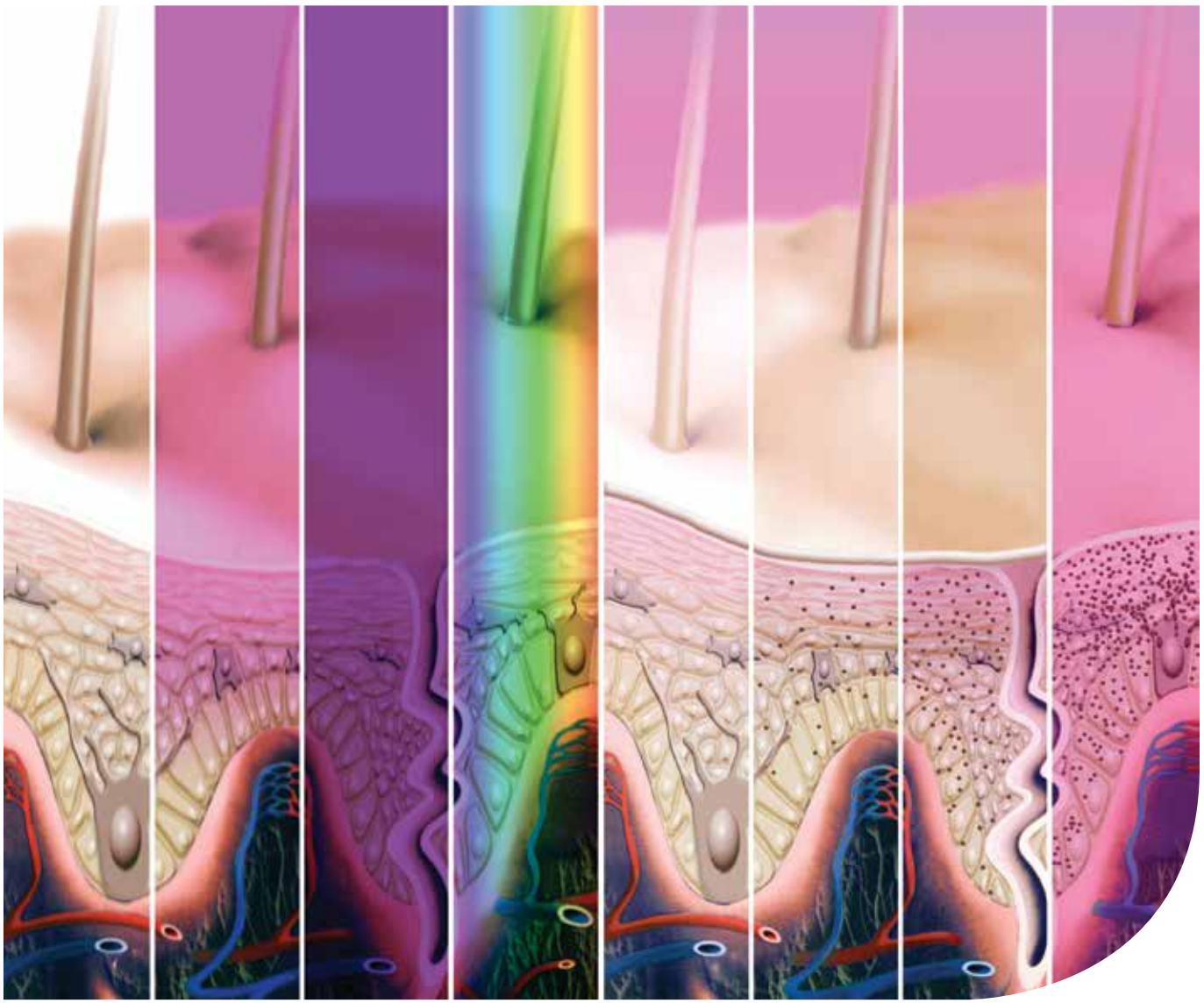
DECEMBER 2016 VOL 1 NO 2

A MEDICINE TODAY PUBLICATION

Dermatology Collection

PEER REVIEWED UPDATES FOR MEDICAL PRACTITIONERS



Reprints in Dermatology

A GP's guide to actinic keratosis

Paediatric psoriasis: a common skin disorder with potential multisystem implications

Update on diagnosis and management of melanoma

Nail disease: is it fungal and how should it be managed?

Nicotinamide and prevention of nonmelanoma skin cancer

Nappy rash: managing eruptions, preventing recurrence

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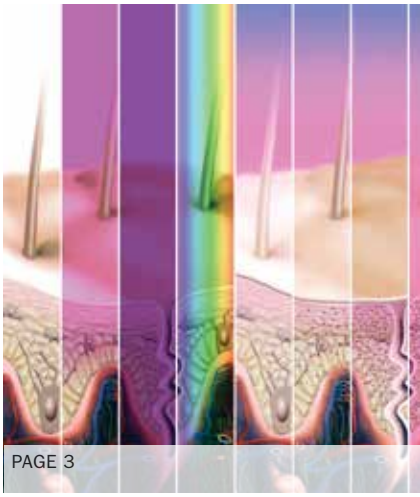

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FOREWORD FROM THE EDITOR-IN-CHIEF, DERMATOLOGY COLLECTION

Dermatology is an important aspect of general practice and GPs are called on to diagnose and treat skin disease on a regular basis. *Medicine Today* is keen to provide regular updates and quizzes on the topic.

In this second issue of *Dermatology Collection* you will find more of the articles that we feel have been among the most important published in *Medicine Today* in recent years.

Skin cancer is a major problem in Australia, with over half of all patients seen in specialist dermatology practice having a sun damage- or skin cancer-related problem, such as actinic keratosis or melanoma. Recently, there have been many advances in the management of patients with melanoma. These topics are of constant interest to all GPs.

Many people in Australia take vitamins, the real value of which is doubtful. However, recent Australian research into the value of the B-group vitamin nicotinamide in reducing the risk of nonmelanoma skin cancer is something that all skin cancer patients should be made aware of.

Additionally, the ever-present condition of nappy rash, the mystery of fungal nail disease and the common skin disorder paediatric psoriasis are also covered in this issue.

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

Gayle Fischer MB BS, MD, FACD
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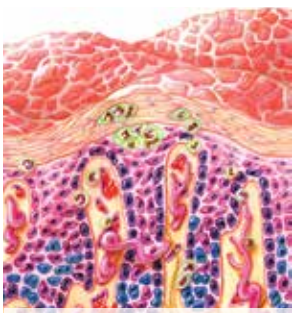
FEATURE ARTICLES PEER REVIEWED



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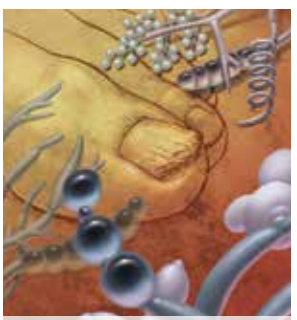

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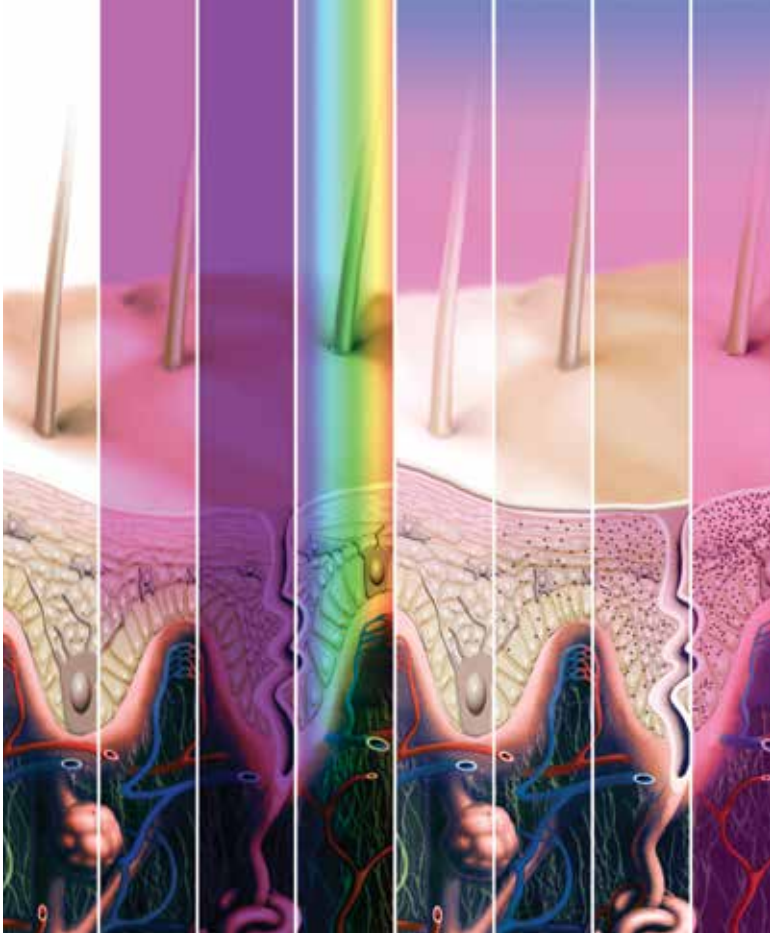
A GP's guide to actinic keratosis

GLORIA FONG BMLSc, MB BS
PATRICIA LOWE MB BS(Hons), MMed, FACD

Australia has the highest prevalence of actinic keratoses in the world. Due to the risk of transformation into invasive squamous cell carcinomas, actinic keratoses are routinely treated with an array of methods to prevent progression to invasive disease.



KEY POINTS

- Actinic keratoses (AKs) are premalignant lesions that have the potential to transform into in situ or invasive squamous cell carcinomas (SCCs).
- The main cause of AKs is chronic ultraviolet radiation-induced skin damage.
- The diagnosis of AKs is a clinical one, although dermoscopy is a useful adjunct to diagnosis.
- The use of high sun protection factor sunscreen and sun protection measures is the most important preventive measure for AKs.
- Other treatment modalities for AK can be broadly divided into lesion-directed and field-directed.
- Dermatologist referral is recommended for patients with lesions suspicious of SCC, extensive photodamage or immunosuppression and those at increased risk of developing SCC due to pre-existing medical conditions.

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Actinic keratoses (AKs) are superficial, discrete, erythematous and scaly skin lesions. They are also known as solar keratoses or 'sunspots'. AKs are found predominantly on sun-exposed areas such as the scalp, face and forearms.[1] Globally, Australians have the highest rate of AK development, resulting in a prevalence of 40 to 60% among the Caucasian population above the age of 40 years.[1,2] Not surprisingly, the treatment of AK often falls under the responsibility of GPs so it is important to be aware of the full range of available treatment options.

Pathogenesis and natural history

AKs arise from chronic ultraviolet (UV) radiation-induced damage to keratinocytes – epithelial cells that produce keratin. In response to UV radiation, a cascade of pathological cellular processes leads to downstream mutagenesis and, ultimately, carcinogenesis of keratinocytes.[1] In AK, the cellular atypia is limited to the epidermis.

The natural history of untreated AKs is:

- regression – spontaneous remission
- no change – stable, without progression, or
- progression – squamous cell carcinoma (SCC) in situ (i.e. Bowen's disease) or invasive SCC.[3]

According to a recent systematic review, the rate of regression of single AK lesions ranges from 15 to 63% per year, with recurrence rates of 15 to 53%.[3] Meanwhile, up to 0.53% of single AKs progress to SCCs each year.[3] SCCs may cross the epidermal basement membrane, invade the dermis and metastasise, causing significant morbidity and mortality.[1] AKs can be regarded as part of a continuum and, in some cases, result in skin cancer development.[4]

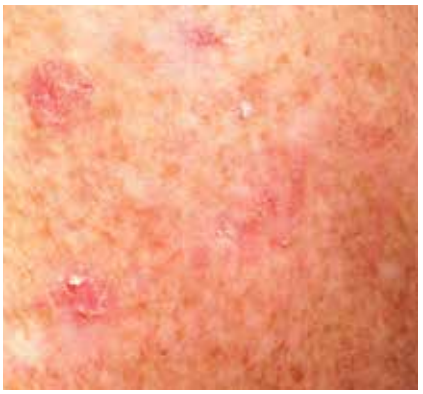


Figure 1. Thin actinic keratosis (clinical grade I).

Although the rates of spontaneous remission and malignant transformation of AKs cannot be definitively elucidated, clinicians should regard and treat all AKs as premalignant lesions.[5]

Another important concept is field damage or 'field cancerisation'. Despite often appearing clinically normal, the skin surrounding AKs, Bowen's disease and SCCs often houses precancerous cells as a result of chronic UV damage.[6] Additionally, AKs, Bowen's disease and SCCs may develop within this area if left untreated. This finding leads to the important consideration of field treatment.

Importance of treatment

AKs are regarded as the precursor of Bowen's disease and SCCs but there is currently no universally accepted definition of AK, which makes reliable identification of these lesions difficult.[7] Nonetheless, clinicians agree that AKs are premalignant lesions and that early identification and treatment are essential in reducing a patient's overall carcinogenic risk.[7,8] This is supported by histology reports showing that 60 to 80% of SCCs arise from AK lesions.[8]

Studies have shown that it takes about two years for previously confirmed AKs to transform into invasive SCCs.[8] Correspondingly, this window presents a golden opportunity for GPs to intervene and treat AKs to reduce the risk of SCC development.

Evaluation in the general practice setting

The diagnosis of AK is predominantly a clinical one. An optimal skin examination requires adequate consultation time, and good lighting and magnification by using hand-held or head-mounted loupes.

Clinically, AKs can be classified according to three grades (Box, Figures 1 to 3a to c):[9]

- I – slightly palpable
- II – moderately thick
- III – very thick and hyperkeratotic.

In reality, grading systems tend to be reserved for teaching purposes and clinical trials. In practice, dermatologists talk about thin, thick or hyperkeratotic AKs, which may remain as discrete lesions or form confluent patches. Variants include pigmented AKs and cutaneous horns. Although usually asymptomatic apart from their cosmetic appearance, AKs can become itchy, or burn and sting.

As an adjunct to diagnosing AK via the clinical grading system, dermoscopy is a useful noninvasive diagnostic technique.[10] The three clinical grades for AKs correspond well with three dermoscopic patterns (Box, Figures 4a to c, Table 1):[9]

- red pseudonetwork
- 'strawberry pattern'
- 'yellow-white keratin'.

Clinical and dermoscopic identification of SCC

Clinical and dermoscopic grading systems can help delineate grades I and II AKs from SCC, because SCCs are more likely to display the vascular patterns that are absent in low-grade (I and II) AKs. The usefulness of these grading systems fall short when attempting to differentiate grade III AK from SCC. Clinically, you would be suspicious of SCC rather than AK if there was:

- bleeding or ulceration
- recent growth
- tenderness or inflammation
- a nodular appearance
- a lesion that is refractory to treatment.

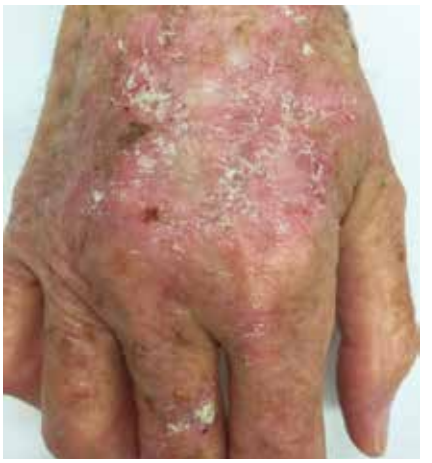


Figure 2. Clinically obvious hyperkeratotic actinic keratosis with field damage (clinical grade III).

Indications for referral to a dermatologist

Although GPs are able to manage most AKs in the primary care setting, referral to a dermatologist is advised for the following:

- patients with lesions that are suspicious for SCC based on clinical and dermoscopic features
- patients with widespread and severe actinic damage
- immunocompromised patients
- young patients with increased risks of developing SCC due to pre-existing medical conditions (e.g. xeroderma pigmentosum).

Treatment options

The treatment modalities for AK are many and varied. Choosing the most appropriate therapy depends on several factors including the number and distribution of lesions, the patient's tolerance to pain, desired cosmetic outcomes, patient adherence to treatment and treatment side effects and costs. It is essential to consider field treatment for prophylaxis in patients with widespread actinic damage or who are immunocompromised. Multimodal or sequential therapy is often required in these patients.

A simplified approach to treatment is provided in Table 2 (modified from the 2015 European Dermatology Forum guidelines).[11]

Treatment of AKs can be broadly divided into lesion-directed treatment and field-directed therapy. Lesion-directed treatments such as cryotherapy and curettage are suitable for treatment of discrete AKs. On the other hand, when there are multiple AKs in an area, and lesion-directed treatment is inappropriate, topical agents such as 5-fluorouracil (5-FU), imiquimod, ingenol mebutate and diclofenac, or conventional or daylight photodynamic therapy (PDT) can be used.

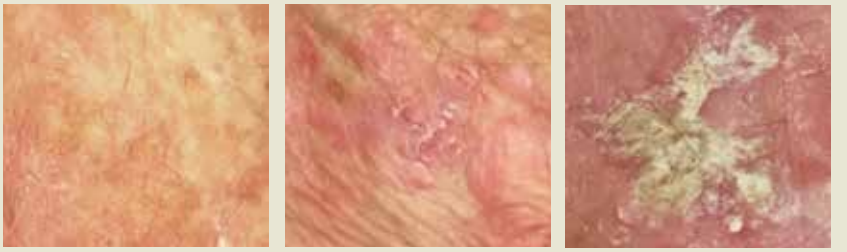
As highlighted from a multinational survey, the consensus is that topical field therapy is the most beneficial treatment for AKs and is preferred over lesion-directed treatment because of the potential to target both clinically visible and subclinical (nonobvious) lesions.[12] However, for field-directed treatments, nonadherence due to local skin reactions is a significant limiting factor.

When prescribing field-directed treatment, agents with the shortest treatment duration are generally preferred, which has led to the development of newer agents such as ingenol mebutate.[12] Table 3 summarises the various treatment modalities, protocols and indications used for AKs.

CLINICAL AND DERMOSCOPIC GRADING OF ACTINIC KERATOSIS[9]

Clinical grades

I – slightly palpable | **II – moderately thick** | **III – hyperkeratotic**



Figures 3a to c. Clinical grades of actinic keratosis.

Dermoscopic grades

I – red pseudonetwork | **II – 'strawberry pattern'** | **III – 'yellow-white keratin'**

Figures 4a to c. Dermoscopic grades of actinic keratosis.

TABLE 1. CLINICAL AND DERMOSCOPIC FEATURES OF ACTINIC KERATOSIS

Grade	Clinical features	Dermoscopic features
I	Slightly palpable – better felt than seen Flat, pink maculae without hyperkeratosis	Red pseudonetwork pattern and discrete white scales
II	Moderately thick – easily felt and seen Moderately thick hyperkeratosis on the background of erythema	'Strawberry pattern' Background erythema intermixed with whitish-yellow, keratotic and enlarged follicular openings
III	Hyperkeratotic – clinically obvious Very thick scale More difficult to differentiate from SCC Background erythema	Structureless, 'yellow-white keratin' Enlarged follicular openings filled with keratotic plugs over a scaly yellow-white background or marked hyperkeratosis

Treatment options

Emollients and keratolytics

Regular application of emollients (with or without keratolytics such as 2 to 5% salicylic acid) reduces scaling in AKs. It is important to use before applying therapeutic modalities because it reduces keratin, allowing therapy to reach the atypical keratinocytes.

Sunscreen and sun protection

The most important preventive measure for AK is the regular use of high sun protection factor (SPF) sunscreen and sun protection, such as protective clothing, and avoiding excessive sun exposure. Sunscreen has been shown to both reduce UV-induced skin mutations and decrease the immunosuppressive effects of UV radiation.[5] Studies have shown that high SPF sunscreen can also reduce the development of new AKs and increase the rates of remission of existing AKs.[1]

A practical tool that GPs can introduce to their patients is a mobile app called SunSmart (www.sunsmart.com.au/tools/interactive-tools/free-sunsmart-app). This app has useful features such as the ability to set alerts for sun protection, daily reminders for times when interval UV levels are damaging and two-hourly reminders to re-apply sunscreen.

Cryotherapy

Cryotherapy with liquid nitrogen is a mainstay of AK treatment and is most effective for thin, less keratotic lesions. Treatment involves a single freeze–thaw cycle with the freezing time lasting for three to seven seconds depending on the site and lesion thickness. This method is effective in removing about 70% of all AKs.[13] This popular method is cost efficient, widely

TABLE 2. TREATMENT OPTIONS FOR ACTINIC KERATOSIS[11]

Treatment	Condition		
	Single or few (<6) distinct AK lesions in the affected area	**Multiple (≥6) distinct AK lesions or widespread actinic damage in the affected area**	**Widespread actinic damage or AK in patients with immunosuppression**
General	Sun protection (broad-spectrum SPF 30+)		
First line	Lesion-directed therapy: • Cryotherapy	Field-directed therapy: • 5-FU • Imiquimod • Ingenol mebutate • Conventional or daylight PDT	Lesion-directed therapy: • Cryotherapy • Curettage and cautery Field-directed therapy: • 5-FU • Imiquimod • Conventional or daylight PDT
Second line	Lesion-directed therapy: • Curettage and cautery	Lesion-directed therapy: • Cryotherapy • Diclofenac	Field-directed and systemic therapy: • Nicotinamide (patients at high risk of nonmelanoma skin cancers) • Acitretin (immunosuppressed patients)

Abbreviations: AK = actinic keratosis; 5-FU = 5-fluorouracil; PDT = photodynamic therapy; SPF = sun protection factor.

available and effective. Limiting factors include pain, risk of wound infection and potential for hypopigmentation.

5-Fluorouracil

5-FU is a topical cytotoxic agent used in 5% concentration to treat discrete or multiple AKs (including field changes), particularly involving the head and neck. It targets atypical keratinocytes in preference to normal skin. The 5-FU cream is usually applied once to twice daily for two to four weeks. A meta-analysis showed clearance and partial response rates of 87.8% and 62.5%, respectively, following one treatment cycle.[14]

5-FU acts by interfering with DNA and RNA synthesis of dysplastic keratinocytes. The most common (and expected) side effect is localised skin inflammation that lasts for two to three weeks (Figure 5). The enzyme required to metabolise 5-FU, dihydropyrimidine dehydrogenase (DPD), is absent in about 5% of the population and mutated in another 3 to 5%. Individuals with deficient or mutated DPD may develop florid skin and even systemic reactions following topical 5-FU use.[15,16] Thus, it is essential to inform patients not only of the expected reactions but also the potential for exaggerated reactions to 5-FU, and instruct them to seek medical attention if unexpected reactions occur.

Currently, it is recommended that the maximum treatment surface area with 5-FU on skin is 500 cm^2 at one time.[15] However, off-label field treatment of widespread AKs on the limbs with topical 5-FU under occlusion (chemowraps) has gained traction in recent years.

In two studies (one with treatment over four to eight weeks and the other over 12 to 14 weeks), topical 5-FU applied to sun-damaged limbs under a zinc-containing occlusive dressing (chemowrap) and reviewed weekly was associated with substantial clinical improvement.[15,16] 5-FU chemowraps have been reported to be accepted by patients due to convenience and a low side effect profile.[15,16]

Imiquimod

Imiquimod is an immune-response modifier. This topical agent activates toll-like receptor 7, resulting in inflammation and subsequent clearance of dysplastic keratinocytes. In Australia, the 5% concentration cream is available and is applied three times weekly for four weeks. Then, after a four-week treatment-free period, the same treatment regimen for another four weeks is undertaken as tolerated.

In a multicentre randomised double-blinded study, imiquimod use was associated with complete and partial AK clearance rates of 45.1% and 59.1%, respectively.[17] Limiting factors for the use of imiquimod include cost (it is not PBS-listed for AK treatment), reduced adherence due to the long duration of treatment and adverse effects such as severe inflammatory reactions, locally and systemically (Figure 6).

Diclofenac

Diclofenac decreases the levels of prostaglandin in skin cells. Although 3% diclofenac is an effective agent for thin AKs, patients are required to apply the agent twice daily for up to 90 days. This long duration of therapy can adversely affect treatment adherence. In a study where diclofenac was applied twice daily for 90 days, complete clearance of target lesions occurred in 50% of AKs, as compared with 20% using placebo.[18] Cost is a limiting factor because diclofenac is not PBS-listed for AK treatment.

Ingenol mebutate

Ingenol mebutate (0.015% or 0.05%, depending on the site) is one of the newest agents on the market used to treat AKs. It preferentially targets dysplastic cells by promoting

TABLE 3. TREATMENT MODALITIES AND INDICATIONS FOR ACTINIC KERATOSIS

Treatment	Protocol	Indications
Cryotherapy	Freeze lesion for about 3 to 7 seconds	Single or few (<6) distinct AK lesions in the affected area
Curettage and electrodessication	Shave lesion superficially followed by curettage (requires local anaesthetic)	Single or few (<6) distinct AK lesions in the affected area
5% Fluorouracil cream	Apply once or twice daily for 3 to 6 weeks depending on site	Multiple (≥6) distinct AK lesions in an area or treatment of field
5% Imiquimod cream	Apply 3 times a week for 4 weeks. Follow this with a 4-week break from treatment, then treat again, applying again 3 times weekly for 4 weeks	Multiple (≥6) distinct AK lesions in an area or treatment of field
3% Diclofenac in 2.5% hyaluronic acid gel	Apply twice daily for 60 to 90 days	Multiple (≥6) distinct AK lesions in an area or treatment of field
0.015% Ingenol mebutate (150 µg/g) gel – face and scalp	Apply once daily for 3 consecutive days	Multiple (≥6) distinct AK lesions in an area or treatment of field
0.05% Ingenol mebutate (500 µg/g) gel – trunk and extremities	Apply once daily for 2 consecutive days	Multiple (≥6) distinct AK lesions in an area or treatment of field
Conventional photodynamic therapy	Apply photosensitiser cream (methyl aminolevulinate [MAL] 160 mg/g) and cover area from light for 3 hours before light treatment	Multiple (≥6) distinct AK lesions in an area or treatment of field
Daylight photodynamic therapy	Apply photosensitiser (MAL, 160 mg/g) and expose to daylight (outdoors) for 2 hours, then remove cream and protect from daylight for the remainder of day	Multiple (≥6) distinct AK lesions in an area or treatment of field
0.05% Topical tretinoin cream	Apply once daily	Multiple (≥6) distinct AK lesions in an area or treatment of field
Systemic acitretin	10 to 25 mg orally daily	Immunosuppressed patients
1% Topical nicotinamide	Apply twice daily	Patients at high risk of developing nonmelanoma skin cancer
Systemic nicotinamide	500 mg orally twice daily	Patients at high risk of developing nonmelanoma skin cancer
Chemical peels	Jessner's solution and 35% trichloroacetic acid applied by experienced operators	Multiple (≥6) distinct AK lesions in an area or treatment of field
Laser resurfacing	Ablative laser such as carbon dioxide and erbium:YAG (yttrium aluminium garnet) performed by experienced operators	Multiple (≥6) distinct AK lesions in an area or treatment of field

apoptosis and induces neutrophil-mediated immunostimulatory effects.[19] This agent is applied once daily for two or three consecutive days, depending on the site. One study reported 35% complete and 53% partial response rates.[20] Due to the short treatment period, ingenol mebutate is associated with high patient satisfaction.[19,21] In practice, however, severe irritant reactions have occurred without achieving sustained clearance. A limitation of treatment is cost, as ingenol mebutate is not PBS-listed, and the small packaging size is single use for up to 25 cm^2, about the size of the dorsum of the hand.[19]

Curettage and electrodessication

Curettage and electrodessication (or cautery) is a modality well known to dermatologists, particularly for hyperkeratotic AK. This technique involves a superficial shave of the lesion, followed by curettage using a sharp-edged spoon curette (disposable or autoclavable). Ballpoint cautery or electrodessication of the superficial dermis follows. This procedure requires the use of local anaesthetic.

Light curettage is often used to debride hyperkeratotic lesions before cryotherapy or PDT. The drawbacks to curettage include the need for local anaesthesia and the potential for hypopigmented scarring and wound infection.

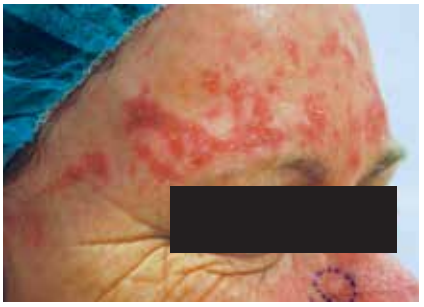


Figure 5. Common self-limiting localised skin inflammation associated with 5-fluorouracil.

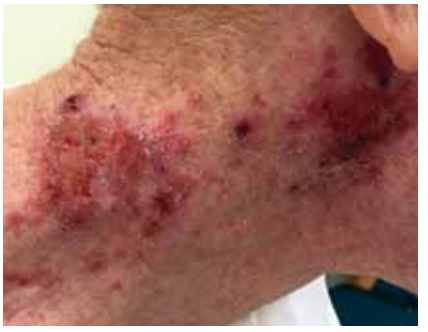


Figure 6. Local reaction to imiquimod.

Figure 7. Actinic field damage on the scalp, suitable for treatment by daylight photodynamic therapy.

Photodynamic therapy

Over the past three decades, conventional PDT has increased in popularity. Although it is more commonly used in the treatment of nonmelanoma skin cancers such as Bowen's disease and basal cell carcinoma (BCC), it has been adopted by some to treat large or hyperkeratotic AKs or as field treatment. Lesion treatment comprises gentle curettage of surface scale, followed by application of the photosensitiser cream, methyl aminolevulinate (MAL) 160 mg/g. This area is protected from light for three hours, during which time the abnormal cells preferentially accumulate the MAL. The area is then illuminated with a red light source at a dose of 37 J/cm^2 at a distance of 5 to 8 cm. Depending on the lamp, it can take 8 to 15 minutes to deliver this energy. A photodynamic reaction between the chemical MAL and light occurs, known as the photodynamic reaction, creating free oxygen radicals which destroy the cancerous cells. The efficacy rates are between 80% and 85%.[13] Limiting factors include cost, because it is not PBS-subsidised, and pain during treatment often requiring local anaesthesia.

Daylight photodynamic therapy

As for PDT, the MAL photosensitiser cream is applied but instead of covering the cream, the patient is advised to sit outdoors in daylight (the light source). Prior to this, the area has been gently debrided and a chemical sunscreen has been applied to the exposed skin. Immediately after application of the MAL cream, patients should be exposed to daylight for two hours, after which the excess MAL cream is removed. Patients must subsequently avoid outdoor light for the remainder of the day.[22]

Many patients prefer daylight PDT over conventional PDT because it is less painful and associated with a lower incidence of post-treatment inflammation. Generally, this treatment can be performed all year round in Australia; however, treatment is limited by the location of the AKs and if they are in an area usually covered by clothes. The Australian consensus supports use of daylight PDT to treat extensive chronic actinic damage that can be exposed easily to daylight, particularly grade I and II AKs on the face and scalp (Figure 7).[23]

Weather conditions can render the treatment less effective or necessitate the use of a greenhouse as an alternative to daylight illumination.[22] Currently, indoor 'daylight PDT' using artificial light sources are being trialled.[22]

Retinoids – topical and oral

Topical retinoids interact with nuclear retinoic acid receptors and promote cellular differentiation, therefore reducing dysplasia in AKs and promoting new collagen formation. The treatment duration of topical retinoid therapy, such as 0.05% tretinoin, is once daily for variable time periods, depending on tolerability. As a pretreatment before 5-FU treatment, it is used up to four weeks beforehand. As maintenance therapy, it is used daily in an ongoing manner.

Oral retinoids are used in the management of widespread AKs, especially in the immunosuppressed population. Low-dose systemic retinoids, such as acitretin at a dose of 10 to 25 mg daily, have been shown to be effective in the secondary prevention of AKs in patients who have undergone renal transplantation. The low dose is generally well tolerated by patients, with a reasonable side effect profile. Refer to a dermatologist for prescription of oral retinoids in this setting.

Nicotinamide – topical and oral

It has been established that topical and oral nicotinamide (vitamin B3) are safe and inexpensive treatment options to reduce AKs because of the photoprotective effects of nicotinamide against carcinogenesis and immune suppression in keratinocytes.[24] In a randomised, double-blinded, placebo-controlled study, the topical application of 1% nicotinamide resulted in a significant reduction in AKs within the first six months of treatment, suggesting that nicotinamide may accelerate the natural seasonal resolution of AKs by reducing UV-induced immunosuppression.[25]

Furthermore, 500 mg of oral nicotinamide twice daily resulted in a 13% reduction of AKs in patients using nicotinamide compared with matched placebo in a study after 12 months.[26] Oral nicotinamide has been shown to be beneficial for patients with extensive AKs or at high risk of developing nonmelanoma skin cancer; however, it has not been shown to be of value in patients without a significant history of skin cancer nor is it recommended for children.[27]

Oral nicotinamide has also been suggested as an effective and safe chemopreventive agent in transplant patients according to a recent phase 2 clinical trial.[28] The routine use of nicotinamide is,

however, not currently recommended until a phase 3 clinical trial is performed to ensure safety in this patient population.

It is important to note that oral chemoprevention (with retinoids and/or nicotinamide) does not negate the need for sun protection measures and regular cutaneous surveillance, commensurate with an individual's skin cancer risk profile.

Chemical peels

Superficial, medium and deep chemical peels have been used for decades to reduce field epidermal dysplasia. A common medium depth peel is a combination of Jessner's solution and 35% trichloroacetic acid, but the procedure needs to be performed by an experienced operator because irreversible scarring may occur.

Laser resurfacing

Ablative laser treatments such as carbon dioxide and erbium:YAG (yttrium aluminium garnet) have water as their chromophore and emit wavelengths that are able to penetrate the epidermis to varying depths. In the 1980s and 1990s, full resurfacing was used to remove field actinic damage but it was fraught with loss of pigment and demarcation lines at the jaw line. Fractionated systems now exist but as they leave columns of cells to repopulate, AK recurrence is not uncommon. Lasers are best used in conjunction with other modalities.

Other treatments

A variety of other agents, predominantly with antioxidant properties, have been proposed as potential AK treatments, including beta-carotene, vitamin E, lycopene and green tea extracts. However, the evidence is not strong to support their use.

Conclusion

AKs are cutaneous, premalignant lesions found on sun-exposed areas that have the potential to transform into SCCs. Therefore, early identification and treatment of AKs are essential to prevent the progression to invasive disease. The most important and often forgotten measure to treat AKs is sun protection with high SPF sunscreen, protective clothing and reduced sun exposure. In addition, a number of treatment modalities, divided into lesion-direct or field-directed treatments, can be used. Given the spectrum of AK, a patient may require multimodal or sequential therapies. Follow up is essential to ensure that clearance of AK has occurred and, more importantly, to detect recurrence or progression to malignancy. MT

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COMPETING INTERESTS: None.

Nappy rash

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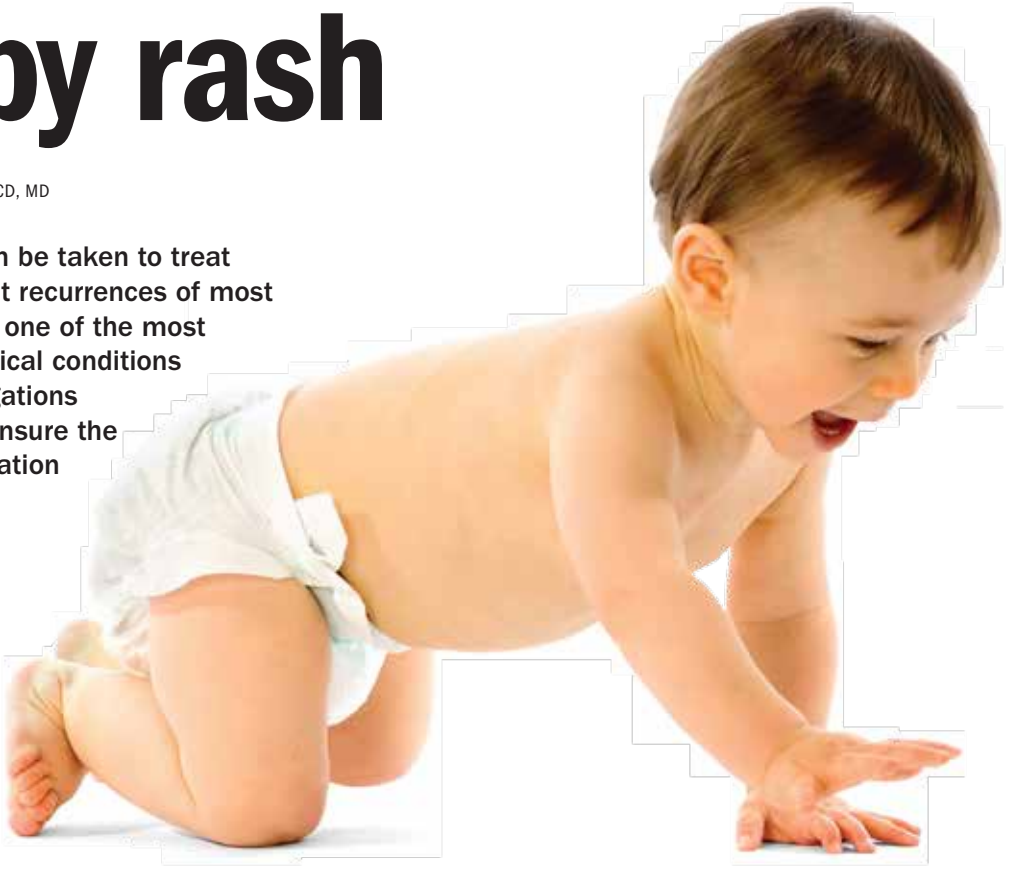
Simple measures can be taken to treat eruptions and prevent recurrences of most cases of nappy rash, one of the most common dermatological conditions in childhood. Investigations may be required to ensure the rash is not a presentation of a more serious condition.



Nappy rash most often affects babies who are in nappies at all times. However, older children with enuresis who still wear night nappies and incontinent adults who wear pads and absorbent underwear may also experience nappy rash.

What causes nappy rash?

The cause of an eruption under a nappy is very often multifactorial. Most often the eruption is due to an irritant dermatitis often coupled with superinfection and aggravation by a variety of topical treatments.

Loss of barrier function

It was once believed that ammonia in urine was the cause of nappy rash, and in early textbooks it was termed 'ammoniacal dermatitis'. However, this has been disproved. It is now accepted that overhydration of skin under the nappy is the most likely basis

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KEY POINTS

- The most common causes of nappy rash are overhydration, heat and friction under the nappy.
- *Candida albicans* usually colonises persistent nappy rash and antifungal creams improve outcome.
- Some rare but serious conditions can present as nappy rash unresponsive to treatment.
- Nappy rash can ulcerate. This is not a sinister sign and the ulceration improves with the usual nappy rash treatment.
- When nappy rash involves the flexures, the presence of an underlying dermatosis such as psoriasis should be considered.
- Seborrhoeic dermatitis is common in young babies, and looks much worse than it is.
- Any persistent perianal rash should be cultured for the presence of beta-haemolytic Group A streptococci.
- A pustular rash under the nappy may be due to *Staphylococcus aureus* and less commonly herpes simplex.
- Most parents are very concerned about the use of topical corticosteroids, and will need firm reassurance that corticosteroids are a safe, appropriate treatment for this condition.

for nappy rash. Increased skin hydration predisposes a child to injury from friction and increased susceptibility to irritants and micro-organisms.

Some children are more prone to nappy rash than others. Published studies have shown that in children from birth to 2 years of age, those under 12 months of age have the greater incidence of nappy rash. However, older children and adults who wear nappies or pads can have substantial problems with the skin under the nappy.

Faeces and urine

Pancreatic and bacterial enzymes found in faeces are undoubtedly skin irritants. Bottle-fed babies may be more prone to nappy rash than breastfed babies because of an increase in enzyme-producing bacteria. Normal newborn infant skin has a slightly acidic pH. The surface pH of the skin covered by the nappy is higher than in other areas and this is increased by occlusion from the nappy as well as faecal bacteria.

Irritating substances

The same substances that tend to aggravate dermatitis often play a role in nappy rash. These include bubble baths and soaps. Most parents start treating nappy rash themselves with over-the-counter barrier creams and medications from the pharmacist.

A recent study has found that nappy rash creams could predispose babies to nappy rash.[1] The effects of these creams may not always be helpful and may complicate the clinical picture because of increased redness and irritation. In general, greasy emollients containing zinc oxide or white soft paraffin are most effective.

True contact allergy is unusual in babies, but is seen in older children and adults. Commercial wet wipes have been shown to be no more effective than a wet cloth and there have been recent reports of reactions to the preservative methylisothiazolinone in wet wipes causing allergic contact dermatitis in babies. Allergic contact dermatitis tends to be much more severe than irritant dermatitis, often erodes and blisters and is likely to spread further than the area in direct contact with the nappy.[2,3]

Nappies

Considering the importance of maceration, heat and friction as causes of nappy rash, it is easy to appreciate that the use of cloth nappies usually causes more problems than the use of disposable nappies. Cloth nappies are usually used with nappy liners, plastic pants and overpants, all of which contribute to nappy rash. Many studies have demonstrated that the introduction of absorbent gel materials in good-quality disposable nappies has led to a decrease in the incidence of nappy rash.

Underlying dermatological conditions

Some children who have no other skin problems seem to have a tendency to develop nappy rash. Although some research suggests that atopic dermatitis may present as a rash in the nappy area, such rashes are in fact uncommon in babies with atopic dermatitis and dry skin, where the nappy area may be the only part spared because of increased hydration. By contrast, older children with atopic dermatitis are often irritated by night nappies.

There are several dermatoses that may present as nappy rashes. Rarely, severe systemic diseases may present in this way. These are considered in more detail later in this article.

Candida albicans and other infections

The presence of *Candida albicans* plays an important role in the development of nappy rash. *C. albicans* is frequently isolated from macerated genital skin in babies and adults, although not in prepubertal children. There is a correlation between the severity of nappy rash and levels of *C. albicans* in faeces and in cultures from the genital skin and mouth. *Candida* is more often a colonist that aggravates an underlying dermatitis than a true pathogen, although it can certainly occur as a true pathogen.

Candidal nappy rash presents with a very inflammatory rash that involves the flexures and is classically surrounded by satellite pustules.

It is uncommon for infections from other micro-organisms to cause nappy rash, but *Staphylococcus aureus* may cause folliculitis or impetigo of the nappy area. Group A beta-haemolytic *Streptococcus pyogenes* may cause a persistent perianal rash and sometimes acute vulvitis or balanitis. *S. aureus* has been reported to cause an indistinguishable perianal rash. Herpes simplex virus may cause a very painful vesiculopustular or ulcerated rash, and hand foot and mouth disease, most commonly due to Coxsackie virus A-16 and Enterovirus 71, may also cause a vesicular nappy rash. Dermatophyte infections can occur, often causing nonspecific but difficult-to-treat rashes. Rarely, babies with congenital syphilis may present with a nappy rash.

Diarrhoea due to various causes

Children with diarrhoea often develop acute episodes of nappy rash. Although many parents attribute nappy rash to

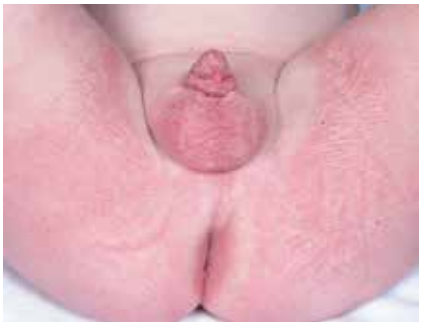

Figure 1. Irritant nappy rash.

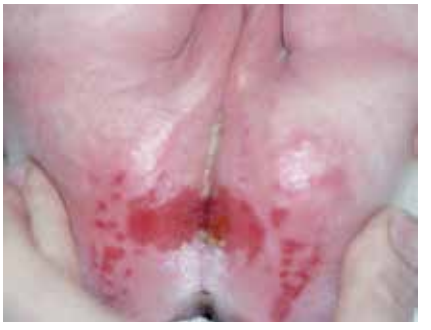

Figure 2. Eroded nappy rash.

teething, there is no evidence supporting a direct association. Infants who are teething may experience increased drooling and diarrhoea, and the diarrhoea may temporarily aggravate a child's tendency to develop nappy rash. Viral gastroenteritis with diarrhoea may also aggravate nappy rash. In small babies, diarrhoea may result in rapid erosion of the perianal skin.

Clinical presentation and diagnosis

Irritant (flexural sparing) nappy rash

Irritant nappy rash is the most common form of nappy rash, and is most often seen between the ages of 1 and 12 months. The usual clinical features of irritant nappy rash are confluent erythema and scaling of the convex surfaces that come into contact with the nappy (Figure 1). The groin flexures are typically normal ('flexural sparing'). In some children, the rash occurs only at the margins of the nappy around the waist and thighs where most friction is encountered. Particularly in young babies, the rash may be confined to the perianal area.

Irritant nappy rash is a dermatitis and shows the characteristic signs of erythema, scale and weeping. As the problem becomes more severe, erosions and ulcers may occur and the appearance may become quite alarming (Figure 2), raising the possibility of herpetic ulceration or even child abuse. The baby is often distressed by bathing and passing urine. Acute retention of urine may occur.

If the rash is longstanding, lichenification may occur. In the healing phase, desquamation is common. Rarely, the rash may become nodular. This is known as pseudoverrucous papules (see below).[4]

Nappy rash in the older child

The clinical presentation of nappy rash in the older child differs from the classic rash seen in babies. The rash in the older child is not usually acutely inflamed, but presents as a low-grade dermatitis, often with miliaria or folliculitis on the buttocks. Friction lines at the edge of the nappy are often involved.

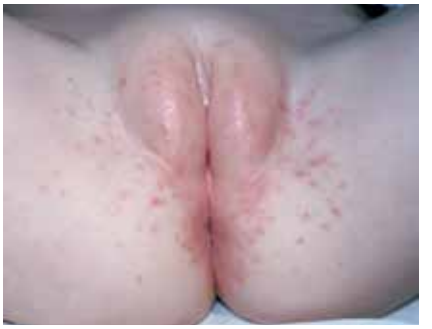

Figure 3. Acute candidiasis.

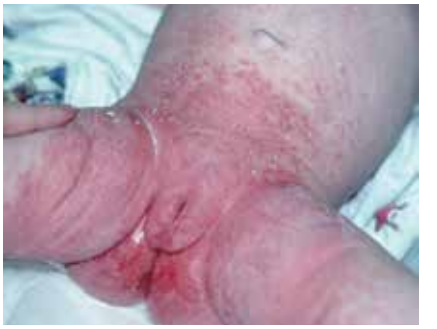

Figure 4. Seborrhoeic dermatitis.

'Nappy' rashes in incontinent adults

'Nappy' rashes in incontinent adults present as persistent, low-grade dermatitis of the vulva or balanitis or erythema of the scrotum and adjacent groin, which seem resistant to treatment. Adults are often embarrassed by incontinence and do not volunteer during history taking that they wear absorbent underwear.

On examination, the skin is often macerated. In immobile, incontinent people in nursing homes, this can be an intractable problem. Candidal and staphylococcal superinfection is common.

Miliaria

Miliaria, a very common condition in babies, is also known as heat rash. It results from mild inflammation around sweat gland orifices due to sweat retention when the baby is hot because of hot weather, excessive clothing or fever. Miliaria may complicate or predominate in any case of nappy rash. The eruption, which is usually asymptomatic, consists of tiny vesicles or pustules on an erythematous base. Miliaria is harmless but can cause diagnostic confusion, particularly with folliculitis. It is self-limiting and responds to any measure that diminishes overheating.

Rashes that involve the flexures

When rashes are due to underlying dermatoses or infection, rather than irritation to the skin from the nappy, the typical sparing of the groin folds is lost. There are so many causes that loss of flexural sparing is only a diagnostic clue insofar as it indicates that something more than common irritant nappy rash is occurring.

Acute candidiasis

Most nappy rashes are colonised by the yeast *C. albicans* and respond better to treatment that includes an antifungal agent. However, *Candida* may become a true pathogen, often for no apparent reason. In this situation, the rash involves the flexures, often becomes much more inflammatory and is surrounded by small peripheral pustules or 'satellite lesions' (Figure 3). The infection is easily proven with a swab for microscopy and bacterial culture (which is able to detect *C. albicans*).

Infantile seborrhoeic dermatitis

Infantile seborrhoeic dermatitis is a relatively common skin condition of small babies that usually involves the nappy area but often other parts of the skin as well. The onset is usually in the first two months of life. The first areas involved are the nappy area, face and scalp. The eruption may then generalise, involving the axillae, umbilicus and neck. Discoid lesions may involve the skin of the trunk.

The rash is erythematous and scaly (Figure 4). The scale tends to have a greasy feel in hairy areas. Although the rash may look quite dramatic, the baby is well and not distressed or itchy.

The long-term prognosis of children with infantile seborrhoeic dermatitis is variable, and it is important not to prognosticate too soon. Studies have shown that about half the cases have an idiopathic

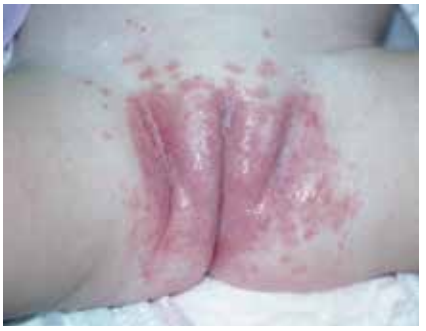

Figure 5. Napkin psoriasis.

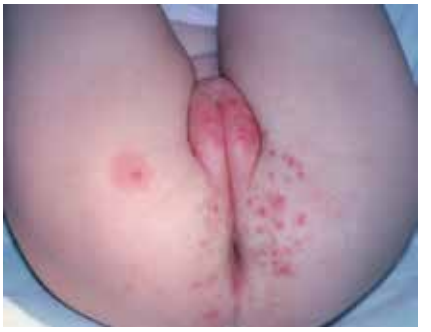

Figure 6. Folliculitis.

condition that is self-limiting, resolving by about 4 months of age. Simple dermatitis treatment is all that is needed.

However, seborrhoeic dermatitis may also be the first sign of either psoriasis or atopic dermatitis. If the rash persists, these diagnoses should be considered. Eventually the true nature of the child's problem will declare itself.

Napkin psoriasis

When psoriasis appears for the first time in infancy it usually localises to the nappy area, scalp, face and around the ears. The onset of the eruption may be quite acute, and the rash may rapidly generalise to involve other parts of the skin. The appearance may be indistinguishable from seborrhoeic dermatitis, but it may also be typical of psoriasis, with bright pink plaques and dry white scales.

In the nappy area, psoriasis appears as bright red, glazed, slightly raised plaques (Figure 5). The pattern is bilaterally symmetrical and the flexures are involved. There is little or no scale. Sometimes the whole area in contact with the nappy is persistently red.

There is often a family history of psoriasis. Clues to the diagnosis include cradle cap, postauricular rashes and nail changes (such as pitting).

Contact dermatitis

Most nappy rashes are a form of irritant contact dermatitis. True allergic contact dermatitis is unusual under nappies, partly because infants are too young to have been sensitised; however, it is becoming more common. Potential allergens are most often over-the-counter medications, antifungal creams, fragrances and preservatives in baby wipes, particularly methylisothiazolinone, and latex gloves. Occasionally, allergens such as dyes and other chemicals in the disposable nappy itself seem to cause a problem. This has been reported under the title 'diaper dye dermatitis' and the allergen has been identified as blue, pink and green dyes in the nappy.

Another form of contact dermatitis from nappies has been termed 'lucky Luke dermatitis'. The clinical picture is of a rash located in the area where the nappy tabs make contact with the skin on the hips and buttocks, the so-called 'cowboy's gunbelt holsters' pattern, which prompted the name. The allergens are rubber additives found in the stretchy elasticated parts of the nappy.

Irritancy from applied substances is much more common. Potential irritants include wet wipes, soaps, shampoos, bubble baths, creams and even substances that the carer has applied to his or her hands.

Allergic contact dermatitis presents with a dramatic weeping, eroded rash. However, irritant contact dermatitis simply presents as a worsening of previous nappy rash or lack of response to treatment.

Other infections of the nappy area

Staphylococcal folliculitis

S. aureus is the most common bacterium to cause skin infections. Although it is much less common as a cause of infectious nappy rash than *C. albicans*, it may be responsible for folliculitis and impetigo in this area.

Folliculitis presents with multiple pustules, usually on the buttocks, but these can occur anywhere under the nappy (Figure 6). The rash may wax and wane, but there are usually a few lesions present. It tends to be itchy rather than tender, and the child is well. The diagnosis is easily confirmed on culture.

Staphylococcal folliculitis can look very similar to the satellite pustules of candidiasis. The difference is that in folliculitis all the lesions are pustules, whereas in candidiasis the pustules are usually seen on the edge of a zone of solid erythema.

Impetigo

Bullous impetigo may occur in the nappy area. The eruption consists of thin-walled blisters that erode to leave moist raw areas. The diagnosis is confirmed by bacterial culture. In neonates, bullous impetigo can generalise and lead to sepsis.

Staphylococcal scalded skin syndrome

Staphylococcal scalded skin syndrome is not a common condition, and is seen almost exclusively in young children. It results from infection with a toxin-producing strain of *S. aureus*. The infection may not be in the nappy area, but the rash may start there with a tender, nonspecific erythema with superficial blistering. At this stage, a very high index of suspicion is needed. If left untreated, the rash will generalise to involve the other flexures and the perioral and periocular areas, with blistering and a generalised erythema. The child will become irritable and unwell because the rash is painful and tender.

Streptococcal dermatitis

Group A beta-haemolytic streptococci infections may cause rashes in the nappy area, particularly in the perianal region. This problem is not confined to babies in nappies and should be considered in any child with a persistent perianal eruption. It is more common in boys.

The tender, itchy rash usually has the appearance of a scaly or weeping erythema surrounding the anus, but it may extend

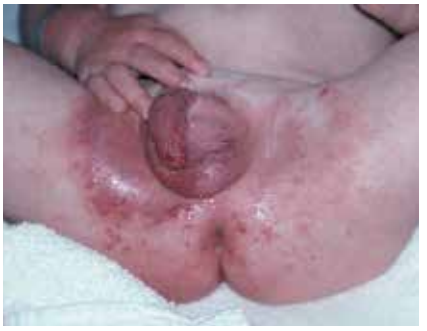

Figure 7. Staphylococcal superinfection.

Figure 8. Herpes simplex virus infection.

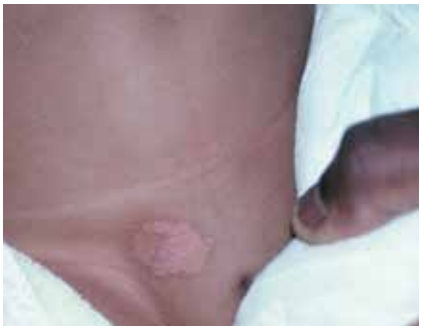

Figure 9. Tinea.

several centimetres and may be complicated by painful fissuring that leads to constipation. Bleeding and discharge may occur. The rest of the nappy area is normal, but the same organism may cause balanitis or vulvitis either concurrently or on another occasion.

Streptococcal dermatitis is not uncommon and is easily missed unless a bacterial culture is performed. A 10-day course of antibiotic cefalexin or roxithromycin in children allergic to β-lactam antibiotics) is essential for effective treatment. Streptococcal infection is a well-recognised trigger of psoriasis, and genital infection may trigger psoriatic nappy rash.

Bacterial superinfection in nappy rash

When a previously responsive nappy rash becomes difficult to treat, the cause may be a bacterial infection. Both staphylococcal (Figure 7) and streptococcal species may be isolated. The appearance of the rash may be indistinguishable from candidal nappy rash, but a swab for microscopy and bacterial culture will easily differentiate bacterial superinfection from a simple candidal rash. Children who suffer from atopic eczema are prone to staphylococcal infections.

Herpes simplex nappy rash

Herpes simplex is a rare cause of rashes in the nappy area. The infection is usually caused by herpes simplex virus type 1, and is usually acquired from the caregiver. A type 2 infection may be acquired congenitally from an infected mother or as a result of child abuse. Children with atopic eczema are more prone than others to herpetic skin infections.

During an initial attack, small grouped vesicles appear on an erythematous base. The initially clear vesicles rapidly become purulent and often erode to cause shallow ulcers (Figure 8). Oedema is often present, and the baby is irritable and unwell because these lesions are painful. Regional lymphadenopathy is present. The diagnosis is confirmed with viral culture and/or rapid immunofluorescence or polymerase chain reaction. There is usually spontaneous clearing in two weeks.

In children with atopic eczema, usually of a severe degree, generalisation and persistence of herpes infection may occur. If infection occurs in the neonatal period, systemic dissemination is a serious concern. These conditions require intravenous treatment with aciclovir.

When herpes infection occurs in the neonatal period, intravenous high-dose aciclovir must be started to prevent the possibility of herpetic encephalitis. A high index of suspicion is essential and treatment should be started immediately.

Varicella

Sometimes varicella infection may present in the nappy area, generalising later. It is less common, although possible, for lesions to be confined to the nappy area. The typical appearance – clear vesicles evolving to umbilicated pustules and then crusts – is present, but diagnostic confusion with herpes simplex and staphylococcal infections may occur.

Other viruses

Hand, foot and mouth disease (due to Coxsackie virus) can produce lesions in the nappy area. Cytomegalovirus and HIV infections can both present with blistering or eroded lesions in the nappy area.

Tinea

True dermatophyte infections of the nappy area are very unusual and always puzzling. The typical signs of tinea are rarely seen, and the rash may present as a difficult-to-treat scaly eczematous eruption that waxes and wanes, continually changing appearance. The clue that it is a tinea infection is that there is a relatively sharp edge to the rash (Figure 9), unlike eczema (which blends into the surrounding skin). A fungal scraping will confirm the diagnosis.

Rare conditions that may present as a nappy rash

Congenital naevi of the nappy area

Almost any congenital naevus can occur in the nappy area, including haemangiomas, epidermal naevi and pigmented naevi. Haemangiomas are the most frequent of these lesions in babies, usually appearing after birth within the first month of life. In the nappy area (Figure 10), unless they form a typical nodule, haemangiomas may be mistaken for nappy rash. Painful ulceration is quite common in this site, and may be extensive enough to obliterate most of the original lesion. Extensive genital haemangiomas have been associated with anatomical abnormalities of the bladder, genital tract and lumbosacral spine. This

Figure 10. Vulval haemangioma.

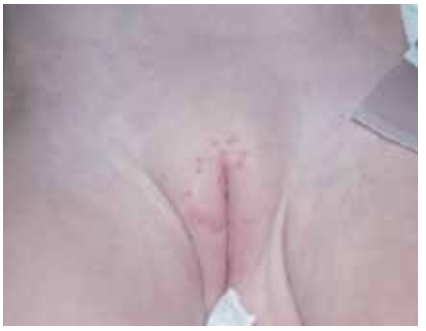

Figure 11. Epidermal naevus.

has been termed PELVIS syndrome.

An extensive epidermal naevus may also be confused with nappy rash, and this is not made any easier by the fact that these lesions can be itchy. Epidermal naevi are rare, and may not be present at birth. They may have the appearance of a scaly, skin-coloured or slightly pigmented plaque (Figure 11), but are usually more raised than a simple rash. If they are causing a great deal of trouble under a nappy, such as around the anus, they may have to be excised.

Traumatic lesions

Most cases of traumatic ulcers in the nappy area are due to nonaccidental injury and child abuse should be considered. Such ulcers are usually noninflammatory and well demarcated. Biopsy shows a result consistent with that seen with a burn in most cases. Infective causes should be ruled out and the child referred to a child protection unit.

Infantile granular parakeratosis

Granular parakeratosis is a rare condition usually described in adults. It is an acquired, idiopathic disorder of keratinisation that results in linear, hyperkeratotic yellow to brown plaques in the inguinal folds as well as geometric plaques underlying pressure points from the nappy or pad. A thick, flaky scale over the plaques is characteristic.

Infantile granular parakeratosis in babies has been reported to be the result of the application of irritating nappy rash creams, particularly those containing zinc oxide. The condition is harmless and resolves once the offending substances are ceased and the child is out of nappies.

Erosive papulonodular dermatosis

Erosive papulonodular dermatosis is also known by several other names, including infantile gluteal granuloma, perianal pseudoverrucous papules and 'Jacquet's erosive dermatitis'. It is an unusual presentation of nappy rash in which red-brown or purple oval, ulcerated nodules appear on a background of typical nappy rash.

The nodules are seen most often on the buttocks. Although it has been attributed to the use of potent topical corticosteroids on the nappy area, erosive papulonodular dermatosis has been reported in the absence of topical corticosteroids and is also seen in older children and incontinent adults. This may indicate that it is a hyperplastic reaction seen in macerated skin exposed to the irritants in faeces and urine, as well as applied topical substances.

Erosive papulonodular dermatosis is well documented in infants and older children with urinary incontinence due to neurological and anatomical abnormalities, as well as in those with chronic diarrhoea due to Hirschsprung's disease.

Although the lesions from erosive papulonodular dermatosis have an alarming appearance, the prognosis is excellent and they regress with appropriate nappy rash treatment.

Zinc deficiency

Zinc deficiency is a rare condition that can occur in babies. This may occur because they have an inability to absorb zinc from food or because they are fully breastfed and their mother's milk is low in zinc.

The highly characteristic rash is a brightly erythematous, eroded rash with a well-defined edge. A similar perioral eruption is also seen, the child may be unwell and irritable, and the rash is resistant to all treatment. It improves rapidly with zinc supplementation.

Rarely, biotin deficiency and cystic fibrosis have been reported to present in a similar way.

Langerhans cell histiocytosis

Langerhans cell histiocytosis is a rare condition that presents in babies and has a predilection for the nappy area, flexures, ears and scalp. It is usual for it to present as a recalcitrant nappy rash or seborrhoeic dermatitis. Careful examination reveals that there are elements of purpura, pustules and erosions in the rash. Diagnosis is by skin biopsy.

Although Langerhans cell histiocytosis is not considered to be a true malignancy, it may involve bone and other organ systems. The condition is treated with chemotherapy.

Kawasaki's disease

Kawasaki's disease is a potentially serious condition of infants and young children and is relatively rare; however, it is a condition to be very aware of because of the implications of leaving it undiagnosed. A prodrome of high fevers for five days or more is followed by cervical lymphadenopathy, conjunctivitis, redness of the lips and mouth, oedema of the hands and feet and a rash. The rash is variable but can be confined to the nappy area only. The child is systemically very unwell, and coronary occlusion is the most serious complication. In the recovery phase, peeling of the hands, feet and perianal area is common.

Congenital syphilis

Congenital syphilis is rare in our community. The affected infants may have no external sign of the disease at birth.

However, it may present in the neonatal period with a rash consisting of round or oval, copper-coloured scaly lesions most often in the nappy area and also on the face, palms of the hands and soles of the feet. Condylomata lata (moist perianal wart-like lesions) may occur and similar lesions may be found around the nose and mouth.

The infant may become unwell, with fever, hepatosplenomegaly, lymphadenopathy and rhinitis. A high index of suspicion is the key to making this diagnosis, which is confirmed by serology and dark field examination of nasal discharge and moist lesions.

Immune deficiencies, ecthyma gangrenosum and pyoderma gangrenosum

Some serious primary immune deficiencies may present with eczematous rashes that seem difficult to treat, and this can include nappy rash. The child is often unwell with recurrent infections, and diagnosis is usually made because of systemic problems.

Ecthyma gangrenosum is an ulcerative skin condition associated with *Pseudomonas aeruginosa* and it usually occurs in immunocompromised patients. It presents with purpuric macules that progress to haemorrhagic bullae, which rapidly necrose leaving ulcers. It can be fatal in infants and is a medical emergency. Very occasionally ecthyma gangrenosum can occur in apparently healthy infants, most often after antibiotic treatment. However, any child with this condition should be investigated for septicaemia and subtle immunological abnormalities.

Pyoderma gangrenosum has been reported in the nappy area and is usually associated with immunocompromise, haematological disease and inflammatory bowel diseases.

Managing nappy rash

What to do about nappies

A recent Cochrane review examined the subject of the use of disposable nappies for preventing napkin dermatitis in infants.[5] It found that there is not enough evidence from good-quality randomised controlled trials to either support or refute the use of disposable nappies to prevent nappy rash. This finding, however, probably relates more to the quality of the research trials than to the use of disposable nappies in reality.

As the cause of most cases of nappy rash is a combination of overhydration, friction and heat, the aim of treatment is to reverse or minimise these factors. Common sense would dictate that the simplest way to do this is to use good-quality disposable nappies that contain absorbent polymers that trap water molecules under the surface so that the layer next to the skin is dry. It has been shown that this type of nappy maintains the skin's normally slightly acidic pH, thus protecting it from activation of faecal enzymes. Another advantage is that disposable nappies are less likely to result in overheating, particularly if they have a 'breathable' cover. This is because they are thinner than cloth nappies and can be used without the plastic and/or nylon overpants that are often used to stop leakage and to hold cloth nappies in place.

Many parents express a concern about environmental issues with regard to disposable nappies. Others find that the good-quality ones that are required are prohibitively expensive. In these cases, parents may be encouraged to use disposable nappies just in situations where it will be difficult to change the baby very frequently, such as overnight or when outside the home.

If cloth nappies are to be worn, they need to be changed as soon as they become wet. Plastic pants and occlusive nappy liners should not be used. The nappies should be machine washed in hot water, well rinsed to remove laundry products and dried in a tumble dryer to make them softer.

Nappies of any sort should be changed as soon as the child defaecates, because of the irritancy of faeces. This may involve having to wake the baby at night. It is often the best sleepers who have the worst nappy rash. Nappies should be changed at least every three to four hours.

Leaving a baby out of nappies altogether is helpful but rarely practical, particularly in winter.

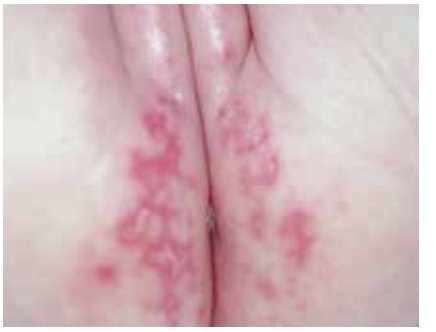

Figure 12. Healing erosions.

Protecting the skin in the nappy area

As most cases of nappy rash are dermatitic, the general principles of treating dermatitis apply. It is important to find out what products the parents have been using on the baby and eliminate anything that may have aggravated the situation. Soaps, bubble baths, perfumed products, antiseptics, wet wipes and powder should be avoided. Shampooing hair while the child sits in the bath results in exposure to detergent as the child sits in the shampoo-filled water.

Although the concept of using a 'barrier cream' is popular, there is no cream capable of creating a highly effective barrier between the skin and the nappy. Products such as zinc and castor oil cream have gained popularity because of this concept, but their value is as emollients.

Emolliation is important in treating all types of dermatitis, because it prevents the skin cracking and fissuring, which allows infection to supervene. Emollients should be applied at every nappy change in babies prone to nappy rash. Any greasy product is satisfactory, including zinc and castor oil cream, wool alcohol ointment, white soft paraffin and emulsifying ointment. These products tend not to sting but if the baby screams in pain when the cream is applied, the cream should be discontinued. Where erosion or ulceration has occurred, an emollient paste is helpful to protect these areas and promote healing (Figure 12).

WHEN TO REFER A BABY OR CHILD WITH NAPPY RASH

- When a stronger product than hydrocortisone is required – this is rarely necessary, but the situation may arise if the child is allergic to hydrocortisone or when psoriasis is present.
- When, despite all treatment strategies, there is no response – the child may have a rare condition such as zinc deficiency or Langerhans cell histiocytosis.
- When the parents are reluctant to use topical corticosteroids – they may require extra reassurance from a specialist that using such products is safe.
- When the child seems unwell and febrile, and the rash is of sudden onset – a serious condition such as staphylococcal scalded skin or Kawasaki's disease may be present.
- If a herpetic infection is suspected – aciclovir may be required.
- If there is a lump or a lesion, or an underlying haemangioma is suspected – ulcer dressings or surgical treatment may be necessary.

A dispersible bath oil is helpful when bathing the baby. When changing the nappy, a damp washer with some emollient or soap-free cleanser is preferable to commercial wipes, which contain potential irritants and will probably cause discomfort. Baby wipe technology has developed more suitable products for infant skin in the past few years; however, the safest course of action is simply to keep a bottle of water and some small towels in a ziplock bag to use instead.

Harsh soaps, particularly those containing antiseptics, should be avoided. Soap-free cleansers are the best option.

Use of topical corticosteroids

A mild topical corticosteroid is the treatment of choice for nappy rash in general. Hydrocortisone 1% ointment should be applied three times daily until the eruption has cleared. The preparation is then used as required for recurrences and exacerbations. Topical anticandidal agents are usually used concurrently with corticosteroids if *Candida* infection is suspected. More potent topical corticosteroids are rarely required, and carry the risk of inducing atrophy, striae or gluteal granuloma. The exception to this is napkin psoriasis which may be quite resistant to 1% hydrocortisone and require a moderate potency preparation before there is a response to treatment.

Never underestimate the reluctance many parents feel about using topical corticosteroids on their children. Most have heard stories of the dangers of these products, and doubt their safety even when prescribed by a doctor. Strong reassurance about the safety of hydrocortisone 1% is worth giving when prescribing the product. Beware of suggesting that parents use the preparation carefully or sparingly. It is unnecessary to be sparing and such a suggestion sends a message that it is hazardous, which may result in noncompliance.

There are case reports of iatrogenic Cushing's syndrome from the use of topical corticosteroids to treat nappy rash. It is important to realise that this resulted from inappropriate overuse or use of inappropriate strength topical corticosteroids under the nappy. Preparations stronger than hydrocortisone 1% should not be used, but the 1% cream is very safe if used appropriately. A child with nappy rash that does not clear despite ongoing use of topical corticosteroids should be referred to a dermatologist.

Complications of topical therapy

All topical preparations, even corticosteroids, have the potential to cause allergic reactions. These reactions usually present with a gradual worsening of the rash to a weeping dermatitis of such severity that oral prednisone may be required to treat it.

A much more common situation is irritancy rather than true allergy. The child may scream whenever the medication is applied because of stinging, and the rash may look more erythematous. This is seen most often from overuse of azole-containing antifungals.

Allergy to topical corticosteroids can be very subtle and present only with a failure of the rash to respond to treatment.

Treatment of infection

Due to the frequency with which nappy rash is colonised with *C. albicans*, it is convenient to concurrently use a topical antifungal, such as nystatin or an imidazole like miconazole, with a topical corticosteroid. Although clioquinol plus hydrocortisone was previously widely used and highly effective, there has recently been concern regarding its potential for neurological toxicity and it is no longer recommended for the treatment of patients with nappy rash. Long-term use of imidazoles may become irritating and nystatin is a safer choice.

If the addition of an antifungal cream makes no difference, a swab should be taken for bacterial culture. If there is oedema, ulceration or vesicles, viral culture should be performed. If tinea is suspected, a fungal scraping should be taken.

If infection with *S. aureus* is encountered, treatment with topical mupirocin is as effective as oral antibiotics and often better accepted by parents. However, for bullous impetigo that is widespread or in a neonate, oral flucloxacillin is the drug of choice. Staphylococcal scalded skin syndrome should be similarly treated. *S. pyogenes* infections should be treated with oral phenoxymethylpenicillin, cefalexin or clindamycin for 10 days, and the concurrent use of mupirocin ointment will help to prevent a recurrence. The addition of chlorine bleach to bathwater has been shown to be highly effective in treating dermatitis that is superinfected with *S. aureus* and is a helpful adjunct to treatment with no potential for allergy or sensitisation.[6]

Advice for parents and carers

Noncompliance is a major factor in the failure of nappy rash management. Nappy rash is such a common problem that almost everyone will have advice for your patient. As a result, many different treatments may have been tried, but few persevered with. Additionally parents may have unintentionally added to the problem by applying irritants.

As in all dermatitic conditions, there is a tendency to relapse when treatment is ceased and, unless this is clearly explained, patients interpret relapse as treatment failure. Parents need to understand both the benign self-limiting nature of this condition and also its chronicity in many cases. Keeping it simple is a vital part of making treatment a success, and emphasis on the need for ongoing treatment is also essential.

A useful handout for patients is available on page 21.

What to do if treatment fails

Check compliance

Have the parents and other carers been following advice, or is there a reluctance to use the prescribed medications? Has extra advice from well-meaning friends and relatives complicated the issue? Did the parents persevere with treatment for more than a few days? These questions should be asked to check compliance with the treatment prescribed.

Rule out allergy and irritancy

True allergic contact dermatitis is not usually subtle and presents with an acute weeping deterioration of the rash. However, contact irritation is more subtle and may occur with almost any topical preparation, including antifungal and corticosteroid creams, emollients, wet wipes and topical antibiotics.

If one of the preparations being used is suspected of causing a problem, stopping all topical therapy and using only one or two different preparations may remove the irritant. Also, hydrocortisone cream should be changed to an ointment that is preservative free.

Rule out and treat infection

Taking a swab for bacterial microscopy and culture from the skin surface can rule out infection. This sort of swab will detect *C. albicans* as well as bacteria. If vesicles are present, viral culture should be performed as well. In a patient with a recalcitrant, scaly rash, a fungal scraping should be taken to rule out tinea.

Refer to dermatologist

A list of instances when the patient should be referred to a dermatologist is given in the Box.

Prognosis

The prognosis for patients with nappy rash is usually excellent. In most cases, there is a rapid response to simple treatment that keeps skin as dry as possible, eliminates irritants, treats inflammation and involves emolliation with a simple product. However, the course of the condition may remit and exacerbate, and some children are never completely free of it until they are out of all nappies, including night nappies. In this situation, it is important to reassure the parents of the self-limiting nature of the condition and encourage them to aim for the comfort of the child rather than a perfect-looking nappy area.

In cases where the underlying condition is psoriasis or atopic eczema, the prognosis is more guarded. These patients may sometimes go on to have persistent problems in the genital area.

It is not possible in early childhood to predict whether this will happen, and follow up is recommended.

Conclusion

Nappy rash is one of the most common dermatological conditions in childhood. Most cases can be managed successfully in general practice with simple advice regarding use of nappies, good skin care practices and treatment with mild corticosteroid and antifungal creams. Even unusual presentations that may seem alarming, such as ulceration or gluteal granuloma, respond to simple measures.

Occasionally a case is seen where there is continuing deterioration despite treatment. In this situation, superinfection or allergy to a topical medication may have occurred, but more often the parent is simply confused about advice and unable or unwilling to comply. If there has been no response to a reiteration of initial advice and a change of medication, or if an unusual or serious diagnosis is suspected, referral to a dermatologist is justified. MT

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Further reading

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COMPETING INTERESTS: None.

How to prevent and manage nappy rash

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This handout provides information about how to manage nappy rash and prevent any further episodes.

Nappy rash is one of the most common dermatological conditions seen in babies. However, by following some simple advice about the use of nappies, good skin care practices and treatment with mild corticosteroid and antifungal creams, symptoms can be treated and recurrences prevented.

Prevention

Nappy rash results from your baby's skin being kept too hot and damp by the nappy. An easy way to prevent this is to ensure you use good-quality disposable nappies, which keep the skin cooler and drier (Figure 1).

If you prefer to use cloth nappies, the following advice should be considered.

- Change the nappy every two hours.
- Do not use plastic overpants.
- Avoid double nappies.
- Do not use nappy liners.
- Machine wash and rinse the nappies in hot water.
- Tumble dry the nappies.

Changing nappies often can be very difficult overnight or when away from home. Consider using disposable nappies in these situations. Always change the nappy as soon as it is soiled with faeces. Long contact with faeces is irritating to a baby's skin.

Treatment

If your baby has developed nappy rash, follow this advice to treat it.

- Discard all powders and creams other than the ones recommended by your doctor. Use a bland, nonperfumed emollient (moisturising) cream, such as sorbolene cream, on your baby's skin at every nappy change (Figure 2).
- Do not use soap or bubble bath when bathing your baby.
- Avoid commercial wet wipes. Instead use a damp washer with soap-free cleanser.
- Change nappies as soon as they become wet or soiled.
- Apply hydrocortisone 1% ointment and an antifungal cream, as prescribed by your GP, or a hydrocortisone–antifungal mixture, three times a day.
- Do not be concerned that the hydrocortisone is too strong for your baby or is likely to thin the skin. This sort of cortisone is very safe.

Once the skin has recovered you can stop using the hydrocortisone and antifungal creams, but continue to do all the other things above or the rash may come back.

Nappy rash tends to recur. If this happens, just use the hydrocortisone and antifungal creams again. Do not use stronger corticosteroid creams, ointments or lotions. If the rash does not improve, see your doctor.

Some babies never have completely normal skin until they are out of nappies, both day and night. Aim for comfort rather than a perfect appearance. MT

Figure 1. Change the nappy every two hours.

Figure 2. Use a nonperfumed moisturising cream at every nappy change.

When is it melanoma?

An update on diagnosis and management

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Early diagnosis and treatment of melanoma are crucial to maximise the chances of a favourable outcome.

KEY POINTS

- Early diagnosis of melanoma is crucial and is enhanced by identification of high-risk groups and appropriate surveillance. In addition to regular full skin examination, total body photography and sequential digital dermoscopic imaging are useful in selected patients.
- Dermoscopy significantly improves diagnostic accuracy for melanoma and other skin lesions.
- Clinicians should be aware of atypical presentations (e.g. amelanotic, hypopigmented and nodular melanomas), which are often the most aggressive forms.
- Excisional biopsy is the ideal biopsy method for suspicious lesions, allowing wide local excision to be based on accurate Breslow thickness.
- Referral of patients to a multidisciplinary melanoma unit should be considered.
- Careful follow up is important to detect disease recurrence and subsequent primary melanomas.

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Australia has the world's highest incidence of melanoma, and the incidence continues to rise.[1] Melanoma was the fourth most common cancer diagnosed in Australia in 2014 (excluding nonmelanoma skin cancer), with 12,640 new cases reported.[2] As survival strongly correlates with melanoma thickness, early diagnosis is essential. The five-year survival rate is more than 95% for patients with tumours thinner than 1 mm, but less than 65% for those with tumours more than 4 mm in thickness.[3]

Clinicians should be aware of both typical and atypical melanomas, the latter often representing the most aggressive forms. Avoiding misdiagnosis of unusual melanomas is important in light of a study from an Australian medical defence organisation, which found about 60% of claims against primary care clinicians for skin conditions were related to melanoma.[4] This article highlights the diagnosis and treatment of typical and atypical melanomas. Clinical practice guidelines and other useful resources for the diagnosis and management of melanoma are listed in Box 1.[1]

Risk factors

Both environmental and genetic factors influence the risk of melanoma development. These factors are listed in Box 2.[5,6] Early diagnosis will be improved if clinicians are aware of high-risk groups of patients, and if individuals in these groups are aware of their increased risk.

Clinical assessment

Fewer than half of melanomas are detected by doctors opportunistically or at the time of a skin cancer check. More than half are detected by patients who notice a new or changing lesion.[7] Clinical assessment of patients for melanoma includes paying close attention to any history of change, even if the lesion shows no typical clinical features of melanoma.[8] Atypical melanomas are often the most

aggressive forms and are associated with a history of recent change. Therefore, even if a lesion does not look like a melanoma, if the patient expresses concern and gives a clear history of change then referral or excisional biopsy should be considered.

Complete skin examination

A complete skin examination is indicated based on patient concern or skin cancer risk factors. It should be performed under good lighting and should include the scalp, breasts, buttocks, soles of the feet and between the toes. Most melanomas are pigmented and present with an initial flat phase (radial growth phase). The features of these melanomas have been summarised by the acronym ABCD: asymmetry, border irregularity, colour variation and large diameter.[9,10] A lesion with one or more of these features should be considered a possible melanoma.

However, there are limitations to the ABCD system, which applies only to melanomas with a radial growth phase. Aggressive melanomas, such as nodular melanomas, grow vertically from the outset and do not show ABCD features. EFG criteria (elevated, firm and growing progressively for more than a month) may help diagnosis of these lesions.[11]

Dermoscopy

Dermoscopy (epiluminescence microscopy) is a useful diagnostic technique that permits visualisation of morphological features not visible to the naked eye. In experienced hands, it improves diagnostic accuracy of melanoma and other skin lesions.[12] A meta-analysis concluded that the diagnostic accuracy for melanoma, as measured by diagnostic odds ratio, was 15.6 times higher for dermoscopy compared with naked-eye examination.[12] Several studies in a primary care setting have demonstrated that dermoscopy improves diagnostic accuracy after the examiner has undergone a short period of formal training.[13-15] Later in this article, we will detail dermoscopic features suspicious for melanoma. A two-step dermoscopic method to diagnose pigmented skin lesions was described in detail in a previous issue of *Medicine Today*.[16]

1. RESOURCES FOR MELANOMA DIAGNOSIS AND MANAGEMENT

- Australian Cancer Network Melanoma Guidelines Revision Working Party. *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand*. Wellington, NZ: Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008 (www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp111.pdf).
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- Melanoma prognosis online calculator, based on the American Joint Committee on Cancer Melanoma Database (www.melanomaprognosis.org).

2. RISK FACTORS FOR MELANOMA DEVELOPMENT

Stronger risk factors

- Previous melanoma
- Multiple dysplastic naevi
- Multiple naevi
- Family history (first-degree relative affected)
- Multiple nonmelanoma skin cancers

Weaker risk factors

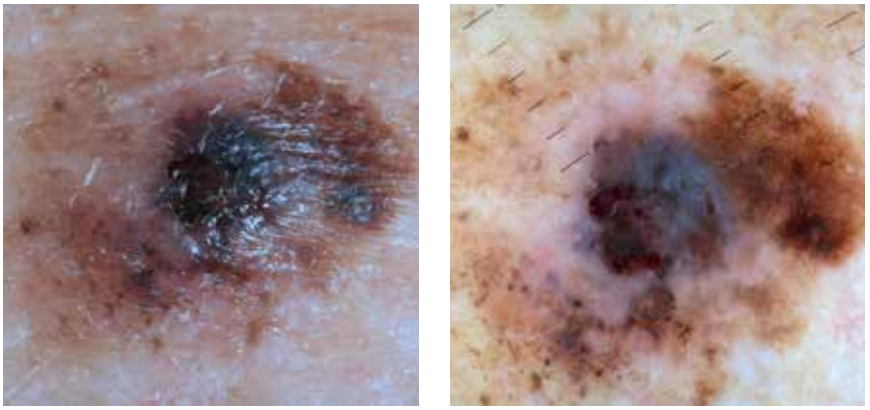
- History of blistering sunburn
- Type I skin (burns without tanning)
- Freckling
- Red hair
- Blue eyes
- Immunosuppression
- Solarium use

Surveillance of high-risk patients

It is recommended that high-risk patients undergo increased surveillance to aid earlier melanoma diagnosis. Depending on the individual patient's risk and access to specialist care, full skin examination by a doctor is recommended at six to 12-monthly intervals. Regular skin self-examination should also be encouraged, with the aid of a mirror and if possible a partner.

Total body photography

Total body photography is a useful adjunct to skin surveillance in patients with high naevus counts or multiple dysplastic naevi, in whom detection of new or changed pigmented lesions is difficult. It should be noted that although some melanomas arise in pre-existing naevi, many melanomas arise on normal skin.



Figures 1a and b. a, left. Superficial spreading melanoma (1.0 mm thick). b, right. Dermoscopy shows an asymmetrical pigmentation pattern, broadened pigment network, multiple brown dots and blue-white veil.

Sequential digital dermoscopic imaging

Digital total body photography of the skin surface can be combined with digital dermoscopic imaging of naevi with atypical features. Regular follow-up examinations allow comparison of sequential images over time, and this technique has been shown to detect early melanomas even before they develop specific dermoscopic diagnostic criteria for melanoma.

Sequential digital dermoscopic imaging may be performed in two settings as follows.

- Long-term monitoring involves examination of nonsuspicious pigmented lesions, usually at 12-month intervals.
- Short-term monitoring, usually over three months, examines individual suspicious lesions that lack diagnostic evidence of melanoma. A study in a primary care setting found the combination of dermoscopy and short-term sequential digital dermoscopic imaging reduced the excision rate of benign pigmented lesions by more than half, while nearly doubling the sensitivity for the diagnosis of melanoma.[17]

Sequential dermoscopy should not be used for lesions with features that suggest melanoma or for raised lesions that might already be invasive.

Characteristics of melanoma subtypes

Superficial spreading melanoma

Superficial spreading melanoma (Figures 1a and b) is the most common melanoma subtype, accounting for 70% of in situ melanomas (noninvasive melanomas confined to the epidermis) and invasive melanomas (those that have invaded the dermis). Superficial spreading melanomas are archetypal ABCD melanomas, and typically present as gradually enlarging, asymmetrical lesions with variegated pigmentation and irregular borders. Differential diagnoses include dysplastic naevus, seborrhoeic keratosis, dermatofibroma and nonmelanoma skin cancer.

Dermoscopy is useful for differentiating between melanomas and other pigmented lesions, and several algorithms have been developed for this purpose. Among others, the Menzies method is useful to support the decision to perform a biopsy or to refer the patient to a dermatologist, and is outlined in Box 3.[18] The Menzies method has a sensitivity of 85 to 95% and a specificity of 38 to 78% among examiners with various degrees of experience.[14,18-20]

Nodular melanoma

Nodular melanoma comprises only 10 to 15% of melanomas in Australia but is an aggressive subtype that accounts for most thick melanomas and most skin cancer deaths.[21] Nodular melanomas grow vertically from their inception and develop faster than radial growth-phase melanomas. They are more commonly seen on the head and neck and in older people.[22] About 50% of nodular melanomas are amelanotic or hypopigmented and appear as pink or red nodules.[8] When pigmentation is present, it is usually evenly distributed throughout the tumour.

Nodular melanomas begin raised and grow progressively as a firm, round nodule (Figures 2a and b). They are often symmetrical and well circumscribed.[8] After a period of growth they may ulcerate, bleed and crust. Because of their atypical presentation, nodular melanomas are frequently misdiagnosed as nonmelanoma skin cancer or benign lesions such as dermatofibroma, pyogenic granuloma, haemangioma or intradermal naevi. As previously discussed, the ABCD features apply poorly to nodular melanomas, and the EFG criteria are more useful.[11]

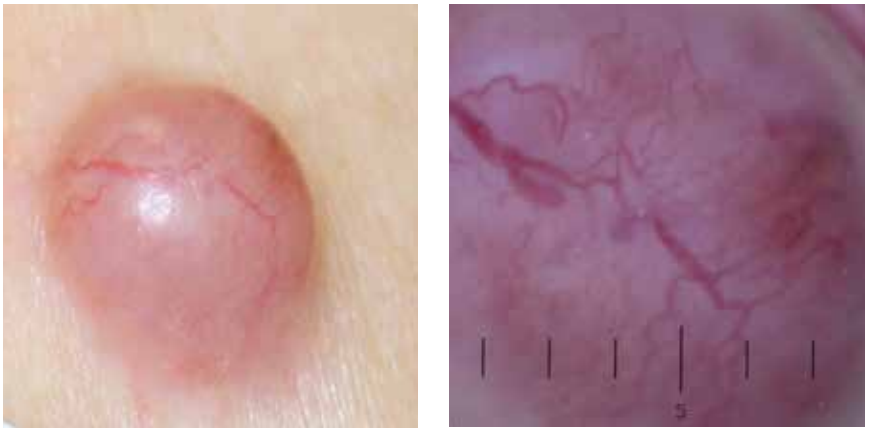
Dermoscopically, pigmented nodular

3. MENZIES METHOD FOR DIAGNOSIS OF MELANOMA

In the Menzies scoring method for the dermoscopic differentiation of melanoma from benign pigmented lesions, a lesion satisfying both of the following criteria is diagnosed as a melanoma.

- The lesion must have neither of the two negative features:
  - symmetry of pigmentation pattern
  - presence of only a single colour
- The lesion must have at least one of the nine positive features:
  - blue-white veil
  - multiple brown dots
  - radial streaming
  - pseudopods
  - scar-like depigmentation
  - peripheral black dots or globules
  - multiple (five to six) colours
  - multiple blue-grey dots
  - broadened pigment network

melanomas may exhibit multiple colours, blue-grey veil and an atypical vascular pattern. Although a typical hypomelanotic nodular melanoma might appear pink or red to the naked eye, subtle pigment may be visualised with dermoscopy in 90% of lesions. Other important dermoscopic clues include milky pink areas and atypical vascular structures.[23,24] However, the diagnosis of completely amelanotic nodular melanomas is especially challenging because they lack both clinical and dermoscopic evidence of pigmentation. As a general rule, a growing firm nodule that has been present long enough to make an inflammatory lesion unlikely (more than one month) should be excised without delay if there is any diagnostic uncertainty.[25]

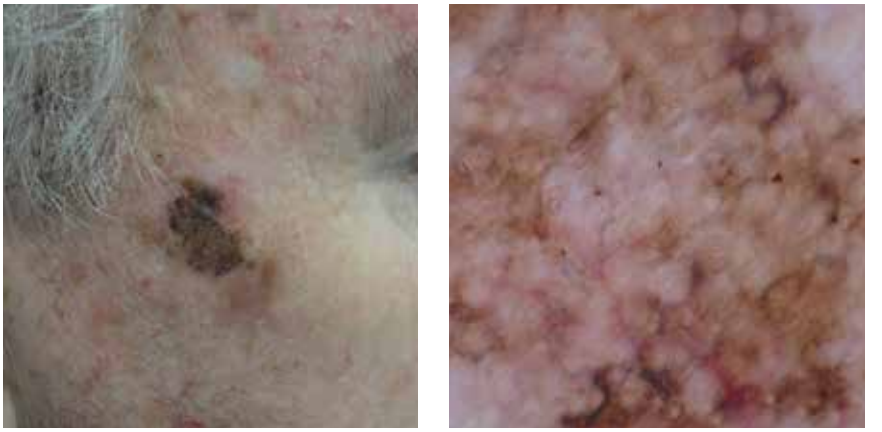


Figures 2a and b. a, left. Amelanotic nodular melanoma (11.2 mm thick). Clinically this was a rapidly enlarging, firm, symmetrical pink nodule. b, right. Dermoscopy shows atypical vessels and milky pink areas.

Lentigo maligna and lentigo maligna melanoma

Lentigo maligna (Hutchinson's melanotic freckle) and its invasive counterpart, lentigo maligna melanoma, comprise 10 to 15% of all melanomas. This subtype tends to occur on chronically sun-exposed areas such as the head and neck.

Clinically, lentigo maligna presents as an ill-defined and variably pigmented macule with ABCD features (Figures 3a and b). Diagnosis can be challenging on severely sun-damaged skin, and differential diagnoses include solar lentigo, pigmented solar keratosis, pigmented intraepidermal carcinoma and pigmented seborrhoeic keratosis. Dermoscopy is a valuable diagnostic aid, as lentigo maligna exhibits a number of unique features including asymmetric perifollicular pigmentation, rhomboidal structures and annular granular structures.[26]



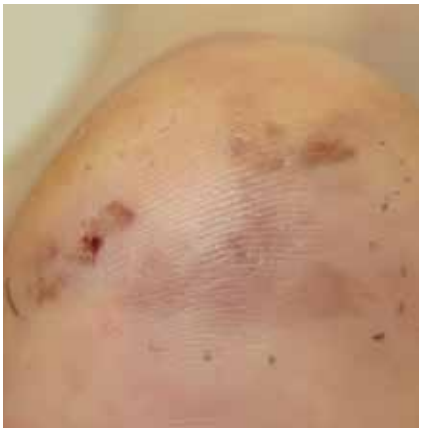
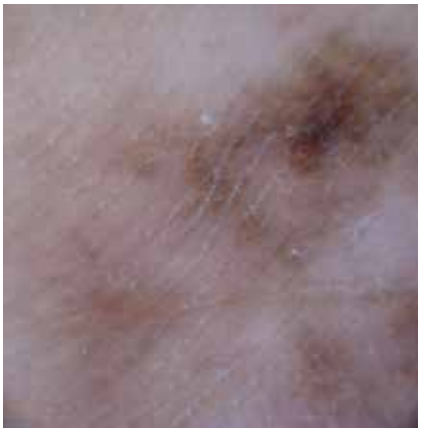
Figures 3a and b. a, left. Lentigo maligna melanoma (0.2 mm thick) on the cheek. b, right. Dermoscopy shows rhomboidal structures, asymmetric perifollicular pigmentation and annular granular structures.

Acral lentiginous melanoma

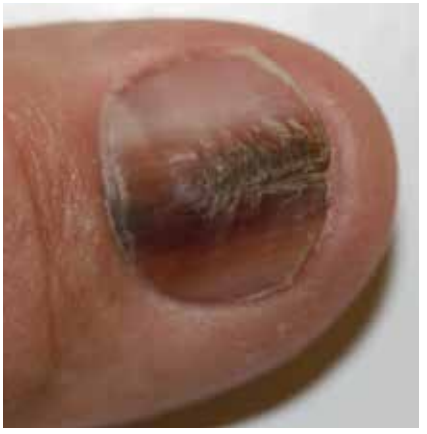
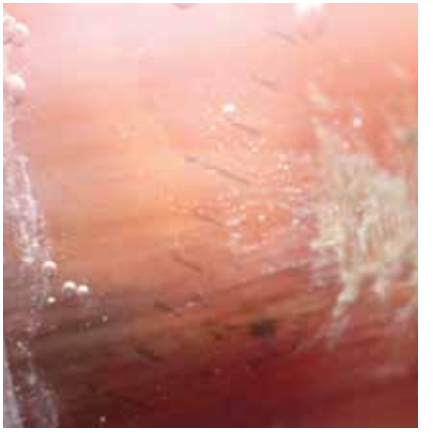
Acral lentiginous melanoma accounts for 0.5 to 1.0% of melanomas in Australia and occurs on the sole, palm and nail apparatus (Figures 4a and b). Uniquely among melanomas, acral lentiginous melanoma is not thought to be related to ultraviolet light exposure.[27] It is the most common subtype of melanoma in people with deeply pigmented or Asian skin.

Clinically, these melanomas present as pigmented macules that appear similar to superficial spreading melanomas. However, they are more often light coloured or pink.[27] Not uncommonly, they may be mistaken for a wart or fungal infection. Any warty acral lesion or erythematous patch responding poorly to treatment should be biopsied. Although melanomas on acral areas may appear relatively flat, this can be deceiving, and many have invaded to a significant depth histopathologically. Acral lentiginous melanoma is associated with a poorer prognosis because of delayed diagnosis and advanced thickness at diagnosis. A parallel ridge pattern on dermoscopy is highly specific for this type of melanoma.

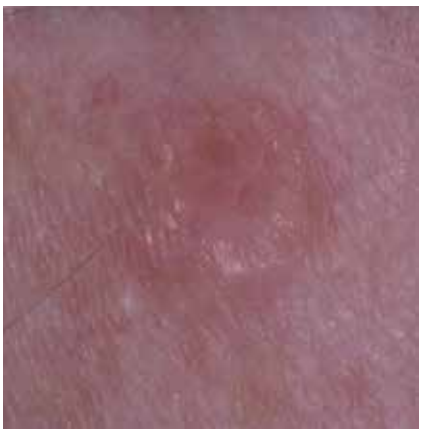
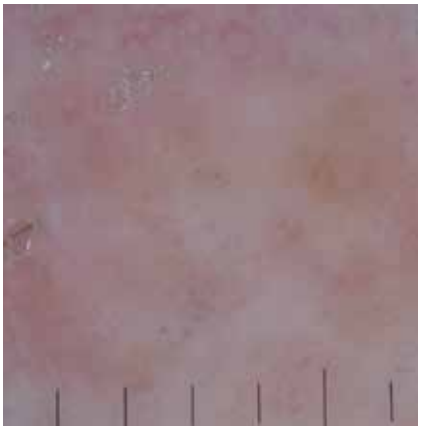
Subungual melanoma, a variant of acral lentiginous melanoma, originates within the nail matrix and presents as a broad and expanding pigmented band, referred to as longitudinal melanonychia (Figures 5a and b).[28] Adjacent nail fold pigmentation may be seen, known as Hutchinson's sign. The major differential diagnosis is subungual haematoma. However, subungual haematoma has a different colour (red through to blue-black) and does not conform to the band-like pattern of melanoma.

Figures 4a and b. a, left. In situ acral lentiginous melanoma on the heel. b, right. Dermoscopy shows an irregular pigment pattern.

Figures 5a and b. a, left. In situ subungual melanoma of the thumb presenting as longitudinal melanonychia with associated nail dystrophy. b, right. Dermoscopy shows the longitudinal pigmented band.

Figures 6a and b. a, left. A desmoplastic melanoma (3.9 mm thick) with a clinically banal appearance, which is easily misdiagnosed. b, right. Dermoscopy shows a completely amelanotic lesion. A history of change was crucial to the diagnosis.

Desmoplastic melanoma

Desmoplastic melanoma is a rare spindle cell melanoma that produces a scar-like tissue reaction and is frequently associated with perineural invasion. It is more common in elderly people and on the head and neck.[29]

Desmoplastic melanoma often appears as an amelanotic plaque or nodule (Figures 6a and b). They typically have a firm, sclerotic or indurated quality and may appear clinically innocuous. As a result, desmoplastic melanomas are frequently misdiagnosed as nonmelanoma skin cancer, dermatofibroma, scar or even dermatitis. Diagnostic delay is common and these tumours may be deeply invasive at the time of diagnosis. A history of recent appearance or change is often crucial to the diagnosis.

Melanoma mimickers

The clinical and dermoscopic features of common skin lesions that can mimic the appearance of melanoma are listed in Box 4. Pigmented lesions such as dysplastic naevi and seborrhoeic keratoses may appear similar to pigmented melanoma, whereas nonmelanoma skin cancers may resemble amelanotic nodular and desmoplastic melanoma. Figures 7 to 13 illustrate some features of nonmelanoma lesions that assist diagnosis.

Initial biopsy of suspected melanoma

Excisional biopsy

An excisional biopsy with a 2 mm margin is the ideal biopsy method for lesions suspected of being melanoma.[1] Complete excision allows accurate assessment of overall histopathological architecture, cellular detail and tumour depth.

Even with a confident clinical diagnosis of melanoma, excisional biopsy should be performed rather than immediate wide local excision. Immediate wide excision may compromise margins and the opportunity to perform sentinel lymph node biopsy.

Appropriate surgical planning is important for excisional biopsy. The long

4. CLINICAL AND DERMOSCOPIC FEATURES OF COMMON NONMELANOMA CUTANEOUS LESIONS

Melanocytic naevus
Symmetrical with regular pigment network or globules and symmetrical structures (Figures 7a and b)

Dysplastic naevus
Atypical or irregular pigment network without melanoma-specific criteria (Figures 8a and b)

Seborrhoeic keratosis
Milia-like cysts, comedo-like openings, fissures and ridges, fingerprint-like structures, well-defined borders, hairpin vessels (Figures 9a and b)

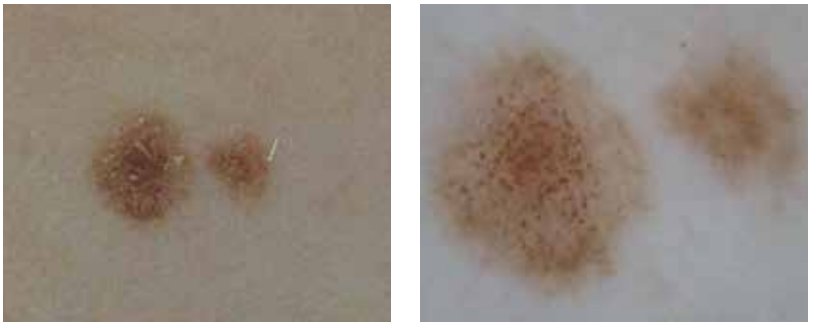
Haemangioma
Venous lakes and lacunes (Figures 10a and b)

Dermatofibroma
Fitzpatrick's 'dimple' sign, central hypopigmentation surrounded by delicate pigment network (Figures 11a and b)

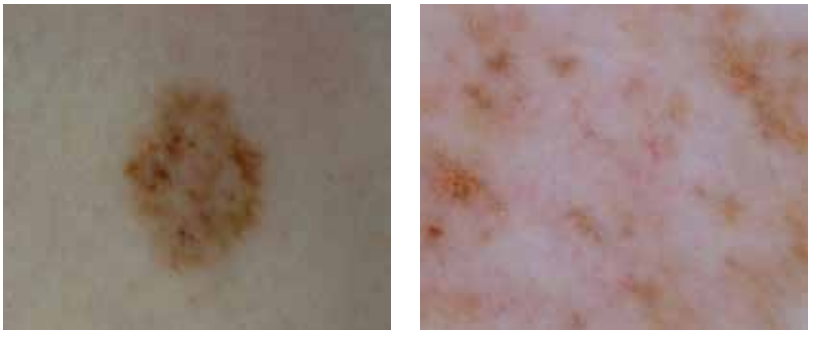
Basal cell carcinoma
Arborising vessels, spoke wheel-like structures, leaf-like areas, blue-grey ovoid nests, multiple nonaggregated blue-grey globules, ulceration (Figures 12a and b)

Squamous cell carcinoma
Hyperkeratosis, white structureless areas, white circles, white dots, keratin pearls, glomerular vessels, hairpin vessels and serpentine vessels (Figures 13a and b)

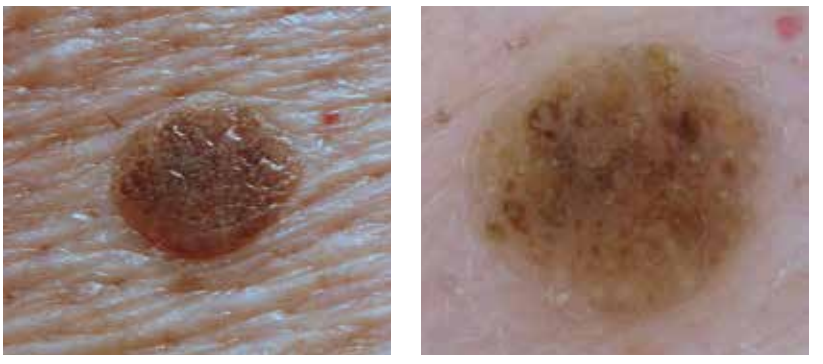
NONMELANOMA LESIONS



Figures 7a and b. a, left. Melanocytic naevus. b, right. Dermoscopy shows a symmetrical lesion with regular pigment network.



Figures 8a and b. a, left. Dysplastic naevus. b, right. Dermoscopy shows an irregular pigmentation pattern but no melanoma-specific features.



Figures 9a and b. a, left. Seborrhoeic keratosis. This lesion has a 'stuck on' appearance with well-defined borders. b, right. Dermoscopy reveals fissures and ridges, milia-like cysts and irregularly shaped crypts.

axis of an elliptical excisional biopsy should follow the lines of relaxed skin tension as this may allow subsequent re-excision to be closed primarily rather than with a graft or flap. Complicated skin closure with local flaps should be avoided, as flap closure distorts skin architecture and complicates wide local excision. Skin flaps may also interfere with lymphatic drainage and decrease the accuracy of sentinel lymph node biopsy.

Partial biopsy

Partial biopsy techniques (punch, shave, curettage or incision) should be avoided if possible. Partial biopsy increases the chance of medical errors, including histopathological misdiagnosis through misrepresentative sampling, and can interfere with assessment of tumour thickness and induce pseudomelanoma (a recurrent naevus that mimics melanoma). A recent study showed that 24% of punch biopsies for melanoma failed to detect its presence, and punch biopsies were 20 times more likely to lead to misdiagnosis than excisional biopsies.[30] This is reflected in the finding that partial biopsies are a significant cause of litigation.[31]

Nevertheless, an excisional biopsy may not be appropriate in all circumstances. For instance, a partial biopsy may be needed if the lesion is large or located in a cosmetically or functionally important area such as the face or acral skin. A superficial shave biopsy is often used for investigation of an atypical pigmented macule, particularly on the face, to diagnose early lentigo maligna. For superficial melanomas, a well-performed shave excision can be used to remove the complete lesion. However, for invasive tumours, saucerisation biopsy commonly transects the base, irreparably compromising assessment of tumour depth, the most important prognostic indicator.

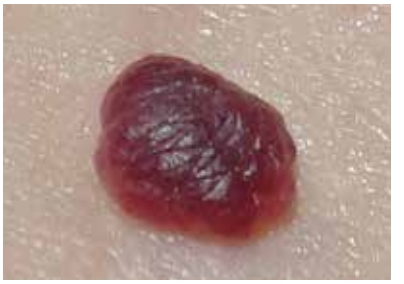
When a partial biopsy is performed, it should include the most suspicious areas of the lesion. Dermoscopy may assist in identifying these areas, and partial biopsies are best undertaken by those with expertise in the clinical diagnosis of cutaneous lesions. As a rule, the smaller the proportion of the lesion that is biopsied, the greater the potential for error. When partial biopsy is performed, histopathological conclusions need to be interpreted cautiously and with full understanding of the limitations of the biopsy method. If there is discordance between the clinical impression and the histopathology, or if there is diagnostic uncertainty, a better sample should be obtained, preferably through excisional biopsy.

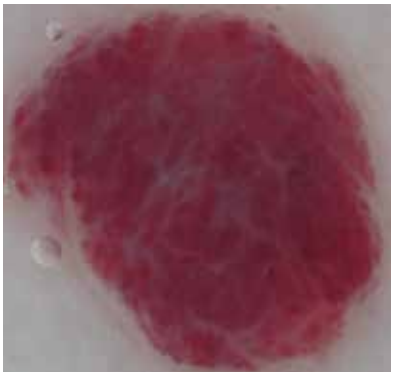
Treatment of primary melanoma

Wide local excision

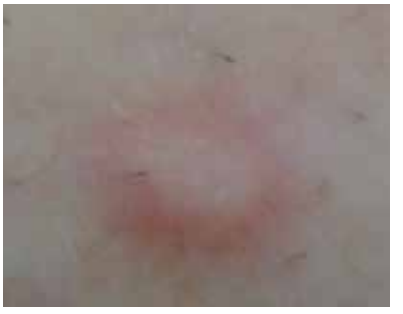
After initial biopsy, the treatment for histopathologically confirmed primary melanoma is wide local excision of the skin and subcutaneous tissues around the melanoma. The recommendations for minimum radial excision margins are based on the maximum Breslow thickness of the primary melanoma (Table).[1] However, it should be noted that there are inadequate data on whether a margin greater than 1 cm offers any survival advantage or reduces risk of local recurrence.[32-34]

NONMELANOMA LESIONS (continued)

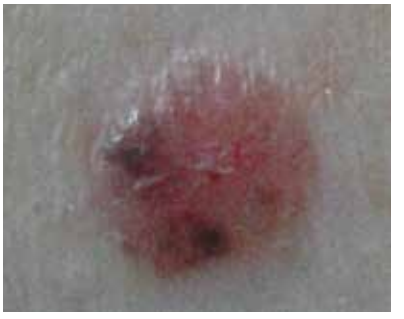


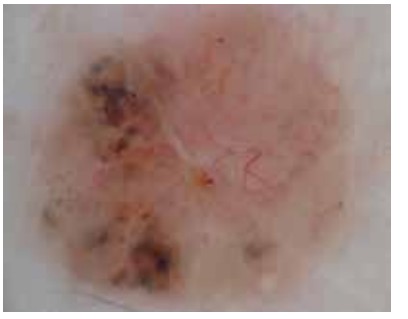


Figures 10a and b.
a, above. Haemangioma.
b, right. Dermoscopy shows vascular lakes.

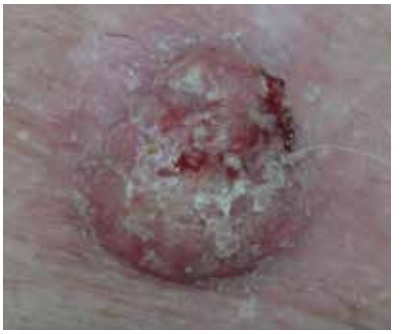


Figures 11a and b. a, left. Dermatofibroma. b, right. Dermoscopy reveals a central scar-like area.





Figures 12a and b. a, left. Pigmented basal cell carcinoma. b, right. Dermoscopy shows crisply focused arborising vessels, blue-grey ovoid nests and blue-grey globules.



Figures 13a and b. a, left. Nodular squamous cell carcinoma. b, right. Dermoscopy shows an amelanotic nodule with hyperkeratosis, white structureless areas, white circles and linear irregular vessels.

TABLE. RECOMMENDED MARGINS FOR RADIAL SURGICAL EXCISION OF PRIMARY MELANOMA

Melanoma Breslow thickness*	Margin
In situ	5 mm
<1.0 mm	1 cm
1.0 to 4.0 mm	1 to 2 cm
>4.0 mm	2 cm

* Breslow thickness is measured from the granular layer of the epidermis down to the deepest invasive tumour cell. This is the single most important prognostic factor for clinically localised primary melanoma.

Sentinel lymph node biopsy

A sentinel lymph node is the first lymph node reached by metastasising cancer cells from the primary tumour site. This node can be identified by injecting dye and radioactive tracer at the primary tumour site before wide local excision. During sentinel lymph node biopsy, the sentinel node is located by a gamma probe and confirmed with blue dye staining, then removed for histological analysis. This allows assessment for nodal micrometastases. The status of the sentinel lymph node provides prognostic information additional to that obtained from the primary lesion.[3] However, the results of a large randomised controlled trial showed no overall survival benefit in patients who underwent sentinel lymph node biopsy.[35] Thus, the role of this procedure is currently an area of great debate.

Current guidelines recommend that patients with a melanoma greater than 1.0 mm in thickness be given the opportunity to discuss use of sentinel lymph node biopsy to provide prognostic information.[1] It is also sometimes offered for thinner melanomas with other high-risk histopathological features, such as ulceration or increased mitotic rate. The decision whether to undergo sentinel lymph node biopsy should be made in conjunction with a specialist in the field before the wide local excision is planned.

Staging investigations

Staging investigations, including blood tests, CT and PET (positron emission tomography) scans, are not recommended in patients who have no clinical evidence of metastatic disease.

New treatment options for advanced melanoma

New therapies developed over the past decade have led to substantial improvements in treatment options for patients with metastatic melanoma. Specific mutations in the *BRAF* gene, which are present in about 40% of advanced melanomas, drive the MAPK pathway, promoting proliferation. Patients with metastatic melanoma should have tissue assessed for the presence of *BRAF* gene mutations. For those patients with a known *BRAF* mutation, targeted inhibition of the MAPK pathway is a treatment option. Such inhibitors include *BRAF* inhibitors (e.g. dabrafenib[36]) which may be combined for increased efficacy with *MEK* inhibitors (e.g. trametinib[37]). Immunotherapy is another treatment option for some patients with metastatic melanoma. Immune checkpoint inhibition of CTLA-4 (such as with ipilimumab[38-41]) or PD1 (such as with pembrolizumab[42]), used singly or in combination, have been shown to result in survival benefit for a significant proportion of patients with advanced melanoma.

Counselling patients about prognosis

The American Joint Committee on Cancer has produced an online prognostic calculator based on analysis of a large dataset of patients with long-term follow up (see Box 1). In addition to thickness and sentinel lymph node status, important negative prognostic factors are high mitotic rate, ulceration, male sex, axial location (trunk, head and neck) and older age.

Multidisciplinary melanoma units

There are several multidisciplinary melanoma units in Australia. These units offer specialist assessment and advice on all aspects of management for biopsy-proven localised melanoma and metastatic melanoma. Services provided by these units are outlined in Box 5.

Follow up

Patients with melanoma are followed up for two main reasons: to detect recurrence and, more importantly, to facilitate early detection of subsequent primary melanomas.

To detect recurrence, an important part of each follow-up consultation involves careful examination of the scar and lymph node status. Lymph nodes containing metastatic melanoma often rapidly increase in size and are firm to hard in consistency. However, studies have shown that three-quarters of patients detect their own recurrences if they have received appropriate melanoma education.[43] Therefore, patient self-examination is also essential and should be taught. Ultrasonography is increasingly being used as an adjunct to clinical examination for patients at higher risk of regional nodal metastasis, but there is insufficient evidence at present to support the inclusion of this technique in routine melanoma follow up.

For recurrence detection, there is little evidence to guide follow-up intervals, but it is generally recommended that patients at greatest risk of recurrence should be followed up more often than those with a low risk of recurrence. Recurrences from thicker tumours are likely to present in the early years after diagnosis. Thus, a patient with an invasive melanoma less than 1 mm thick might be seen six-monthly, whereas a patient with a melanoma more than 4 mm thick might be checked every three months for the first two years (when

5. SERVICES PROVIDED BY MULTIDISCIPLINARY MELANOMA UNITS

- Histopathology review by an expert dermatopathologist (this is particularly important for difficult histopathology, because 10% of patients seen in multidisciplinary melanoma units have a significant alteration in diagnosis or microstaging based on pathology review)
- Advice regarding the role of sentinel lymph node biopsy and staging investigations
- Wide local excision (particularly in cosmetically or functionally important sites or where complicated closure is required)
- Surgery for metastatic disease
- Radiation oncology assessment for treatment, adjuvant therapy and palliation
- Medical oncology assessment for patients with metastatic disease, including enrolment in clinical trials
- Full skin surface examination with dermoscopy
- Melanoma risk assessment, prognostication and advice regarding future surveillance and follow up
- Advice and treatment for unusual melanomas or melanomas on unusual sites
- Psychological support and counselling

the risk of recurrence is greater), four-monthly for the next two years, then six-monthly for two years and annually thereafter.

Secondly, and more importantly, follow up allows early detection of subsequent primary melanomas.[44] Most patients in Australia with melanoma are at greater risk of a subsequent primary melanoma (0.5 to 3.0% annually) than of metastatic disease. Furthermore, early diagnosis of subsequent primary melanoma leads to higher cure rates, whereas early detection of metastatic disease may have no effect on survival, although it helps minimise morbidity. A full skin examination should be performed by the clinician at least once a year. In addition, regular self-examination by patients is essential. Patients should be taught this process and be active partners in their ongoing management. As discussed previously, a program of increased surveillance should be implemented in patients at high risk of developing new melanomas.

Conclusion

Melanoma is one of the most common cancers in Australia and primary care clinicians represent the front line in melanoma management. Prognosis is closely associated with tumour thickness, and early diagnosis and treatment before the melanoma metastasises is crucially important. Clinicians should be aware of both typical and atypical melanoma presentations; the latter often represent the most aggressive tumours. When melanoma is suspected, early excisional biopsy or urgent referral is vital for a favourable outcome. MT

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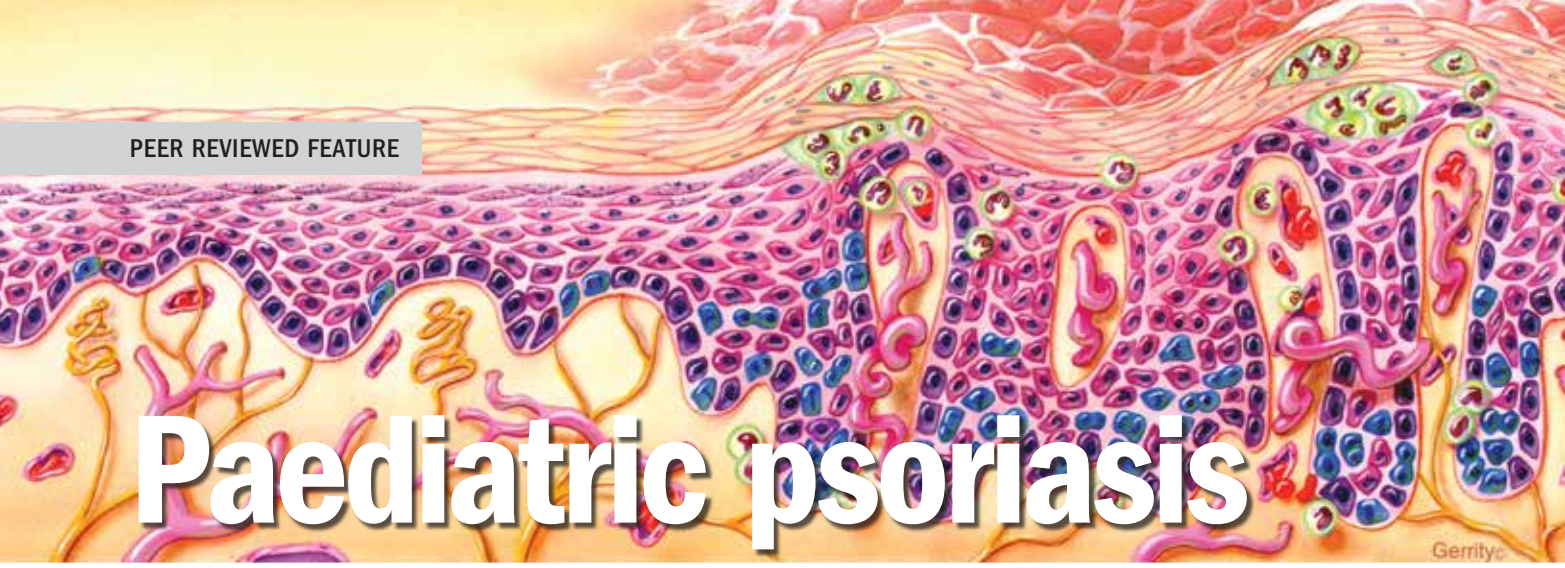
COMPETING INTERESTS: None.



Paediatric psoriasis

A common skin disorder with potential multisystem implications

ANDREW LEE MB BS, MMed
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Paediatric psoriasis is a diagnostic challenge but it can be managed well if recognised and treated correctly. With evidence increasing that children with psoriasis are at greater risk of cardiovascular disease, obesity and metabolic syndrome later in life, a young patient with this chronic skin disorder presents an important opportunity for preventive action to reduce future health risks.

KEY POINTS

- The presentation of psoriasis in children may differ markedly from the typical adult presentation. It can be confused with atopic dermatitis or discoid eczema.
- Psoriasis in children is generally a mild disease, and most cases can be managed successfully with regular topical treatment.
- Narrow-band UVB phototherapy is beneficial and safe for children.
- Specialist referral is recommended for the small group of children who require systemic medication for psoriasis that is severe and widespread.
- Evidence is increasing that children with psoriasis have an increased risk of cardiovascular disease, obesity and metabolic syndrome later in life.

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Psoriasis is a common chronic skin condition that affects around 3% of all people. Retrospective studies indicate that one-third of adult patients recall a childhood onset, and two-thirds of patients have a family history of psoriasis. The results of twin studies are suggestive of a strong genetic component.[1] A number of chromosomal loci have been linked to an increased susceptibility for psoriasis.[2-4]

The typical age of onset for psoriasis is in late childhood and early adulthood, but psoriasis can start at any time in life. Exacerbations and acute attacks may be triggered by certain events, such as trauma or infections, including viral upper respiratory tract infections. Group A streptococcal throat and skin infections are one of the most common causes of acute guttate psoriasis and can worsen pre-existing psoriasis. In susceptible children, streptococcal genital infections often precipitate genital psoriasis. Psoriasis may also be precipitated by certain drugs, particularly beta blockers, antiepileptic drugs, antimalarial agents and lithium.

The pathophysiology of psoriasis is related to an excessively rapid turnover of keratinocytes. Recent studies in adults suggest it to be an immune-mediated condition that is associated with a number of autoimmune disorders and can have systemic implications, particularly arthritis and metabolic syndrome. Studies suggest that children with psoriasis are more likely to be overweight and may be at risk for metabolic syndrome from adolescence onwards.[5-7] Psoriasis is therefore increasingly viewed as being a skin disorder that has potential multisystem implications.

Clinical presentations

Although some children with psoriasis develop the classic plaques seen in adults, the presentation of psoriasis in others may differ markedly from the typical adult presentation.

Paediatric psoriasis is sometimes difficult to recognise and can be confused with atopic dermatitis or discoid eczema (Figure 1). Psoriatic plaques in children tend to be thinner, not as well demarcated, less scaly and less erythematous than in adults. Children may have concurrent psoriasis and atopic dermatitis, which produces a mixed clinical picture.

Infants

In infants, a scaly scalp ('cradle cap') is often one of the first signs of psoriasis (Figure 2). Persistent nappy rash that is resistant to treatment is another common early sign – a psoriatic nappy rash tends to be bright red and well demarcated in this location, and it often involves the groin folds (Figures 3 and 4). It may present as elbow and facial plaques (Figure 5).

Young children

In children of primary school age, the most common presentation of psoriasis is scaly erythematous plaques or papules, typically involving the dorsal surfaces of the knees and elbows. These plaques are usually not as raised, hyperkeratotic or as well defined as in adults (Figures 6a and b).[8] Other common areas of involvement include the scalp, ankles (Figure 7) and the post-auricular and infra-auricular regions (Figure 8). Erythema may be very persistent. Splitting of the skin is common and may affect the soles and palms (Figures 9 and 10); there may also be fingertip redness and fissuring. Excoriations are less common in psoriasis than in atopic dermatitis.

Facial involvement is common in children with psoriasis (rare in adults). It may present as chronic plaques on the cheeks (Figure 11), blepharitis, cheilitis (perlèche; Figure 12) or as a band extending from the frontal hairline to mid-forehead. Facial lesions can be particularly difficult to treat.

Children may present with genital involvement, either alone or as part of more generalised psoriasis. Clinically, this presents as an itchy, sore and red vulva or as erythematous plaques on the scrotum, penis and perianal skin with extension into the natal cleft. A recent study has suggested that psoriasis is the most common cause of vulval itching and rashes in prepubertal girls.[9]

Older children and adolescents

Psoriasis of older children and adolescents begins to resemble typical psoriasis seen in adults. In this age group, many patients who had coexisting atopic dermatitis when they were younger will experience remission of atopic dermatitis and be left with a clinical picture of psoriasis only.

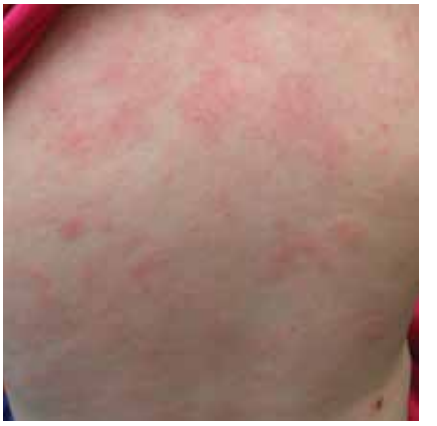
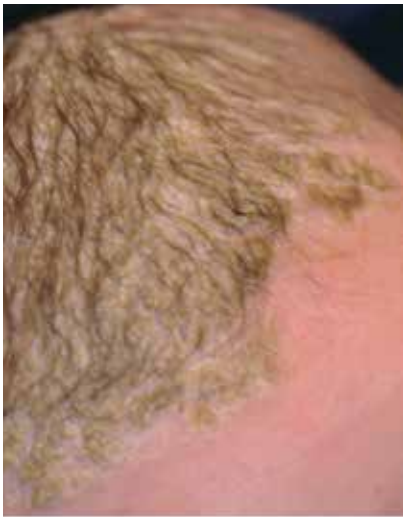
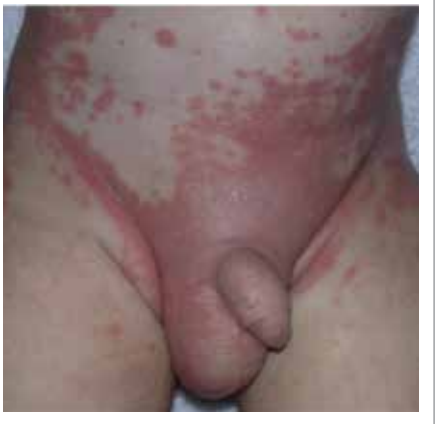
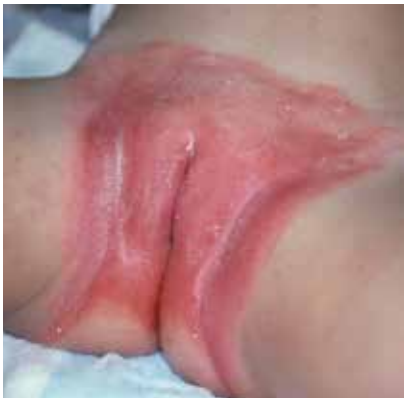


Figure 1. Extensive paediatric psoriasis resembling eczema.

PSORIASIS IN INFANTS







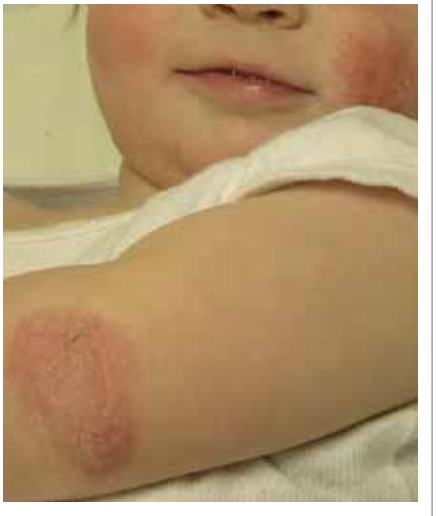
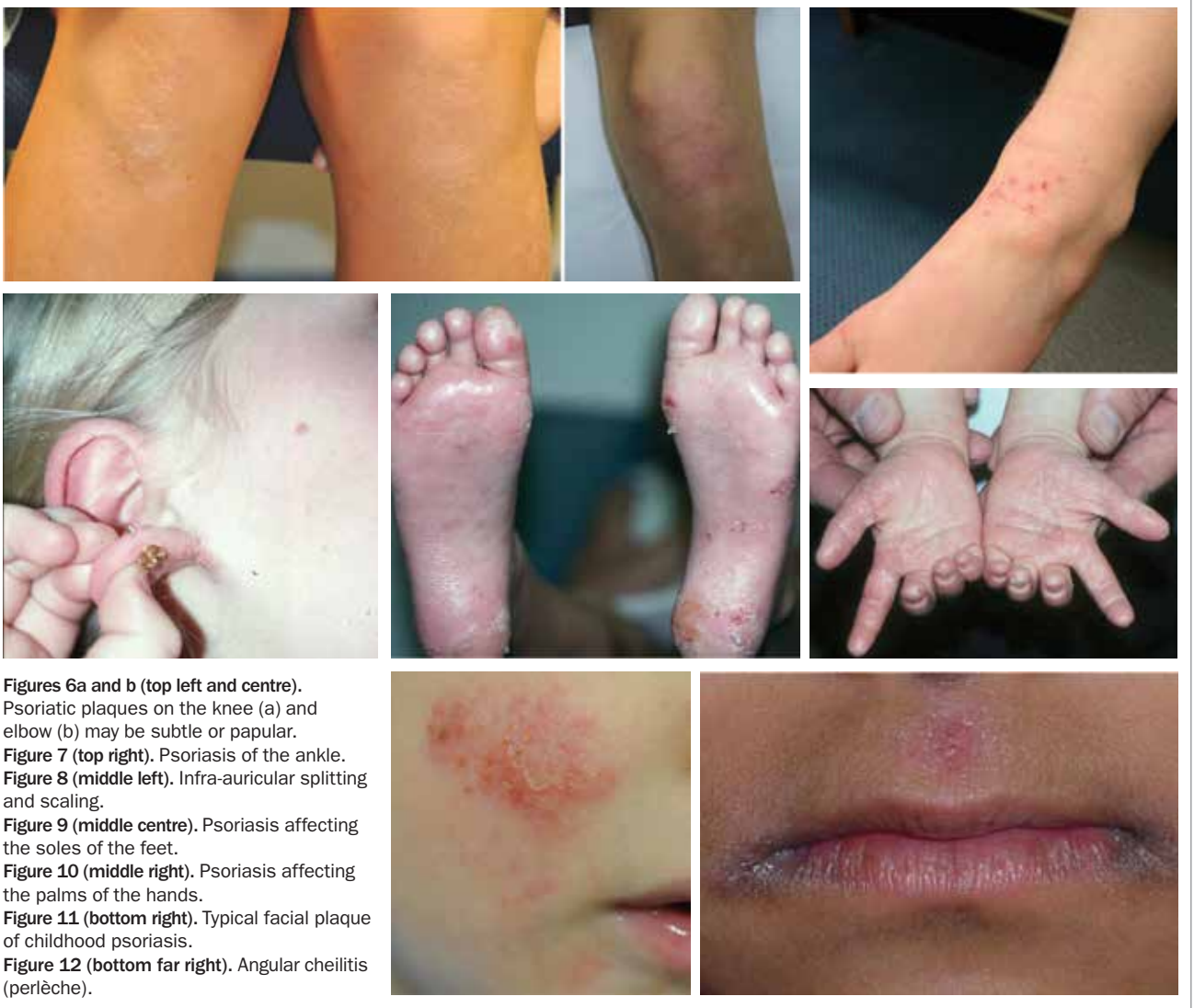


Figure 2 (top left). Severe hyperkeratotic scalp ('cradle cap') caused by psoriasis.
Figure 3 (top right). Typical psoriatic nappy rash.
Figure 4 (bottom left). Persistent and severe psoriatic nappy rash with well-demarcated edge.
Figure 5 (bottom right). A baby with a typical elbow plaque and similar plaques on the cheeks.

PSORIASIS IN YOUNG CHILDREN



Figures 6a and b (top left and centre). Psoriatic plaques on the knee (a) and elbow (b) may be subtle or papular.
Figure 7 (top right). Psoriasis of the ankle.
Figure 8 (middle left). Infra-auricular splitting and scaling.
Figure 9 (middle centre). Psoriasis affecting the soles of the feet.
Figure 10 (middle right). Psoriasis affecting the palms of the hands.
Figure 11 (bottom right). Typical facial plaque of childhood psoriasis.
Figure 12 (bottom far right). Angular cheilitis (perlèche).

In older children and adolescents, psoriasis typically presents as thickened scaly plaques with involvement of the dorsal knees (Figure 13), elbows (Figure 14), feet and hands, and scattered patches of involvement elsewhere. They may also have a red and scaly scalp. Nail involvement is common but usually minimal and may not be evident if pitting is the only sign (Figure 15). However, other nail changes can be seen in patients with more severe disease (Figure 16). Changes include lifting of the nail plate (onycholysis), discolouration ('salmon patches') and thickening (subungual hyperkeratosis).

Differential diagnosis

Other diagnoses to consider in children with suspected psoriasis include atopic dermatitis, fungal infection and discoid eczema. In babies and adolescents, seborrhoeic dermatitis is another possibility.

Atopic dermatitis usually responds very well to potent topical corticosteroids and emollients, whereas psoriasis is typically more resistant to treatment, displaying only a partial response to even the more potent topical corticosteroids and a rebound flare on cessation of treatment. Atopic dermatitis is characteristically distributed in a different pattern to psoriasis, with involvement of the cubital and popliteal fossae, and is associated with generalised xerosis. It tends to be significantly more itchy than psoriasis and has a tendency to interrupt sleep. However, psoriasis in children may be very itchy, particularly when there is also an element of atopic dermatitis.

PSORIASIS IN OLDER CHILDREN AND ADOLESCENTS

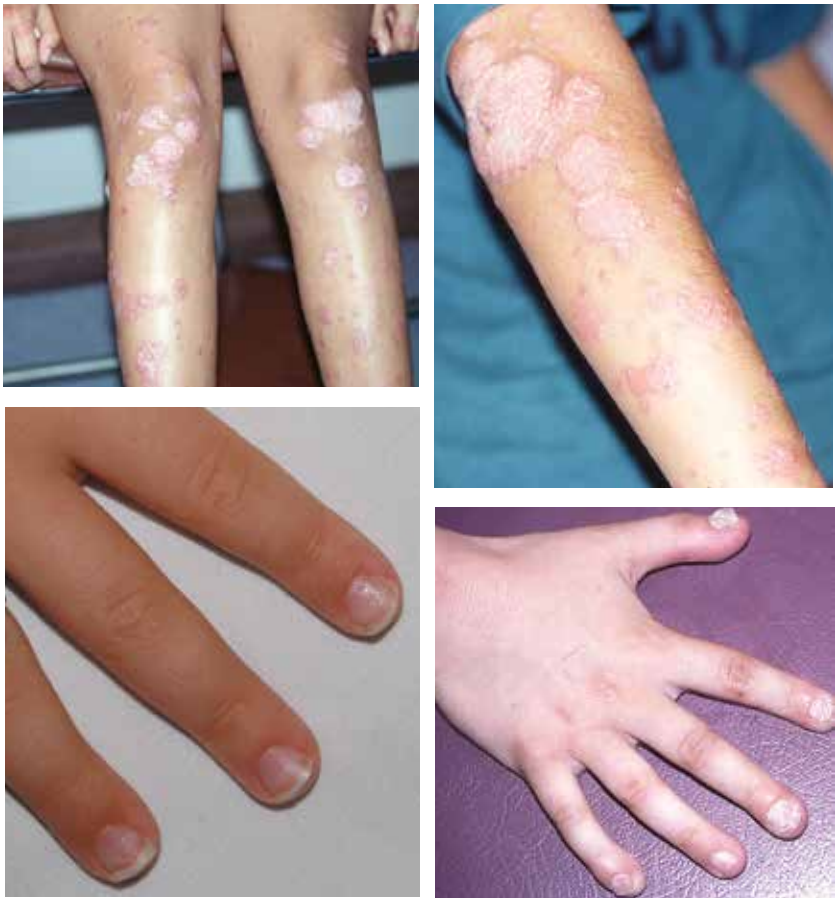


Figure 13 (top left). Psoriatic plaques on the knees and lower legs.
Figure 14 (top right). Typical elbow psoriasis.
Figure 15 (bottom left). Typical nail pitting in psoriasis.
Figure 16 (bottom right). Severe dystrophic nail change in psoriasis.

Tinea may mimic psoriasis of the hands and feet and may cause scalp scaling (almost always with alopecia) and scaly patches on the skin. It can be suppressed by topical corticosteroids and, like psoriasis, flare on cessation of treatment.

Discoid eczema may closely mimic psoriasis but is very itchy and randomly distributed. In some children, discoid eczema evolves into psoriasis.

'Seborrhoeic dermatitis' as a phenotype may evolve into psoriasis and can be the first sign of psoriasis in babies. It can be self-limiting and readily suppressed with topical corticosteroids, but if it persists beyond 1 year of age then psoriasis is a more likely diagnosis. In adolescents, seborrhoeic dermatitis resembles the typical presentation in adults, with scaly scalp, eyelids and axillae, groin rash and paranasal scale and erythema. However, it may resemble psoriasis very closely.

Zinc deficiency may closely mimic psoriasis in babies. However, this is very rare and would only be suspected where there was no response to appropriate treatment for psoriasis and in the setting of a very unwell child with failure to thrive.

Investigations

Psoriasis is a clinical diagnosis. Skin biopsies are not always diagnostic and are not required or justified in a child. For scenarios where the presentation is atypical, taking a fungal scraping or skin swab at the edge of the active lesion for culture may be worthwhile to rule out infection.

In a child presenting with sudden-onset guttate psoriasis (Figures 17a and b), a full blood count and C-reactive protein (CRP) measurement are indicated to rule out active infection (particularly streptococcal infection). Raised inflammatory markers and antistreptolysin-O titre (ASOT) and DNAase-B level indicate infection with *Streptococcus pyogenes*. In some children, chronic guttate psoriasis has an association with chronic ear, nose and throat infections; such patients may benefit from oral antibiotics and tonsillectomy and may require referral to an ENT specialist.[10]

Approach to management

It is important for parents and children to understand that psoriasis is a chronic condition and that it is distinct from atopic eczema. Some patients improve with time, with remission or indolent disease, but in our experience children with severe psoriasis maintain this pattern into adolescence. It is very difficult, however, to predict long-term outcome.

The Psoriasis Area and Severity Index (PASI; www.pasitraining.com) and the Dermatology Life Quality Index (DLQI) can be used to assess disease severity (mild, moderate or severe) and identify treatment goals.[11] The PASI measures the extent and intensity of psoriasis. The DLQI measures the extent to which psoriasis is affecting a patient's life; a modified version exists for children (Children's DLQI [CDLQI]; www.cardiff.ac.uk/dermatology/quality-of-life/childrens-dermatology-life-quality-index-cdlqi/). A PASI score of more than 10 indicates moderate to severe psoriasis. A CDLQI score of more than 10 indicates a moderate to severe effect on a child's life.[11]

A diagnosis of psoriasis in a child can be devastating for parents if they conceptualise it to be an incurable condition. It can also induce feelings of guilt in a parent who is also a sufferer. Part of

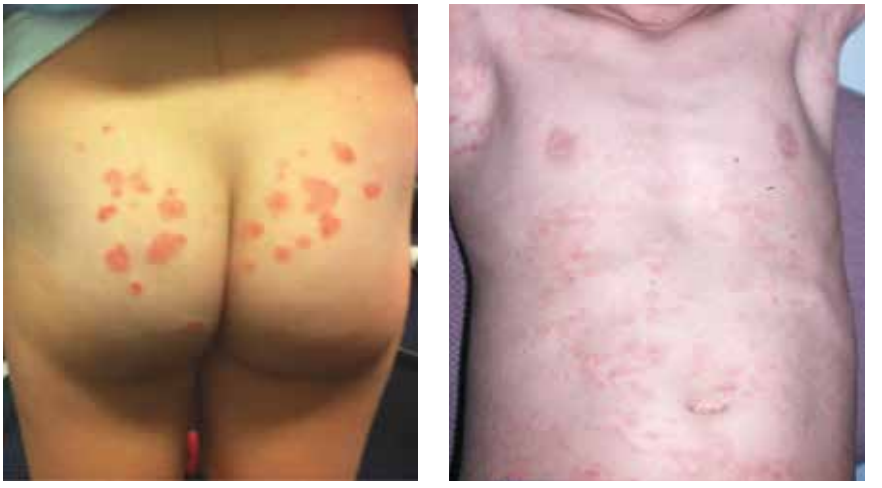
management involves addressing these feelings and providing reassurance about the relatively good prognosis of this condition in childhood, despite the fact that there are no good quality data on long-term outcomes.

Topical treatment

Psoriasis in children is generally a mild disease compared with psoriasis in adults, and most cases can be managed successfully with regular topical treatment. It is important that parents be made aware that good control of psoriasis is very dependent on regular treatment.

For children with psoriasis, the initial treatment of flares is focused on the use of basic emollients and topical corticosteroids, with the choice depending on the severity of the flare. For facial plaques, a mild to moderate topical corticosteroid could be suitable (e.g. hydrocortisone 1% or methylprednisolone aceponate 0.1%). For plaques on the body, a moderate potent topical corticosteroid is required. Betamethasone dipropionate in combination with calcipotriol, which is more effective for psoriasis than either component alone, is particularly helpful and can be applied once or twice a day. Scalp psoriasis can initially be treated with a topical corticosteroid lotion, such as methylprednisolone aceponate 0.1% or betamethasone dipropionate/calcipotriol gel. Corticosteroid lotions that are alcohol-based (e.g. mometasone furoate 0.1% or betamethasone dipropionate 0.05%) usually cause stinging and are poorly tolerated in children.

As the severity of the flare reduces and there is less inflammation and excoriation, an attempt should be made to introduce maintenance therapy with tar preparations. Treatment with liquor picis carbonis (LPC), in either aqueous cream or emulsifying ointment, is generally well tolerated; however, some children find that it stings and others do not tolerate the odour. A typical regimen would include 2% LPC for the face and 4% LPC for the body, applied once daily after bathing.



Figures 17a and b. Guttate psoriasis.

For maintenance treatment of scalp psoriasis, a tar-based shampoo can be recommended. Instructions should be given to rub the product into the scalp and leave it on for five to 10 minutes before rinsing out and then washing the hair as normal. Many patients use such products as shampoo to wash hair rather than as a scalp treatment, and it is important to explain correct application. The treatment is applied daily until the scalp is normal and then once or twice a week as needed.

Phototherapy

For children with patches of psoriasis that are resistant to treatment, narrow-band UVB phototherapy is beneficial and safe.[12,13] Phototherapy is especially useful for children with psoriasis that covers a large surface area of the body and for areas that are notoriously difficult to treat, such as the hands and feet. Even small children can receive phototherapy, although its administration sometimes requires patience on the part of the practitioner.

Systemic medications

Systemic medications are required for the small group of children who have psoriasis that is severe and widespread, and specialist referral is recommended in this situation. Acitretin and methotrexate are commonly used – these medications are effective and have a good safety profile in children. The biological agent etanercept has been approved for use in children over 4 years of age with difficult to control psoriasis and has shown positive results.[14] Referral to a dermatologist is recommended.

Comorbidities

As a result of extensive studies required for the introduction of biological agents, psoriasis in adults has been found to be a multisystem disorder that has associations with autoimmune disease, mental health disorders, cardiovascular disease and malignancies. Fortunately, psoriasis in children is not commonly associated with other medical conditions, possibly because of the inadequate duration to cause the systemic effects that result from a chronic inflammatory condition.

There is, however, increasing evidence that children with psoriasis are at greater risk of cardiovascular disease, obesity and metabolic syndrome later in life.[5-7] This presents an opportunity for preventive action to reduce future health risks. Older children and adolescents with psoriasis are almost twice as likely to be overweight or obese, and psoriasis severity has been correlated with an increased risk of being overweight.[5-7]

Children can be identified as being overweight through a sex- and age-adjusted BMI percentile or height-to-weight ratio.

The waist-to-height ratio has been proposed as a simpler measure for identifying children who have increased central adiposity, with a waist circumference more than half of the height in a child or adolescent being highly specific for increased cardiometabolic risk.[15-18] However, the waist-to-height ratio has not been validated in children under the age of 5 years, so it should not be used in this age group.

For children with psoriasis who are over the age of 10 years and who are found on screening to be at cardiometabolic risk, it would be appropriate to perform metabolic screening (including fasting lipid and blood sugar levels). All parents of children with psoriasis should be educated about the risks of obesity and the importance of a healthy lifestyle.

Psoriatic arthritis

Although it has been reported, true psoriatic arthritis in children has a very low incidence, about 1%.[19,20] The clinical course of psoriatic arthritis in children is unpredictable, and the majority of mild cases can be treated with an NSAID such as naproxen or ibuprofen. It is important to educate parents of affected children about the potential chronic nature of psoriatic arthritis. Early assessment by a rheumatologist is ideal to achieve optimal outcomes.

Conclusion

Psoriasis in children is a chronic skin condition that can be managed well if recognised and treated specifically. The disease is less likely to be severe in children and is more responsive to treatment. Accurate diagnosis and appropriate management are essential to achieving adequate disease control. The involvement of a dermatologist is recommended for children with psoriasis that is severe or difficult to treat. MT

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COMPETING INTERESTS: None.

Nail disease

Is it fungal and how should it be managed?

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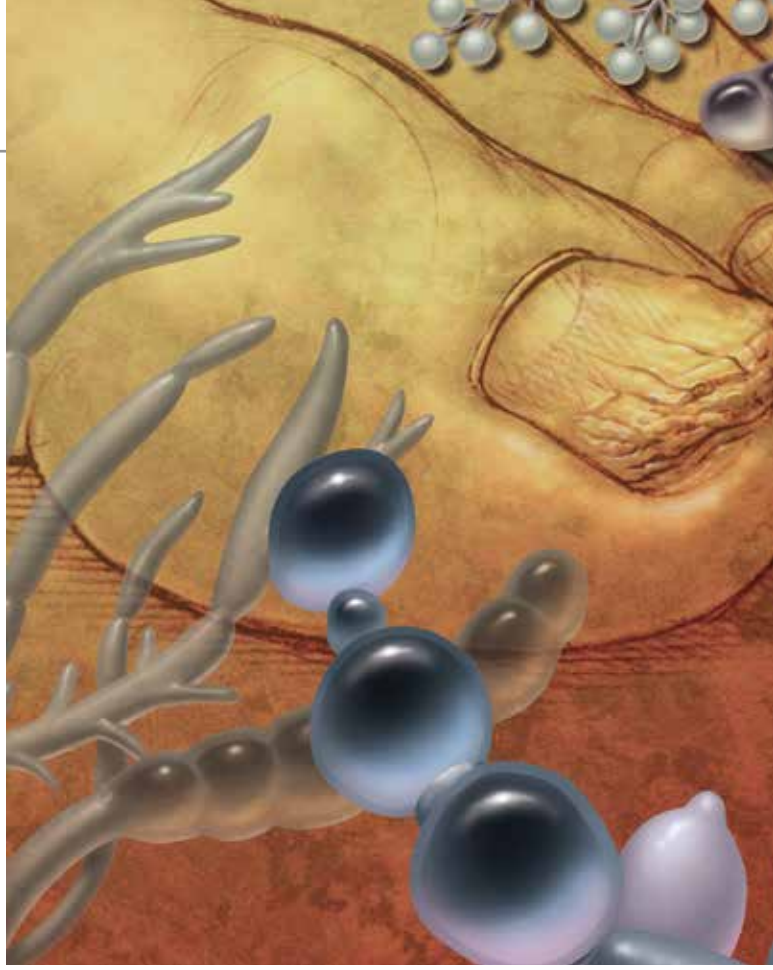
Fungal infection accounts for about half of all nail abnormalities. Differential diagnoses include psoriasis, lichen planus and *Pseudomonas* infection. Treatment usually requires long-term continuous or pulsed antifungal therapy.



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KEY POINTS

- Onychomycosis is typically asymptomatic and subclinical, representing a cosmetic problem.
- Dermatophyte moulds are the most common cause.
- Differential diagnoses that should be considered in patients with nail abnormalities include psoriasis, lichen planus and *Pseudomonas* infection.
- Keeping the feet and toenails dry can help prevent onychomycosis.
- Systemic agents have the highest success rates in treating onychomycosis; they include terbinafine, itraconazole and fluconazole.
- Topical treatments are typically useful only for superficial white onychomycosis and very mild subungual onychomycosis; they include amorolfine, bifonazole, ciclopirox and miconazole.

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Fungal infection of the fingernail or toenail plate is termed onychomycosis or tinea unguium. It accounts for about one-third of all fungal infections and half of all nail abnormalities. Onychomycosis has a prevalence of about 10%, varying geographically. The prevalence increases with age. It is mostly asymptomatic and subclinical; patients present only when affected by its clinical appearance. However, onychomycosis can be the source of dermatophytes that cause tinea on other parts of the body. Treatment typically requires a protracted course of an oral antifungal agent.

This article outlines a practical approach to the management of onychomycosis. The pharmacology of topical and oral antifungal agents used in dermatology was discussed in a previous article on dermatophyte infections, in the June 2014 issue of *Medicine Today*.[1]

Dermatophyte vs nondermatophyte moulds

Most cases of onychomycosis are caused by dermatophyte moulds. These fungi are ubiquitous; they are found in almost any environment that can support their existence. Dermatophytes grow on keratinised tissues – the 'dead' component of skin and its appendages. The most common dermatophyte infecting nails and skin is *Trichophyton rubrum*. This anthropophilic organism has a worldwide distribution and is abundant in any moist, warm area frequented by humans. Other dermatophyte species can also affect the nail plate. Dermatophyte infections are typically easier to treat than nondermatophyte infections, as most respond to oral antifungal preparations.

Saprophytic nondermatophyte moulds can also infect the

nail plate, albeit uncommonly. Typically, these moulds do not grow on other keratinised tissues, such as the skin. *Scopulariopsis brevicaulis* is the most common nondermatophyte to infect the undamaged nail plate, whereas *Acremonium*, *Aspergillus* and *Fusarium* spp. can cause superficial white onychomycosis. Infections with nondermatophyte moulds are often more difficult to treat than dermatophyte infections, especially if deep-seated; itraconazole with or without nail plate avulsion is required.

In addition, *Candida* spp. can infect the nail plate and associated nail fold. Infection can take the form of paronychia and associated nail dystrophy or, more rarely, total nail plate involvement and destruction in the setting of chronic mucocutaneous candidiasis.

Presentation

There are several types of onychomycosis, based on the mechanism of infection and clinical appearance of the nail plate.

Superficial white onychomycosis

Superficial white onychomycosis describes a very superficial infection, where the fungal elements are found on the surface of the nail plate. Powdery, white, circumscribed patches are seen (Figure 1). This is typically caused by *Trichophyton interdigitale*. *T. rubrum* and nondermatophytes can also be causative.

Distal and lateral subungual onychomycosis

Distal and lateral subungual onychomycosis is the most common type of onychomycosis, with the infection gaining access via the distal free nail plate and extending proximally (Figure 2). Yellow, brown or white discolouration of the nail plate occurs. The nail plate may thicken and is lifted up by subungual hyperkeratosis as the infection moves upwards. Chards (streaks) of infection can be seen running up the nail plate. Eventually the nail plate can be completely involved and destroyed. Distal and lateral subungual onychomycosis may start in the nail plate of one digit and extend to the others.

Proximal subungual onychomycosis

Proximal subungual onychomycosis is unusual, where whitening of the nail starts proximally as the fungus is able to access the nail plate via the proximal nail fold. Proximal subungual onychomycosis is more common in patients who are immunosuppressed, such as in HIV infection. *T. rubrum* is the most common cause.

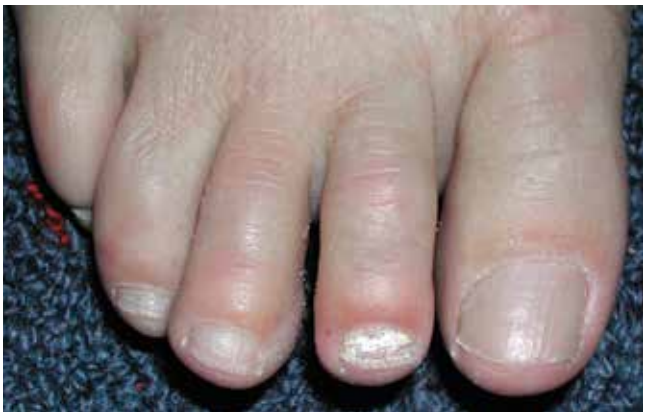

Figure 1. Superficial white onychomycosis, showing a powdery white infection of the superficial part of the nail plate of the second toe.

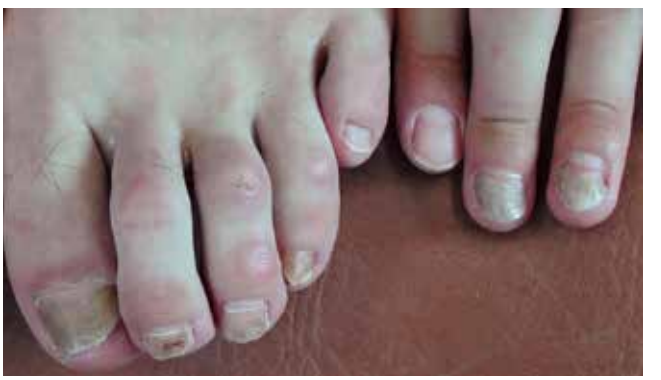

Figure 2. Classic distal and lateral subungual onychomycosis involving multiple toe and finger nails. Note the yellow-green discolouration visible on the surface of the nail, representing tinea in the nail plate and subungual hyperkeratosis, and onycholysis of the fingernails, in contrast with the normal fingernail.

Endonyx onychomycosis

Endonyx onychomycosis is a highly unusual variant, where the nail plate becomes secondarily involved by an infection that begins in the finger or toe pulp. Extension of the infection to the nail plate leads to nail pits, lamellar splits, subungual hyperkeratosis and onycholysis. Endonyx onychomycosis is caused by fungal species responsible for endothrix infection (infection of the substance of the hair shaft), such as *Trichophyton soudanense*.

Differential diagnoses

Although onychomycosis is exceedingly common and in most circumstances easy to diagnose, several differential diagnoses should always be considered. It is also important to note that

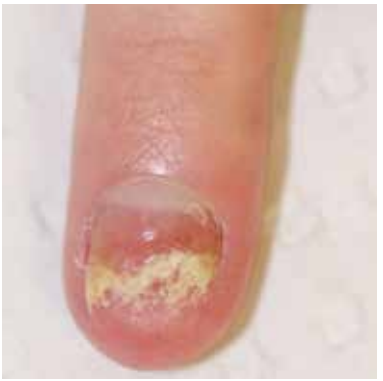

Figure 3. Nail psoriasis showing subungual hyperkeratosis, which is commonly misdiagnosed as tinea. Note the absence of the yellow-green streaks expected in dermatophyte infection, and the presence of the salmon-pink 'oil drop' sign just proximal to the hyperkeratosis.

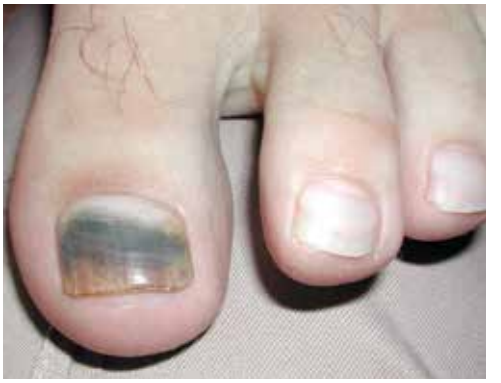

Figure 4. *Pseudomonas* infection of the nail plate showing a greenish discolouration that is not seen in tinea.

onychomycosis can be a secondary infection or coexist with any other nail dystrophy.

Psoriasis

Psoriasis can cause nail dystrophy and discolouration, subungual hyperkeratosis and onycholysis. It can be very difficult to differentiate clinically from onychomycosis. However, features of psoriasis that help in this differentiation include:

- a different quality of the dystrophic nail, with less yellow discolouration and no white/yellow streaks
- early involvement of multiple nails
- changes such as distinctive nail pits in a regular pattern
- the salmon pink 'oil drop' sign of subungual discolouration (Figure 3)
- psoriasis present elsewhere on the skin.

Pseudomonas infection

Pseudomonas infection should always be considered in patients who do a lot of 'wet work'. It leads to onycholysis with green discolouration of the nails (Figure 4). There is typically no subungual hyperkeratosis or nail destruction, although an accompanying chronic paronychia may lead to nail plate distortion or dystrophy.

Lichen planus

Lichen planus is an inflammatory condition that leads to destruction of the nail complex. The characteristic feature is a pterygium. In the context of the nail apparatus, this is a scarring process in which the proximal nail fold adheres to the nail plate and is dragged along as the nail grows. The end product is a scarred nail bed with no nail plate.

Simple traumatic onycholysis

Simple traumatic onycholysis is very common. In the fingernails, this is caused by excessive wet work and hand washing, as well as fastidious nail care where the patient cleans under the nail to remove debris, inadvertently lifting the nail further. The toenails can be lifted by excessive walking and exercise in tight shoes. Scraping of the great toenail along the ceiling of the toe box of the shoe can shear the nail plate from the bed. Subungual hyperkeratosis, chards of infection and discolouration are not seen, although secondary *Pseudomonas* infection may produce a green tinge.

Onychogryphosis

Onychogryphosis can affect elderly patients and involves gross thickening of the nail plate related to age and chronic trauma. Tinea of the nail plate can often coexist with onychogryphosis.

Investigations for onychomycosis

The 'gold standard' for the laboratory diagnosis of onychomycosis is a positive fungal culture of nail clippings. Although isolation of a fungus is diagnostic, culture is an insensitive test, and a negative result does not rule out onychomycosis. When a nail specimen is harvested for microscopy and culture, the greater the volume of material submitted the greater the chance of a positive culture. The soft, macerated subungual debris gives the greatest load of fungal elements. A small (2 mm) bone or skin curette is useful for scraping underneath the nail plate.

Fungal elements can also be seen on histopathology of the nail plate and are easily identified by the periodic acid-Schiff stain. This method can have a much higher positivity rate for diagnosis of onychomycosis, but the disadvantage is the lack of culture confirmation.

Prevention

General measures

Dermatophytes are ubiquitous organisms found in the soil and on animals and humans. Thus patients can potentially be infected from anywhere, and it is impossible to strictly avoid the fungi. The key to preventing any fungal infection is to deny the organisms favourable conditions to flourish – that is, a warm, moist, protected environment. The feet and toenails should be kept relatively dry. Open shoes are ideal, allowing the toe and webs to air dry. After a shower, the feet and web spaces can be blow dried with a hair dryer. People

who must wear closed shoes and socks for work should choose styles that are more ventilated (e.g. fabric rather than leather construction). Heavy safety boots can be ventilated with grommets and perforations by a shoe maker.

Another practical approach is to sprinkle antifungal powder into shoes. This does not treat onychomycosis but may prevent reinfection after the patient has received adequate therapy. Older shoes, which are likely to carry the fungus, should be replaced. Hot washing of socks will reduce their fungal load.

Wearing thongs or shoes in public amenities such as swimming pools and change rooms may help avoid gross contamination of the feet with detritus, but incidental contact with fungus-infested surfaces is almost unavoidable. Thorough washing and drying of the feet is important to prevent the fungus flourishing.

Predisposing factors

Predisposing factors for onychomycosis include:

- age-related changes in the toenails
- diabetes
- HIV infection
- peripheral vascular disease
- peripheral neuropathies
- sporting activities
- traumatic nail problems
- pedal anatomical abnormalities.

Good control of diabetes and peripheral vascular disease is likely to keep the skin of the feet in good condition and thus reduce the risk of infection. Patients with diabetes, peripheral vascular disease or neuropathy should inspect their feet daily for problems including onychomycosis and tinea to allow prompt treatment. However, onychomycosis is exceedingly common, and clinicians should not equate its presence with any predisposing disease.

Treatment

Both topical and systemic options are available for the treatment of patients with onychomycosis. In most cases, onychomycosis is not a major clinical problem, and no treatment is also a legitimate option.

Systemic agents have higher success rates than topical agents in treating onychomycosis and are typically safe but, like all drugs, may have side effects. Patients need to be happy to use a systemic agent with its inherent risks to treat an essentially cosmetic issue.

As an alternative to systemic therapy, superficial white onychomycosis and very mild cases of distal and lateral onychomycosis can be treated with topical agents. These act slowly and have significant failure rates. Patients should be reminded of the need to be persistent and regular in applying topical therapy and also to observe for worsening onychomycosis, at which time an oral agent may be considered.

The pharmacology of therapies for cutaneous fungal infections was discussed in a previous article in the June 2014 issue of *Medicine Today*.[1]

Systemic therapy

The aim of treatment is a normal-looking nail. It is important to recognise that mycological cure is not equivalent to clinical cure. After the traditional three-month course of an oral antifungal agent, mycological cure is possible but the nail may still look abnormal. Patients need to recognise that the nails grow slowly and, even if there is no active infection, the nail plate may take many more months to grow out completely. Patients should be reassured when the proximal portion of the affected nail appears normal and clear of discolouration.

However, in practice, treatment failure is common after the prescribed three-month course. I consider it advisable to continue treatment until the abnormal nail grows out completely. Cost and exposure to the drug can be minimised by a pulsed regimen. A useful technique to monitor for treatment failure is for a line to be scored into the nail plate at the most proximal portion of the visible infection. The line should move distally with the abnormal nail if mycological cure is achieved. If the chard of fungus grows proximal to the scored line then treatment failure is likely.

Terbinafine

Terbinafine is the most effective agent for dermatophyte onychomycosis. The standard dosing regimen for dermatophyte infection is 250 mg/day for six weeks for fingernail onychomycosis and 12 weeks for toenail disease. Multiple studies have shown the efficacy of this regimen, with a short-term mycological cure rate of about 76 to 78%.[2]

Another recommended approach is to 'pulse' the treatment, by giving 250 mg/day for one week every two to three months until the nail grows out. My preference is to administer the drug daily for one week every month, until the nail grows out to become normal.

When to commence therapy is arbitrary. PBS subsidisation is available for terbinafine if 80% of the great toenail is affected and the infection has been mycologically confirmed. Regardless of the extent of disease, I find it more timely and efficient to write a private script for terbinafine, as the relative cost of the medication is not prohibitive, and this avoids the requisite delay for cultures to be performed. Furthermore, culture often gives false-negative results, and repeated testing simply for PBS subsidisation is undesirable.

Itraconazole

Itraconazole is a relatively expensive agent when used for the treatment of onychomycosis. It is useful when:

- terbinafine is contraindicated

- the fungus is resistant to terbinafine, as determined by treatment failure, or
- a nondermatophyte mould is cultured.

Itraconazole is given at a dose of 400 mg/day for one week each month (seven doses each month). For mycological cure of common dermatophyte tinea, two to three pulses are required for fingernails and three to four pulses for toenails. The short-term mycological cure rate is up to 75%.[2] My preference is to pulse the therapy until the nail grows out to become clinically normal.

Itraconazole is fat-soluble and is best absorbed with a low pH environment in the stomach. If patients have relative achlorhydria or cannot take the medication with a main meal then an acidic drink (such as a cola soft drink) is useful in improving absorption. The newest preparation of itraconazole released in Australia had twice the potency, requiring only half the dose to achieve the same efficacy as the pre-existing preparation.

Fluconazole

Fluconazole is another alternative to terbinafine, although the mycological cure rate is much lower at only about 50%.[2] It is given as pulse therapy, with one dose per week for six months for fingernails and nine months for toenails. Doses in the literature range from 150 to 450 mg/day. My preference is to balance cost with effectiveness, using the 200 mg tablets weekly until the nails grow out completely normally.

Griseofulvin

Griseofulvin is the oldest oral antifungal available for onychomycosis. Being fungistatic rather than fungicidal, it is much less effective than terbinafine or the azoles. A dose of 0.5 to 1.0 mg/day is required for adults; 18 months of therapy may be required before complete clinical clearance of onychomycosis. The other agents discussed are more effective for treatment of onychomycosis.

Topical therapy

There are several topical nail kits currently available in Australia. Although easily accessible by patients as over-the-counter preparations, the cure rates from lengthy use of these agents are typically poor, achieving a mycological cure rate of less than 50% and a clinical cure rate of less than 10%. These topical treatments typically require physical preparation of the nail to aid absorption of the active agent, as described below.

- Amorolfine lacquer is used weekly after sanding down the nail with a nail file.
- Bifonazole cream is applied after a week of nail preparation with urea cream to break down the hyperkeratotic nail plate and allow removal by scraping.
- Ciclopirox lacquer is applied directly to the nail surface, daily until cure, with no nail preparation required.
- Miconazole tincture is applied directly to the nail surface until cure.

Topical treatments may be useful for superficial white onychomycosis and very mild subungual onychomycosis but have little role in well-established distal and lateral subungual onychomycosis.

Physical therapies

Occasionally, the thickened or dystrophic nail plate may be removed for cosmesis or pain. Both surgical and chemical means are available, and should be used in conjunction with a systemic agent for effective cure. Referral to a dermatologist with an interest in nails would be useful.

Use of vascular lasers has been in vogue for the treatment of onychomycosis. The initial enthusiasm for this treatment has waned significantly as practitioners and patients found a low and inconsistent clearance rate.[3] The mechanism of action appears to be thermal destruction of the fungal elements. However, patients are typically unable to tolerate the high temperature and duration of treatment required for effective fungicidal effect.

Conclusion

Onychomycosis is an exceedingly common type of fungal infection that is best treated with a systemic agent. Oral terbinafine is the most effective. Clinical cure is best achieved with an intermittent/pulsed regimen until the affected nail has grown out and been replaced completely with a normal nail plate. MT

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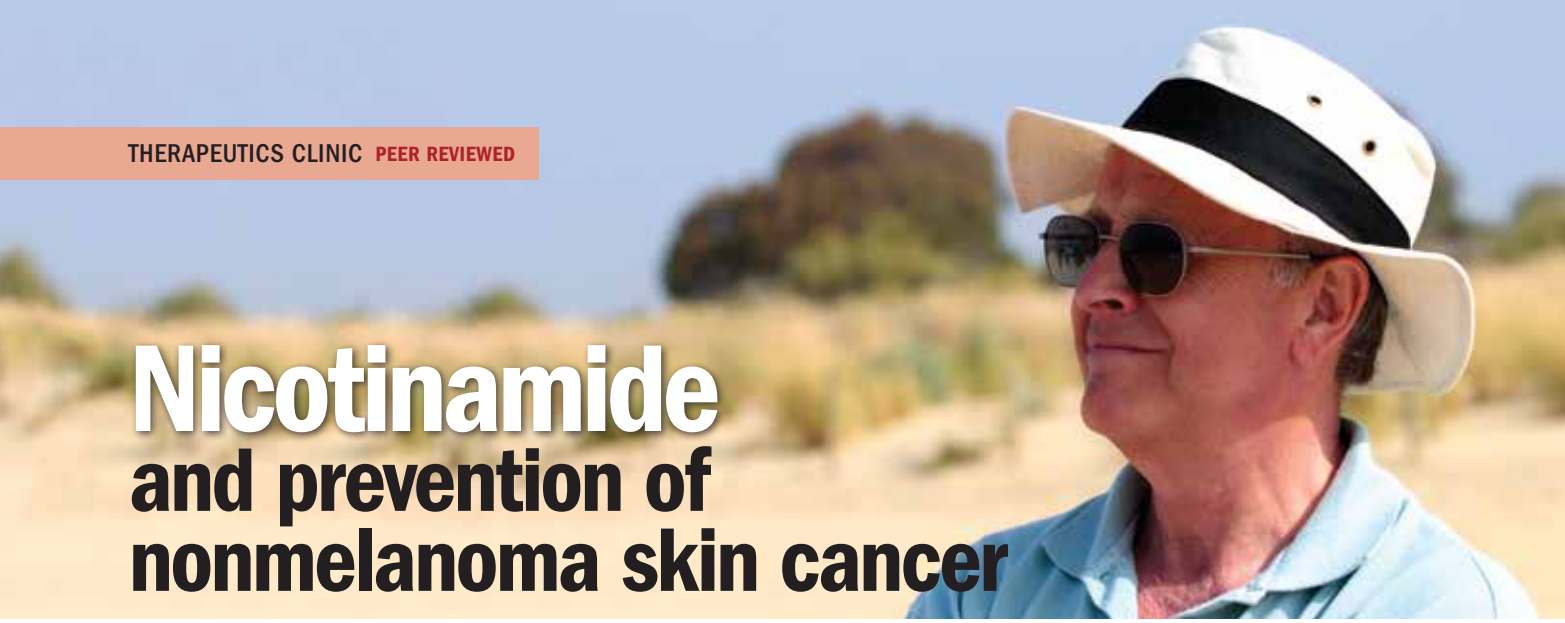
COMPETING INTERESTS: None.



Nicotinamide and prevention of nonmelanoma skin cancer

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ANDREW FREEMAN MB BS

Evidence suggests that nicotinamide supplements can reduce the development of nonmelanoma skin cancer in high-risk patients. It may be a useful adjunct to sun protection for nonmelanoma skin cancer prevention in patients at high risk.

The water-soluble B-group vitamin nicotinamide is central to the function of some of the most important regulatory enzymes involved in DNA repair following exposure to ultraviolet (UV) radiation. Recent trials strongly suggest that nicotinamide supplementation protects against some of the damaging effects of UV exposure.[1,2]

What is nicotinamide?

Nicotinamide is the amide form of vitamin B3 (niacin). It is naturally present in trace amounts in foods such as yeast, meat, fish, nuts, legumes and cremini mushrooms. It is also produced in the body indirectly from tryptophan and directly from niacin. Nicotinamide is readily available in Australia as an inexpensive over-the-counter vitamin supplement.

Nicotinamide has been investigated over the past 50 years for a wide range of therapeutic applications.[3] Current clinical uses of nicotinamide include treatment of autoimmune bullous diseases such as bullous pemphigoid and topical treatment of acne and facial melasma, where it inhibits melanosome transfer.

Role of nicotinamide in skin cancer prevention

UV radiation causes skin cancer via two main mechanisms: DNA damage and UV-induced immunosuppression.[4,5] In Australia, up to 99% of nonmelanoma skin cancers (NMSCs), mainly basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs), can be attributed to UV radiation exposure.[6] UV radiation has a direct damaging effect on DNA.[7] To avoid the risk of genetic mutations, damaged DNA is repaired when possible. When DNA repair is not possible then the cancer-prone cell is cleared by apoptosis. Immune surveillance detects and clears damaged cells that may lead to NMSC. UV-induced immunosuppression increases the risk of damaged cells developing into skin cancer.[4]

Nicotinamide is central to many cellular oxidation–reduction (redox) and non-redox reactions.[2] It is a precursor of the coenzymes nicotinamide adenine dinucleotide (NAD) and NAD phosphate, which function to accept or donate electrons, respectively, in many redox reactions, including catabolism of carbohydrates, fats and proteins and biosynthesis of macromolecules. Apart from its essential role in cellular metabolism and synthesis, nicotinamide is also the sole substrate and an inhibitor of the nuclear enzyme poly-ADP-ribose polymerase 1 (PARP-1). This enzyme is important in DNA repair, stress responses, cell signalling, transcription, regulation, apoptosis, chromatin structure, cell differentiation and the inflammatory response.[8,9] UV damage to DNA leads to PARP activation. Correctly functioning PARP-1 along with sirtuin proteins increases cell resistance to genotoxic insult, which otherwise can lead to mutagenesis and skin cancer formation.[10] UVA also causes an energy crisis in cells, and normalisation of adenosine triphosphate (ATP) with nicotinamide prevents UVA immunosuppression.[11]

Thus, theoretically nicotinamide should be able to aid in skin cancer prevention.

Evidence on nicotinamide and skin cancer

Studies have shown that nicotinamide reduces UV-induced immunosuppression at oral doses of 500 to 1500 mg per day.[12,13] In addition, recent Australian trials have shown that nicotinamide supplementation can reduce numbers of actinic keratoses and the development of NMSC.[1,2]

Actinic keratoses strongly predict a risk of NMSC. Two phase 2 double-blind randomised controlled trials involving 74 people in Sydney found that oral nicotinamide reduced actinic keratoses in patients with sun-damaged skin.[2] At the end of the four-month trials, the number of actinic keratoses was 29% lower among those

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who received nicotinamide 500 mg once daily and 35% lower among those who received nicotinamide 500 mg twice daily than among those who received placebo. The odds of developing at least one skin cancer were significantly lower with nicotinamide treatment, as was the rate of new skin cancers.

More recently, a double-blind randomised controlled trial investigated the effects of oral nicotinamide (500 mg twice daily for 12 months) on the development of new NMSCs in 386 patients in Sydney aged over 18 years who had been diagnosed with at least two NMSCs in the previous five years.[1] Patients diagnosed with invasive melanoma in the previous five years were excluded from the study. Participants had a mean age of 66 years (range 30 to 91 years), and 63% were men. At enrolment, they had been diagnosed with a mean of eight NMSCs in the previous five years (range 0 to 61) and had a mean of 47 actinic keratoses (range 0 to 214). Almost half had used sunscreen in the previous week.

The study found that after 12 months of therapy, the rate of new NMSCs was 23% lower in the nicotinamide group compared with the placebo group (mean of 1.8 *vs* 2.4 NMSCs per person). The rate of new BCCs was reduced by 20% ($p = 0.12$), and the rate of new SCCs was reduced by 30% ($p = 0.05$). The number of actinic keratoses was 13% lower at 12 months ($p = 0.001$). There were no significant differences between placebo and nicotinamide in the number or types of adverse events. There was no evidence of continuing benefit after nicotinamide was discontinued. The authors concluded that oral nicotinamide is safe and effective in reducing the rates of NMSCs and actinic keratoses in high-risk patients.[1]

Tolerability

Nicotinamide has been used at pharmacological doses up to 3 g per day for more than 50 years.[3] Repeated studies have demonstrated its tolerability, with a reported low incidence of side effects. Nausea and gastrointestinal side effects have been reported at doses higher than 3 g per day.[14] At very high doses, reversible hepatotoxicity has been reported in animals and humans.[3] Unlike nicotinic acid and niacin, nicotinamide is not a vasodilator, and therefore flushing is unlikely to occur.

How does nicotinamide fit into NMSC prevention strategies?

Oral nicotinamide supplementation can be proposed as an adjunct to other skin cancer prevention measures in patients who have current evidence of sun damage, either previous NMSC or actinic keratoses. There is no evidence of benefit for patients without a significant history of skin cancer. Chemoprevention with nicotinamide does not reduce the need for ongoing sun protection, sunscreen use and skin surveillance for high-risk patients.

Nicotinamide supplementation to prevent skin cancer should not be recommended for children because there is no evidence of its effectiveness in this age group. There is also a risk that its use might encourage sun overexposure in the belief they are protected. This is the same rationale underlying the limitation on sunscreen labelling to a maximum sun protection factor of 'SPF 50+'.

Other agents currently prescribed for skin cancer prevention include oral retinoids such as acitretin, used especially in patients who have undergone transplantation. However, the effectiveness of this expensive agent tends to wane over time, and its long-term use is associated with significant side effects.

Further studies on nicotinamide are needed, especially to ensure that the reductions in NMSC continue with long-term treatment. Investigation of any effect on melanoma incidence would be a priority for the Australian population.

Conclusion

Recent evidence suggests that nicotinamide at a dose of 500 mg twice daily reduces NMSC incidence by up to 23% in patients with previous NMSC. Nicotinamide appears to have a good safety profile with minimal side effects. It seems reasonable to recommend nicotinamide for motivated patients at high-risk of NMSC as an adjunct to ongoing sun protection, sunscreen use and regular skin checks. There is no evidence of benefit for patients without a significant history of skin cancer and no evidence to recommend this treatment in children. MT

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