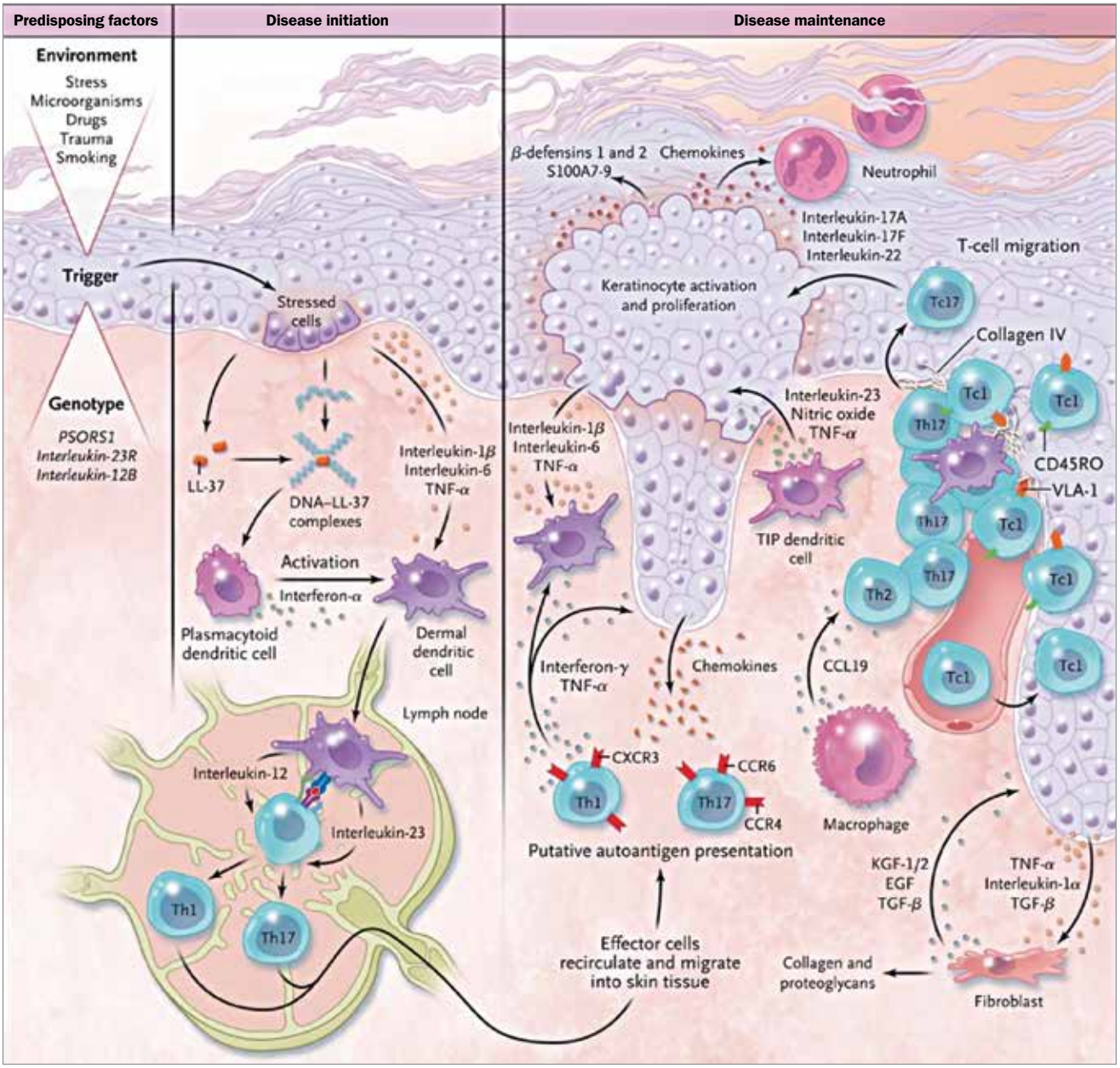

Figure 3. Proposed schema for the evolution of a psoriatic lesion from initiation to maintenance of disease.

Abbreviations: CCL-19 = chemokine (C-C motif) ligand 19; CCR4 = chemokine receptor 4; CCR6 = chemokine receptor 6; CD45RO = cluster designation 45RO; CXCR3 = chemokine (C-X-C motif) receptor 3; LL-37 = cathelicidin antimicrobial peptide, 18 kDa; PORS1 = psoriasis susceptibility locus 1; S100A7-9 = S100 regulatory proteins A7 (psoriasin), A8/9 (calprotectin); Tc1 = type 1 cytotoxic T cell; Tc17 = type 17 cytotoxic T cell; Th1 = type 1 T-helper cell; Th17 = type 17 T-helper cell; TIP dendritic cell = nitric oxide synthase-producing dendritic cell; TNF-α = tumour necrosis factor-alpha; VLA-1 = very late antigen 1.

Reproduced with permission from Nestle et al. Psoriasis. N Engl J Med 2009; 361: 496-509.[7]

myeloid dendritic cells. Subsequent secretion of IL-12 and IL-23 induces naïve T cells to differentiate into effector cells, such as type 1 and type 17 T-helper cells and cytotoxic T cells. The type 1 T cells release interferon-gamma and tumour necrosis factor (TNF)-alpha, and the type 17 T cells produce interleukins-17A, 17F and 22 (Figure 4).[7] These interleukins and TNF-alpha lead to keratinocyte activation and proliferation and subsequent production of antimicrobial peptides and chemokines. T cells migrate from the dermis to the epidermis in psoriasis. The microvasculature in psoriasis is also seen as leaky, and dendritic cells and T cells form perivascular clusters around blood vessels.[2,7]

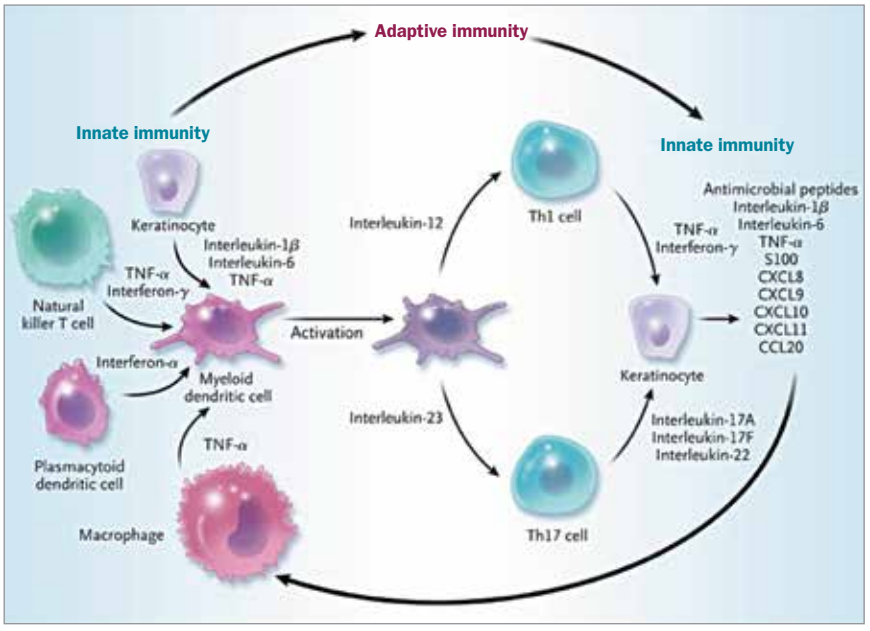

Figure 4. Key cells and mediators in the transition from innate to adaptive immunity in psoriasis. Innate immune cells produce key cytokines (tumour necrosis factor, interferons and interleukins) that activate myeloid dendritic cells. The activated cells present antigens and secrete mediators such as interleukins 12 and 23, leading to the differentiation of T-helper cells types 1 and 17. The T cells, in turn, secrete mediators (e.g. interleukins 17A, 17F and 22) that activate keratinocytes and induce the production of antimicrobial peptides, proinflammatory cytokines, chemokines and S100 proteins. These soluble mediators feed back into the proinflammatory disease cycle and shape the inflammatory infiltrate.

Abbreviations: Th1 = type 1 helper T cell; Th17 = type 17 helper T cell; TNF = tumour necrosis factor.
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Conventional treatments

The traditional aim of psoriasis therapy has revolved around decreasing skin turnover. Medications used include topical corticosteroids, coal tar (with or without salicylic acid), vitamin D derivatives, vitamin A derivatives and dithranol. Phototherapy with narrow-band ultraviolet B (UVB) or psoralen plus ultraviolet A (PUVA) is also used. These therapies may be used as monotherapy or in combinations.

Patients with more severe or generalised psoriasis may require systemic therapy with the oral vitamin A derivative acitretin or an immunosuppressant such as methotrexate or ciclosporin. Referral to a dermatologist for management is encouraged for this group.[2,3]

Other patients with psoriasis who require specialist referral because of the therapeutic challenge include:

- patients with severe nail psoriasis or pustular psoriasis
- children
- pregnant women
- patients with acquired immunodeficiency.[8]

Nonpharmacological treatments

Patient education and nonpharmacological management should be explored in all patients with psoriasis. This includes avoidance of triggers such as stress, infection, trauma, xerosis and potential culprit medications.

Topical corticosteroids

Topical corticosteroids are used to reduce inflammation. Low-potency corticosteroids should be used on the face, axillae and groin, where the skin is more sensitive, and concomitantly higher potency agents are typically needed on thicker plaques and patches on the palms and soles. Adverse effects of inappropriate use may include thinning of skin and the development of striae; caution is required to avoid a rebound flare following cessation. Topical corticosteroids are often used in conjunction with other treatments listed below that have complementary effects.[9]

Coal tar with or without salicylic acid

Coal tar therapy is available in various forms and combinations with other agents such as salicylic acid. Coal tar in its natural form is thick and black and can be obtained over the counter. Coal tar in combination with agents such as salicylic acid requires a prescription.

The exact mechanism of action of tar in patients with psoriasis is not completely understood, but it is believed to suppress DNA synthesis and thereby to inhibit keratinocyte proliferation.[10] As well as this keratoplastic effect, tar is proposed to have antimicrobial and antipruritic effects.[11] Salicylic acid is a keratolytic that causes shedding of the epidermis and scale, improving penetration of other topical medications.

The benefit of tar therapy is its low cost, but it may cause local irritation, has an unpleasant smell and can stain skin and clothing.[12]

Vitamin D derivatives (calcipotriol)

Natural vitamin D3 (calcitriol) requires activation through skin exposure to ultraviolet light. Calcipotriol is an already active form of vitamin D. Calcipotriol is included in topical treatments that are used once or twice daily, often in combination with corticosteroids. A fixed combination of calcipotriol with betamethasone dipropionate can be used daily.[9] Adverse effects of calcipotriol include local irritation and disturbances of calcium metabolism. However, only 1% of calcipotriol is absorbed through the skin and the risk of hypercalcaemia is significantly lower than for natural vitamin D3 (100 to 200 times lower risk).[13,14] As salicylic acid deactivates calcipotriol, the two medications should not be used concurrently.

Vitamin A (retinol) and synthetic derivatives

Vitamin A is needed for normal skin growth. Vitamin A (retinol) and synthetic vitamin A derivatives bind to nuclear retinoic acid receptors in the skin and reduce the rate at which skin cells develop and renew themselves; they also reduce inflammation. Tazarotene is the first topical receptor-selective retinoid approved for use to treat psoriasis. It binds only to the cell receptors in the epidermis and hence has a lower adverse effect profile.[3] However, local irritation is still common, and it is usually used along with topical corticosteroids to counteract this.

Oral retinoids such as acitretin are usually reserved for patients with severe psoriasis and are particularly useful for those with the pustular or erythrodermic type of psoriasis.[15] Adverse effects can include more significant local irritation, with redness and dry skin, and emollients should be used. Caution is needed with oral retinoids in patients with liver abnormalities, and they must not be used by women who are pregnant or for at least two years before pregnancy, because of potential teratogenic effects.

Topical and oral retinoids are typically used in combination with other therapies, such as topical corticosteroids and phototherapy.[16]

Dithranol

Dithranol (also known as anthralin) is a natural anthraquinone derivative that controls skin growth by reducing DNA synthesis and mitotic activity in the hyperplastic epidermis. This restores a normal rate of cell proliferation and keratinisation. Dithranol also has anti-inflammatory effects. It is available as a cream, ointment or paste, but is less commonly used today.[17]

Phototherapy (narrow-band UVB or psoralen plus UVA)

Patients with psoriasis that is widespread or difficult to control should be referred to a dermatologist. Phototherapy, methotrexate and ciclosporin are reserved for these groups of patients.

In phototherapy, UV light reduces inflammation and slows the production of skin cells. Treatment involves exposing the skin to UV light for a set duration on a regular schedule, usually three times a week. The most common modality is narrow-band UVB (311 nm). UV light seems effective in combination with topical medications. Psoralen increases the skin's responsiveness to UVA light. For this reason, psoralen plus UVA is generally more effective than UVB but has a greater risk of adverse effects. Phototherapy can be time consuming for patients and may cause phototoxicity, photoageing and increased risk of skin malignancy.[3] As the risk of skin malignancy increases with greater DNA damage, PUVA carries a greater risk than narrow-band UVB therapy.[4] All patients receiving phototherapy should use standard sun protection measures.

Methotrexate

Systemic options such as methotrexate and ciclosporin are useful to treat psoriasis as they prevent T cell activation. Methotrexate is a folic acid antagonist that inhibits DNA synthesis and cell replication by competitively inhibiting the conversion of folic acid to folinic acid. It has cytotoxic, immunosuppressive and anti-inflammatory actions that are beneficial in psoriasis. A low-dose weekly regimen of either oral or subcutaneous methotrexate is recommended. Adverse effects include hepatic impairment, bone marrow suppression with neutropenia or pancytopenia, renal impairment and pulmonary toxicity.[18]

Ciclosporin

Ciclosporin is a calcineurin inhibitor that blocks the action of calcineurin in activated T cells, hence downregulating inflammatory interleukins and T-cell proliferation. As with methotrexate, care should be taken with toxicity and adverse effects such as renal impairment and hypertension.[19,20]

Novel targeted therapies

Improved understanding of the complex immune process underlying psoriasis has suggested a therapeutic role for agents that target the immune system. This pathogenesis-based approach to therapy for psoriasis is effective and overall well tolerated, validating the theories about the underlying immune mechanisms.

The biologic therapies in current use target cytokines. Therapies that target T cells, such as alefacept, are no longer used as more effective targeted therapies have become available. The initial cytokine-targeted therapies targeted TNF. Therapies that target interleukins were then explored; these are delivered subcutaneously. Janus kinase (JAK) inhibitors and phosphodiesterase-4 (PD4) inhibitors are oral targeted therapies that may also have a role in changing the face of psoriasis treatment.

Biologic therapies for psoriasis are available on the PBS for patients who fulfil specific criteria, which typically include failure of several other systemic treatments. This includes failure to achieve an adequate response, intolerance or a contraindication to two of the following four treatments for psoriasis: acitretin, phototherapy, methotrexate or ciclosporin (with specific doses and durations applicable). In addition, biologic therapies for psoriasis must be prescribed by a dermatologist.[21]

Anti-tumour necrosis factor-alpha

Anti-TNF-alpha therapies are cytokine modulators that bind to TNF-alpha and inhibit its activity. They include infliximab, adalimumab and etanercept. Anti-TNF-alpha therapies therefore reduce activation of myeloid dendritic cells and downstream inflammatory pathways. Adverse effects include potential infections, exacerbation of psoriasis (because of blocking of other anti-inflammatory effects), triggering of autoimmune processes, cutaneous malignancies and blood dyscrasias.[22,23] Cardiac failure is also reported but is infrequent.

Anti-interleukin-23

Anti-IL-23 therapies include ustekinumab, guselkumab, tildrakizumab and risankizumab. Anti-IL-23 therapies bind to the p40 subunit of IL-12 and IL-23 or to the

PSORIASIS AREA AND SEVERITY INDEX

A Psoriasis Area and Severity Index (PASI) is a quantitative rating scale for measuring the severity of psoriatic lesions based on area coverage and plaque appearance. Please complete **all** sections of the table and shade in the affected areas on the body diagrams below.

Plaque characteristic	Rating score	Body region (and weighting factor)			
		Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None 1 = Slight 2 = Moderate 3 = Severe 4 = Very severe				
Thickness					
Scaling					
Add together each of the 3 scores for each of the body regions to give 4 separate sub totals.					
Sub Totals		A1=	A2=	A3=	A4=
Multiply each sub total by the amount of body surface area represented by that region i.e. A1 x 0.1 for head, A2 x 0.2 for upper limbs, A3 x 0.3 for trunk, A4 x 0.4 for lower limbs to give a value B1, B2, B3 and B4 for each body region respectively					
		A1 x 0.1 = B1	A2 x 0.2 = B2	A3 x 0.3 = B3	A4 x 0.4 = B4
		B1=	B2=	B3=	B4=
Degree of involvement as % for each body region affected (score each region with score between 0–6)	0 = None 1 = 1–9% 2 = 10–29% 3 = 30–49% 4 = 50–69% 5 = 70–89% 6 = 90–100%				
For each body region multiply sub total B1, B2, B3 and B4 by the score (0–6) of the % of body region involved to give 4 subtotals C1, C2, C3 and C4					
		B1 x score = C1	B2 x score = C2	B3 x score = C3	B4 x score = C4
		C1=	**C2=**	**C3=**	**C4=**
The patient's PASI score is the sum of C1+C2+C3+C4				**PASI=**	

Please shade in the affected areas

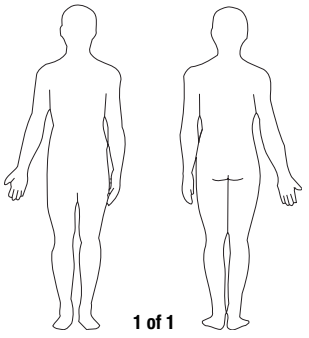

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Figure 5. Form for calculation of the Psoriasis Area and Severity Index (PASI; https://www.humanservices.gov.au/organisations/health-professionals/forms/pb115).[26]

p19 subunit of IL-23, preventing these interleukins binding to cell-surface receptors. This prevents IL-23 or IL-12-mediated activation and differentiation of T cells, interrupting signalling and cytokine cascades involved in psoriasis pathology.[7] Side effects to consider include reactivation of infections such as inactive hepatitis B or latent tuberculosis.

Anti-interleukin-17

Anti-IL-17 therapies include secukinumab and ixekizumab. Like anti-IL-23 therapies, anti-IL-17 therapies act as cytokine modulators by selectively binding and neutralising cytokine IL-17A. This blocks IL-17A from forming a complex with the IL-17 receptor, and thereby inhibits activation of keratinocytes and release of proinflammatory cytokines, chemokines and mediators of tissue damage.[3] Adverse effects are similar to those of IL-23 agents; ixekizumab can cause site reactions. Another anti-IL-17 agent, brodalumab, is available in other countries but has not been taken to market in Australia because of a black box warning following a study that reported two suicides, despite its impressive efficacy in clinical trials.

Janus kinase inhibitors

JAK inhibitors include tofacitinib and deucravacitinib. JAK enzymes include four types: JAK 1, JAK 2, JAK 3 and Tyk2. They act in pairs on the intracytoplasmic portion of cytokine receptors. Each JAK pair can be activated by different cytokines and in turn activates different signal transducer and activator of transcription (STAT) proteins. Activated STAT proteins control the expression of nuclear gene targets, inducing the transcription of pro-inflammatory genes. Hence, JAK inhibition decreases production of inflammatory cytokines.[7] Adverse effects are determined by the selectivity profile but can include bone marrow dysfunction and increased risk of gastrointestinal perforation.[24] Other drugs metabolised by the cytochrome P450 3A4 (CYP3A4) enzyme should be avoided. None of the JAK inhibitors are currently approved in Australia for use in psoriasis.

Phosphodiesterase-4 inhibitors

PD4 inhibitors act as cytokine modulators by inhibiting PD4 in many cells, including T cells and keratinocytes. This in turn reduces production of pro-inflammatory cytokines, including TNF-alpha, interferon-gamma, IL-17 and IL-23, and also increases anti-inflammatory cytokines such as IL-10. PD4 inhibitors include apremilast, which is available on the PBS for patients who have not responded to methotrexate, and is prescribed by a dermatologist. Adverse effects include gastrointestinal upset, renal impairment and depression.[25]

Treatment monitoring

Psoriasis causes significant discomfort and has associated comorbidities, which can affect patients' quality of life. Treatment monitoring should include not only skin assessment but also a measure of quality of life.[2]

The skin can be assessed with the Psoriasis Area and Severity Index (PASI). This rates severity on a scale of 0 to 72 based on area of coverage and plaque appearance (erythema, thickness and scaling) for each body region. A pro forma is available at: www.humanservices.gov.au/

organisations/health-professionals/forms/pb115 (Figure 5).[26] Quality of life can be assessed with the Dermatology Life Quality Index (DLQI), a 10-question questionnaire that measures the impact of a skin problem on the patient's life over the previous week (http://sites.cardiff.ac.uk/dermatology/quality-of-life-dermatology-quality-of-life-index-dlqi).

The 2013 Australian consensus on treatment goals for psoriasis agreed that treatment success is a reduction in PASI score of 75% or more at the end of the induction phase of treatment.[27] Treatment failure was defined as a reduction in PASI score of 50% or less at the end of induction, indicating the need to modify the treatment regimen. It was also considered highly relevant to assess quality of life when assessing psoriasis severity and treatment, because an absolute PASI score and skin appearance may not be clinically meaningful measures if they do not correlate with quality of life.[27]

Since the introduction of anti-interleukin therapies, greater improvements in PASI score are expected. A reduction in PASI score of 90% or more has been considered a more appropriate standard.[28] Some studies include a 100% reduction in PASI score as a secondary endpoint. This change highlights our higher expectations; as new therapies evolve, we can aim for patients with psoriasis to have clear, or almost clear, skin. This is a shift from the traditional view that only lesion control is achievable.[4]

Conclusion

Psoriasis is a chronic inflammatory disease that has not only physical but also psychological, social and economic implications. Conventional topical and systemic immunosuppressants have not met the treatment needs of all patients with psoriasis. However, newer pathogenesis-targeted therapies that act as cytokine modulators have shown their effectiveness. Although these biologic therapies must be prescribed by specialists, it is important for the wider medical community to understand their role in the evolving management of psoriasis. These newer therapies have shown appropriate long-term risk-benefit and cost profiles. An exciting frontier includes further research into the role of these therapies in treating patients with associated inflammatory diseases.[29] MT

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COMPETING INTERESTS: None.

Recurrent painful intertriginous nodules

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GAYLE FISCHER OAM, MB BS, MD, FACD

Test your diagnostic skills in our regular dermatology quiz. What is the cause of these painful lesions occurring on a woman's vulva and groin?

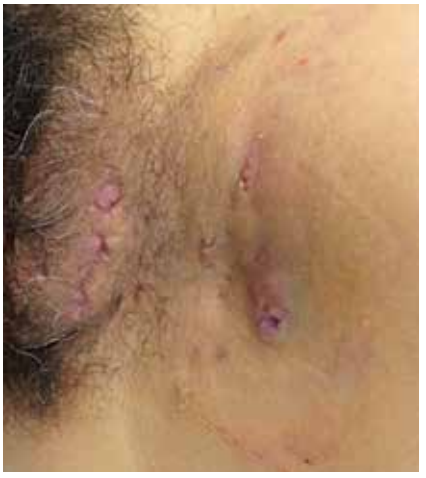

Figure 1. Multiple lesions in the groin area (case patient).

Case presentation

A 32-year-old woman presents with recurrent nodules and pustules on the left side of the vulva and extending to the groin (Figure 1). The lesions are painful and exude pus. She has been treated for the condition several times with antibiotics, despite bacterial swabs consistently returning negative results.

Differential diagnoses

Conditions to consider among the differential diagnoses include the following.

- **Recurrent furunculosis.** Colloquially known as a 'boil', a furuncle is a deep bacterial infection of the hair follicle. It is most commonly caused by *Staphylococcus aureus* but Gram-negative bacteria can also cause anogenital furunculosis.[1] Risk factors include crowded living environments, chronic *S. aureus* carriage in the anterior nares, obesity, diabetes mellitus, HIV infection, atopic dermatitis and chronic wounds, but recurrent furunculosis can occur in healthy individuals.[1] Furuncles present as painful, erythematous, indurated nodules that can occur anywhere there is hair-bearing skin, but the lesions are most common on the face, neck, perineum and sites of trauma or friction.[1] Patients are systemically well, although there may be associated regional lymphadenopathy.[1] A bacterial swab for culture is indicated in each episode of recurrent furunculosis to guide systemic antibiotic therapy and ensure coverage for potential underlying methicillin-resistant *S. aureus* infection.
- **Crohn's disease (CD).** A chronic inflammatory granulomatous disease affecting the entire gastrointestinal tract, CD is characterised by noncaseating granulomatous lesions that can cause debilitating strictures, fistulae and abscesses.[2] CD commonly occurs between the second and fourth decades of life.[2] Dermatological manifestations are the most common extra-intestinal finding, affecting up to 75% of individuals with CD and preceding intestinal diagnosis in 25% of cases.[2] Cutaneous CD lesions are classified as granulomatous extension of gastrointestinal CD (e.g. perianal skin tags, fistulae, sinuses [Figure 2], oral aphthous ulcers), reactive lesions (e.g. erythema nodosum, pyoderma gangrenosum), or lesions resulting from CD-related chronic malnutrition (e.g. acrodermatitis enteropathica-like syndrome).[2] Lesions may therefore be contiguous with the gastrointestinal tract in the perianal region or metastatic, occurring on other parts of the skin. Early contiguous CD lesions begin as erythematous papules that evolve into nodules that then ulcerate with purulent discharge.[2] Metastatic CD is rare but can occur in the genital region where it is characterised by erythema and swelling; nongenital

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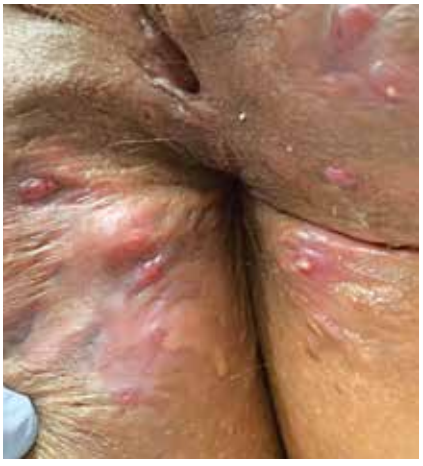

Figure 2. Perianal nodules caused by Crohn's disease.

metastatic CD varies and can present as erythematous papules, plaques and nodules.[2] Biopsy is diagnostic and shows noncaseating granulomas with multinucleated giant cells affecting the dermis that are negative for Gram, periodic acid schiff (PAS) and Ziehl-Neelsen stains.[2]

- **Epidermoid cyst.** Epidermoid cysts (inclusion cysts) are well-demarcated, pink to yellow fluctuant nodules with a central punctum indicating a keratin plug communicating with the skin surface. They can arise anywhere but commonly occur on the back, face and anterior chest wall;[3] multiple epidermoid cysts can occur on genital skin. These nodular lesions commonly remain dormant but can grow, with subsequent rupture provoking a localised inflammatory response and resultant exudate.[3] The cysts can arise in the setting of follicular occlusion (e.g. acne vulgaris) and drug treatments (e.g. BRAF inhibitors).[4] Biopsy shows a true cyst – that is, a keratin-filled cyst lined by stratified squamous epithelium.[3] Epidermoid cysts occurring in uncommon areas or in conjunction with lipomas, fibromas and pilomatricomas are seen in Gardner syndrome, a variant of the autosomal-dominant familial adenomatous polyposis – these patients require colectomy because of the risk of colorectal adenocarcinoma.[3]
- **Mycobacterial abscess.** Cutaneous infections caused by the *Mycobacterium* genus have diverse clinical presentations. They are classified by the causative organism:
  - (i) *Mycobacterium tuberculosis* complex
  - (ii) *Mycobacterium leprae* and *Mycobacterium lepromatosis*
  - (iii) nontuberculous mycobacteria (which includes both slow and rapidly growing mycobacteria).[5]

  Cutaneous tuberculosis (TB) is uncommon, with a prevalence of 2% in those with mycobacterial infection, and rarely coexists with pulmonary or extrapulmonary TB.[5] Scrofuloderma is a worrisome harbinger of concomitant visceral and cutaneous TB and is due to localised cutaneous extension of an underlying TB-infected structure, most commonly a lymph node but it can also be a bone or joint.[5] It presents with enlarging indurated subcutaneous nodules, most commonly on the neck, that ulcerate with subsequent sinus tracts exuding purulent or caseous discharge.[5] Biopsy shows caseating granulomas with acid-fast bacilli, typical of mycobacteria.[5]
- **Hidradenitis suppurativa (HS).** This is the correct diagnosis. HS is a chronic inflammatory disease of the pilosebaceous unit resulting in follicular occlusion, rupture and resultant dermal abscess formation.[6] HS occurs in intertriginous areas where there is an abundance of apocrine glands, such as the axillae, inguinal folds and perineal, anogenital and inframammary areas.[6] Acute HS presents with multiple tender erythematous subcutaneous nodules and abscesses, which over time develop sinus tracts (double-ended pseudocomedones) and hypertrophic scars – these are visible in Figure 1.[6] The sinus tracts express purulent, malodorous exudate, which is typically sterile.[6] HS affects 1% of the population, commonly affecting individuals in their second and third decades of life, and has a predominance in females. However, there is a familial form of HS that has an autosomal-dominant mode of inheritance.[6] It is one of four diseases in the 'follicular occlusion' tetrad – along with acne conglobata, dissecting cellulitis of the scalp and pilonidal cysts – and it is not uncommon for patients to be affected by multiple disorders within the tetrad.[6] Other associations with HS include the autoinflammatory syndromes PASH (pyoderma gangrenosum, acne vulgaris, HS) and PAPASH (pyogenic arthritis and PASH); it is also associated with obesity, smoking and CD.[6]

Diagnosis

HS is a clinical diagnosis. The aim of initial evaluation is to exclude differential diagnoses; this includes bacterial cultures to exclude acute bacterial infection, and biopsy to exclude cutaneous CD.[6] Biopsy of a HS lesion shows follicular plugging and deep dermal fibrotic changes with mixed granulomatous/suppurative infiltrate.[6] HS should be suspected for any chronic relapsing pustular condition of the intertriginous areas associated with scarring, sinuses and comedones, particularly if bacterial swabs do not return positive results on culture.

Management

HS is a chronic debilitating disease that has a significant psychosocial impact

for affected patients. The Hurley staging system is used to classify the extent of the disease but is not reflective of disease activity.[6] For Hurley stage I lesions (abscesses without sinus tract formation or cicatrisation), first-line treatment is antimicrobial agents (systemic and/or topical)[6] and antiandrogen therapy; additional modalities include intralesional corticosteroids and oral zinc.[6] Clindamycin has been shown to achieve reduction in abscesses and pustules and has synergistic benefits when used with other antibiotics (e.g. rifampicin, minocycline), while corticosteroids are useful for the acute management of inflammatory nodules.[6] Higher tier treatment options are reserved for Hurley stage II lesions (separated recurrent abscesses with sinus tract formation and scarring) and stage III lesions (multiple interconnected tracts and abscesses within an area), which include CO_2 laser ablation, immunosuppressive therapies such as adalimumab and surgical excision.[6] Recommended lifestyle modifications for patients with HS include weight loss, smoking cessation and avoidance of tight-fitting clothing.[6]

There are significant clinical complications of HS, which include anogenital strictures and fistulae, anaemia, contractures, cutaneous squamous cell carcinoma, epidural abscess and osteomyelitis.[6] HS is associated with metabolic syndrome and polycystic ovarian disease and patients should be appropriately screened.[7,8]

Outcome

This patient's lesions were consistent with Hurley stage II HS. A biopsy was performed, with results showing nonspecific mixed granulomas. She was started on spironolactone 100 mg daily, which proved ineffective. A six-week course of rifampicin and clindamycin was initially effective, but unfortunately her lesions recurred six months later. She was later treated with adalimumab, with a good outcome. MT

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COMPETING INTERESTS: None.

A sudden outbreak of facial papules and pustules

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Test your diagnostic skills in our regular dermatology quiz. What is the cause of these painful lesions on a woman's face?

Case presentation

A 42-year-old woman presents with an eruption of papules and pustules on her chin and both cheeks (Figure). The lesions are painful and tender and associated with oedema and lymphadenopathy. The lesions appeared suddenly about three weeks ago. She is systemically well and afebrile.

The patient has a history of minor acne as a teenager. She denies taking any medications.

Skin swabs and scrapings have been taken from the lesions and returned negative results for bacteria, herpes viruses and fungi. She has been treated with oral flucloxacillin, but the condition has not improved.

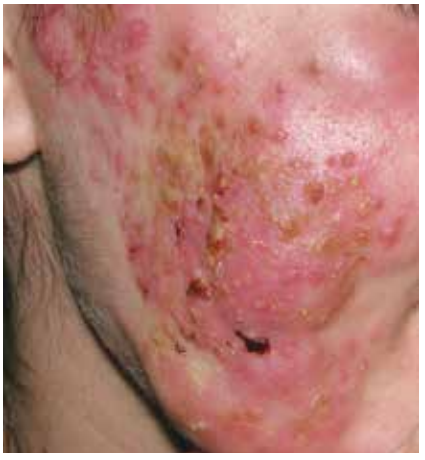

Figure. Papules and pustules on the patient's cheek.

Differential diagnosis

Conditions to consider in the differential diagnosis include the following.

- **Nodulocystic acne.** This severe form of acne presents as pustules, cysts, papules and comedones and is usually seen in adolescents and young adults. There is a subtype (acne fulminans) associated with systemic upset. Severe nodulocystic acne would be very unlikely in a woman who is 42 years of age.
- **Tinea faciei.** Tinea infections are caused by dermatophyte fungi and have a classic appearance of a scaly patch with central clearing. However, tinea infections are occasionally acutely inflammatory and pustular, particularly when the pathogen is acquired from an animal. Even in the presence of dramatic inflammation, patients remain systemically well.
- **Herpes infections.** A primary attack of cutaneous herpes simplex infection may sometimes be severe. The lesions are typically small, closely grouped vesicles on an erythematous base and they may follow a linear (zosteriform) distribution. A severe herpes simplex infection is usually accompanied by lymphadenopathy, pain and fever. Herpes zoster may also present as an acute infection with vesicles that become pustular and erosive – the eruption is nearly always unilateral with a dermatomal distribution – and it is frequently severely painful.
- **Impetigo.** A staphylococcal infection should be considered in the differential diagnosis of any pustular eruption. However, it would be very unlikely to be as severely inflammatory as the skin eruption seen in the case patient presented here. Impetigo would be ruled out by negative bacteriology and a complete lack of response to treatment with flucloxacillin.
- **Sweet's syndrome.** This uncommon inflammatory dermatosis often follows a streptococcal infection but may also be a sign of serious systemic disease. Patients present with acutely inflammatory plaques that may appear vesicular due to oedema. They are usually febrile and unwell, with a neutrophilia and elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).
- **Rosacea fulminans (pyoderma faciale).** This is the correct diagnosis. This uncommon and alarming eruption is generally seen in middle-aged women and is usually confined to the face. The onset is typically acute and, despite the highly inflammatory appearance of the skin eruption, the patient remains well. The pustular lesions and cystic

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swellings, which may be connected by sinuses, are itchy, tender and painful, and these occur on a background of erythema and oedema. Comedones are not part of the clinical picture and there is not always a history of typical rosacea. Rosacea fulminans may occur in pregnancy.[1] There may be residual scarring after the eruption has cleared; this scarring is minimal and not proportionate to the severity of the lesions. Rosacea fulminans is often a clinical diagnosis and one of exclusion. For the case presented here, the skin eruption is consistent with the clinical features of rosacea fulminans; the patient is female and within the typical age range and infective causes have been ruled out.

Cause

It is not clear whether rosacea fulminans is a variant of rosacea or acne vulgaris or a separate entity.[2] It has been suggested that hormones may play a role because rosacea fulminans is a condition that mainly affects females.[1] There have been reported cases with associated inflammatory bowel disease, both Crohn's disease[3] and ulcerative colitis.[4] Rosacea fulminans may be complicated by erythema nodosum.[5]

Diagnosis

Despite the severity of the skin inflammation in patients with rosacea fulminans, there are no systemic symptoms. Typically, no infective organisms are found in the bacterial and fungal cultures of the affected skin. Histopathological examination of skin lesions should be performed in patients for whom Sweet's syndrome is suspected. Biopsies of rosacea fulminans are not diagnostic in themselves, usually showing extensive lymphocytic infiltrate with perifollicular accentuation, mainly in the dermis and extending to the subcutis. Eosinophils, foreign body giant cells and granuloma formation, collagen necrosis and fibrosis have also been described.[6] Patients are otherwise well and further blood tests or investigations are therefore not usually indicated.

Management

Patients with rosacea fulminans should be under the care of a dermatologist and early referral is advised. Treatment is initiated with oral prednisone (0.5 to 1.0 mg daily for one to two weeks) to settle the inflammation. Isotretinoin (0.2 to 0.5 mg/kg daily for three to four months) is then introduced while the prednisone is tapered. Recovery may take up to six months.[7] MT

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A rapidly progressing, blistering eruption in a febrile patient

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Test your diagnostic skills in our regular dermatology quiz. What is the cause of this painful, widespread skin eruption?

Case presentation

A 32-year-old primary school teacher presents to the accident and emergency department with fever associated with a painful and itchy blistering eruption. The lesions involve her trunk, arms, legs, face and scalp (Figure). The illness started with a generalised maculopapular eruption three days ago and progressed rapidly, with lesions cropping every few hours. She feels fatigued and mildly nauseated but is not significantly unwell.

Differential diagnoses

Differential diagnoses to consider in a patient with an evolving, generalised blistering eruption with fever include the following.

- **Sweet's syndrome (acute febrile neutrophilic dermatosis).** Sweet's syndrome is a rare neutrophilic dermatosis characterised by abrupt onset of a generalised, tender, erythematous eruption in an unwell, febrile patient. It can occur at any age, with peak onset between the fourth and seventh decades of life, and has a predominance in females.[1] Triggers include occult malignancy, infection, drugs (e.g. NSAIDs, frusemide, trimethoprim-sulfamethoxazole), inflammatory bowel disease, autoimmune disorders (e.g. systemic lupus erythematosus) and pregnancy.[1] Lesions in Sweet's syndrome are typically nonpruritic, tender erythematous papules that may coalesce into plaques; these can exhibit pseudovesicular and targetoid morphology involving cutaneous surfaces of head, neck and upper limbs, sparing mucosal surfaces.[1] Histopathology shows diffuse nodular perivascular neutrophilic infiltrate without evidence of vasculitis.[1]

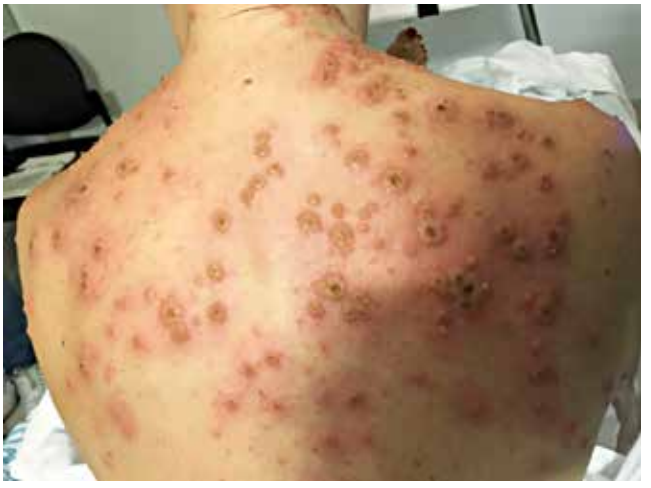

Figure. The case patient's maculopapular eruption in various stages of evolution. Vesicular crusting lesions on an erythematous base are visible.

- **Pityriasis lichenoides et varioliformis acute (PLEVA).** Patients with this condition are usually well and develop diffuse recurrent crops of pruritic and painful erythematous, purpuric papules that may form crusts, vesicles, pustules or ulcers. PLEVA has associations with infections (e.g. HIV, parvovirus B19) and drugs (e.g. 5-fluorouracil, radiocontrast iodide).[2] Histopathology shows predominantly lymphocytic perivascular interface dermatitis, with an absence of vascular fibrinoid necrosis.[2]
- **Staphylococcal folliculitis.** A superficial infection of the hair follicle is most commonly due to *Staphylococcus aureus*, which results in pruritic and tender dome-shaped crusted papules and/or pustules on an erythematous base that may rupture to form a crust.[3] These lesions commonly affect the face, scalp, back, chest, axillae and buttocks. Patients with localised folliculitis are usually well, with leukocytosis and neutrophilia. Bacterial swabs for microscopy, Gram stain and culture will confirm the diagnosis of staphylococcal folliculitis and dictate whether the causative organism is methicillin-sensitive or methicillin-resistant *S. aureus*.[3] Involvement of deep

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soft tissue or large, coalescent erythematous papules in a febrile patient with recalcitrant staphylococcal folliculitis may indicate furunculosis or carbunculosis.[3]

- **Bullous pemphigoid.** Bullous pemphigoid results in a symmetrical distribution of subepidermal vesicles and bullae that tend to involve the flexural surfaces of extremities, lower trunk and mucosal surfaces of the oral cavity, nasopharynx, eyes and anogenital region.[4] Bullous pemphigoid is most commonly seen in the eighth decade of life and can be triggered by trauma, drugs (e.g. spironolactone, NSAIDs, penicillins, ACE inhibitors), and is associated with neuropsychiatric disorders.[4] The typical polymorphic clinical course of bullous pemphigoid occurs in two stages. An initial prodromal nonbullous period with nonspecific pruritus may be accompanied by erythematous papular and/or urticarial lesions. This is followed by a bullous phase characterised by the development of vesicles and bullae containing clear and/or blood-tinged fluid that can erupt causing erosions and crusts, with associated annular urticarial papules and plaques.[4] Perilesional biopsy for direct immunofluorescence will show fine linear continuous deposits of IgG and C3 along the epidermal basement membrane, while blood tests may show a peripheral eosinophilia with IgG auto-antibodies to BP180 and BP230.[4]
- **Erythema multiforme (EM).** This condition is characterised by an abrupt onset of fixed pruritic and painful erythematous papules symmetrically affecting the upper extremities and face, which may evolve into the typical target lesions.[5] The two clinical forms of EM (minor and major) are distinguished by the degree of mucosal involvement, which is more severe in EM major.[5] Patients with EM minor are usually well, whereas systemic features such as fever, lethargy and arthralgias are almost always present in EM major.[5] More than 90% of cases of EM are due to infections, most commonly HSV-1 and HSV-2; less common precipitants include drugs (e.g. NSAIDs, anticonvulsants) and systemic disease (e.g. inflammatory bowel disease, systemic lupus erythematosus).[5] A history of herpes labialis is seen in half of patients with EM, which precedes the EM eruption from 3 to 14 days.
- **Varicella infection.** This is the correct diagnosis. Patients with varicella infection experience prodromal fever, myalgia and malaise, followed by an abrupt onset of a pruritic, erythematous, maculopapular eruption that initially appears on the scalp and face, with later involvement of the trunk, proximal extremities and mucosae, particularly the mucosa in the roof of the oral cavity.[6] Lesions evolve into the characteristic small vesicles with a surrounding red halo within 12 hours, then form pustules with crusting; resolution occurs within 10 days of onset.[6] In contrast to the benign and self-limiting disease course seen in children, varicella infection in adults is more severe, with increased cutaneous involvement and higher incidence of varicella pneumonia, hepatitis and encephalitis.[6] Superimposed cutaneous bacterial infection, usually caused by *Streptococcus pyogenes* or *S. aureus*, is the most common complication.[6] The diagnosis is primarily clinical, by clarifying exposure, previous varicella infection and/or vaccination, and is confirmed by PCR testing from a viral swab of an active vesicular lesion.[6] Because of high levels of immunisation in the community, varicella is not seen as often as it once was.

Management and outcome

The patient was admitted to hospital because she was febrile and the medical team in the accident and emergency department were unsure of the diagnosis. A full blood count and biochemical testing were performed, and a raised white cell count and C-reactive protein were noted. Chest x-ray was performed to exclude pulmonary involvement.

The dermatology team was consulted the next day and made a diagnosis of varicella. The patient was started on oral valaciclovir and cefalexin to cover suspected bacterial superinfection. A bacterial swab subsequently revealed secondary infection with *S. aureus*, and cefalexin was therefore continued for 10 days. A viral swab confirmed the diagnosis of varicella.

The patient recovered completely, fortunately without the significant scarring that can be a complication of varicella. However, she suffered from a significant post-viral syndrome with severe fatigue and lethargy for six weeks and was unable to return to work for two months. MT

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