4 Inflammatory skin diseases

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INTRODUCTION

The diagnosis and management of patients with inflammatory skin disease remains a very challenging and rewarding aspect of 'core' dermatology practice. Thorough history taking and examination, sometimes aided by histopathology, remain at the heart of good management. Skills in the management of chronic disease need to be developed, such as the ability to communicate risk/benefit of different therapy strategies and reach joint decisions with patients. You should try to understand the impact of the disease on the patients' lives.

It is important to become familiar with current published national guidelines in the UK, published by the British Association of Dermatologists (website http://www.bad.org.uk). New topical and systemic therapies are being developed and marketed specifically for psoriasis; remember to take an appropriate cautious approach to new therapies. Over the last 30 years many new drugs have been introduced with much optimism and marketed extensively only to be dropped because of poor effectiveness or side effects; you need to take a long term perspective with your patients who have long term disease.

PSORIASIS

Epidemiology

Two percent of the World's population suffer from psoriasis vulgaris. Countries further from the equator have higher prevalence rates (Northern Europe and North America — up to 4.8%; Africa and Asia — < 1%). Psoriasis can first appear from infancy to the eighth decade, and there is a bimodal onset peak.

- Late teens/early 20s — Often more severe, and with a positive family history.
- 50–60 years.

It affects males and females equally, but onset is often earlier in females.

Aetiology

Psoriasis is thought to arise from an environmental trigger, on top of a genetic susceptibility.

Genetic susceptibility

In psoriasis, the genetics are complex and polygenic. Evidence for genetic factors has been formed from family and twin studies, showing increased concordance in both dizygotic and monozygotic twins. Much work has been done on HLA linkage and genetic loci.

The most important identified so far are:

- HLA Cw6 — strongest association with severe disease of early onset.
- PSORS1 gene (chromosome 6p21.3).

Environmental triggers

- Trauma: Koebner phenomenon — occurrence of psoriasis in an area of trauma or a scar. (Box 4.1 and Figure 4.1)
- Infection: Streptococcal throat infection has a strong association with acute guttate psoriasis (Figure 4.1), and also an important association with chronic plaque psoriasis. HIV infection can make psoriasis worse. This is paradoxical and unexplained — one would expect a T-cell mediated disease such as psoriasis to improve with T-cell depletion.

Box 4.1: Skin conditions which commonly display Koebner phenomenon

- Psoriasis
- Lichen planus
- Viral warts
- Vitiligo

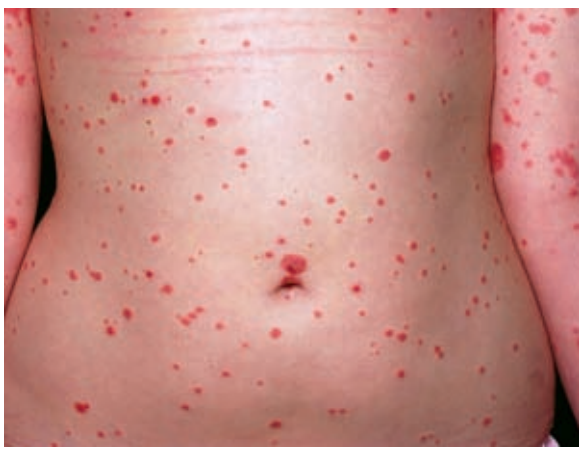


Figure 4.1
Guttate psoriasis. Note the small widespread scaly plaques on arms and torso. Also note the 'Koebner phenomenon' — psoriasis plaques at the umbilicus due to the trauma of 'belly button' piercing.

- Drugs: Some drugs can precipitate or worsen psoriasis (Box 4.2).
- Sunlight: Most patients' psoriasis improves in the sun, but some (about 10%) get worse.
- Metabolic: Pregnancy generally improves psoriasis, but it can worsen post-partum. Generalized pustular psoriasis can be triggered post-partum, or by hypocalcaemia.
- Stress: There is strong evidence that stress can exacerbate psoriasis. Patients with high levels of worry respond less well to therapy.
- Alcohol: Heavy consumption can worsen existing disease.
- Smoking: There is a strong link between smoking and palmoplantar pustular psoriasis, particularly in females.

Pathogenesis

The three main features are:

1. Epidermal proliferation and loss of differentiation — clinically causing scaling and thickening.
2. Dilatation and proliferation of dermal blood vessels — clinically causing erythema.
3. Accumulation of inflammatory cells, mainly neutrophils and T-lymphocytes.

The T-lymphocyte

Psoriasis is a T-cell mediated disease. Th1 helper cells predominate, which, when activated, secrete TNF-α, IL-3, IL-6, GM-CSF and IFN-γ.

TNF-α is the most important and has direct therapy relevance (Table 4.1). IL-8 and IL-10 may have future direct therapy relevance.

Clinical features of chronic plaque psoriasis

- Sharply demarcated, erythematous, papulosquamous plaques occur, mainly on the extensor surfaces (Figure 4.2). They can vary in size from < 1 mm to > 20 cm, and are covered in silvery-white scale, which, when scratched off, may cause pinpoint bleeding. This is known as the 'Auspitz sign', which is *not* recommended to be used. When covered with emollient the plaques will instantly appear more red.
- Erythema at the edge of the plaque indicates active psoriasis, and is useful to assess response to therapy. Post-inflammatory hypo- or hyperpigmentation can occur.

Box 4.2: Drugs which can precipitate or worsen psoriasis

- Lithium
- Beta-blockers
- Withdrawal of corticosteroids
- Non-steroidal anti-inflammatory drugs
- Antimalarials
- ACE inhibitors

Table 4.1: Management of psoriasis

Therapy	Top tips
Bath additives/soap substitutes/emollients	All essential. See Table 4.3 for further details
Topical vitamin D analogues	First line treatment. Can use in combination with topical steroids for limited periods. Some preparations can irritate sensitive areas of skin
Topical corticosteroids	Often first choice for sensitive areas of skin. Potent steroid use or withdrawal can lead to a rebound flare of psoriasis, or transformation to generalized pustular psoriasis
Topical coal tar	Some preparations are messy and smelly. Particularly good for small plaque/guttate psoriasis (apply to all of skin) or scalp
Topical dithranol (anthralin)	Works well on thick plaques. Started at a low concentration and built up. Apply to plaques only. Can irritate surrounding skin. Causes staining of skin
UVB	Main complications burning and skin cancer risk. Patient consent required before commencing. Starting dose determined by Minimum Erythema Dose. Maximum permitted lifetime dose
PUVA	Psoralen can be oral or topical (bath, gel, paint). If taking oral preparation need to protect eyes from UVA for 24 hours (UVA opaque glasses)
Systemics: acitretin methotrexate ciclosporin mycophenolate mofetil	See Chapter 7
The 'biologics'	These are antibodies or receptor blockers to TNF-α. All require intravenous or subcutaneous administration, and multiple doses. The main problems are increased risk of infections, particularly reactivation of tuberculosis, antibody formation, and the expense of the drug. See Chapter 7

Diagnosis

The diagnosis of psoriasis is usually straightforward, but confusion can arise in flexural psoriasis, scalp psoriasis and palmoplantar psoriasis.

Flexural psoriasis

There are some patients who present with indistinct inflammatory lesions in the flexural areas who have inflamed skin at some typical psoriatic sites (always check for psoriasis at the umbilicus in this case), but who also have involvement at sites typical of seborrhoeic dermatitis. The groin area, vulva, axilla, submammary cleft and gluteal cleft can be affected, again with minimal scale, also causing some diagnostic confusion with intertrigo (the two can co-exist). This so-called 'sebo-psoriasis' may need to be treated with a combination of topical antifungals, topical steroids and then standard psoriasis therapies. Do not be worried if this presentation leaves you feeling not sure of the diagnosis — it can be very difficult. A biopsy is usually not helpful as mixed inflammatory features are seen.

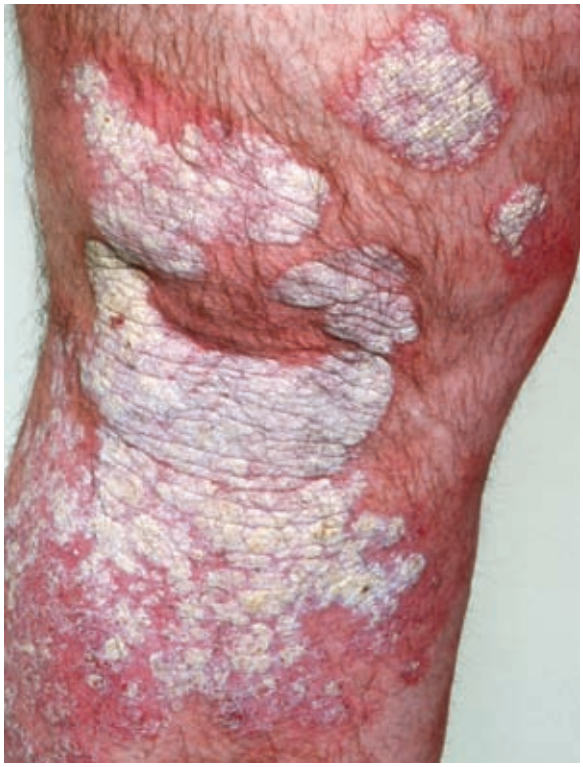


Figure 4.2
Chronic plaque psoriasis. Note the thickened plaque on the knee topped with heavy scaling.

Scalp psoriasis

Scalp psoriasis is usually easy to diagnose; there are typical lesions elsewhere and the lesions are very clearly defined. Plaques on the scalp can develop severe adherent scaling, termed pityriasis amiantacea. Hair growth is usually normal unless severely affected. Occasionally you will see patients misdiagnosed as having scalp psoriasis, even though they have the typical diffuse changes of seborrhoeic dermatitis and no evidence of psoriasis elsewhere. Remember the value of topical antifungals in this setting. Generally, topical coal tar preparations or corticosteroid preparations are used for this condition.

Palmoplantar pustular psoriasis (Figure 4.3)

Psoriasis of the palms or soles can sometimes be difficult to differentiate from chronic eczema. Look carefully for vesicles — these clear sago-like small blebs are diagnostic of eczema. A mixture of large fresh yellow and older brown pustules are typical of palmoplantar pustular psoriasis, but in eczema, vesicles can sometimes get infected, also producing pustules, but no typical burnt-out older brown areas. This is a difficult condition to treat, and potent topical corticosteroids, localized PUVA, or oral retinoids are standard treatments for this condition.

Assessment of disease severity

The reality of most consultations with psoriasis patients is that severity is based on the patient's and clinician's overall view as to whether the disease is getting better or worse.

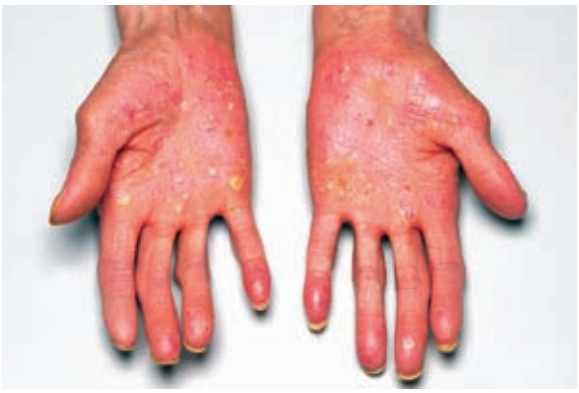


Figure 4.3
Palmar pustular psoriasis. Note the different colours of the pustules indicating different maturity of lesions.

You should, however, know about some basic ways to assess psoriasis severity: these include body surface area estimation (BSA), the PASI (psoriasis area and severity index) scoring system[1] and methods to measure the impact of psoriasis on life quality, e.g. the psoriasis disability index (PDI)[2] or the DLQI (dermatology life quality index).[3]

Body surface area estimation

Use the handprint method. The area of the full palmar aspect of one hand, including the palm and the five digits, is approximately equal to 1% body surface area. It is possible to very quickly estimate BSA by this method, imagining roughly how smaller areas would coalesce into one handprint.

PASI

In this method, an estimate of the severity of redness, scaling and thickness is made in each of the four areas: head, upper limbs, trunk and lower limbs. An estimate of the area involved within each of these areas is also made and the results calculated in a formula, resulting in a score from 0 (no involvement) to 72 (worst possible involvement). A summary of the PASI formula is given in Table 4.2.

DLQI

This is a simple 10 question standard validated questionnaire which can be used across all skin diseases, including psoriasis, to measure the adverse impact of the disease on the patient's life. It takes about 2 minutes to complete and gives a score from 0 (no impact) to 30 (maximum possible impact). The score can be easily interpreted thus: 0–1 = no impact, 2–5 = slight impact, 6–10 = moderate impact, 11–20 = very great impact, 21–30 = extremely great impact. More information is available on www.dlqi.com, or www.dermatology.org.uk.[4]

We have suggested that current severe psoriasis can be defined by the Rule of Tens: BSA > 10% *or* PASI > 10 *or* DLQI > 10.

Variants of psoriasis

Ten percent of all psoriasis sufferers have a variant of the condition.

Pustular psoriasis

Sheets of small, sterile pustules can appear in plaques of otherwise normal-appearing skin. When generalized, the patient can be systemically unwell, and this represents a dermatological emergency. This can appear post-partum, with hypocalcaemia, as a rebound to withdrawal of topical or systemic steroids, or following infection. Oral methotrexate is often the first line treatment for control of this condition.

Nail psoriasis

Nail changes are seen in 25–50% of psoriasis sufferers (Figure 4.4). These include pitting, ridging and discoloration of the nail, subungual hyperkeratosis, onycholysis and a circular 'oil spot' appearance (due to hyperkeratosis of the nail bed).

Table 4.2: Formula for calculation of PASI score

Score	0	1	2	3	4	5	6
Erythema Induration Scaling	none	slight	moderate	severe	very severe		
Area %	0	1–9	10–29	30–49	50–69	70–89	90–100

	Head (H)	Upper limbs (U)	Trunk (T)	Lower limbs (L)
Erythema (E)	–	–	–	–
Induration (I)	–	–	–	–
Scaling (S)	–	–	–	–
Sum = E + I + S =	__	__	__	__
Area	_	_	_	_
Sum × Area =	__	__	__	__
	× 0.1	× 0.2	× 0.3	× 0.4
Total =	__._	__._	__._	__._

PASI score = Total (H) + Total (T) + Total (U) + Total (L) = __._

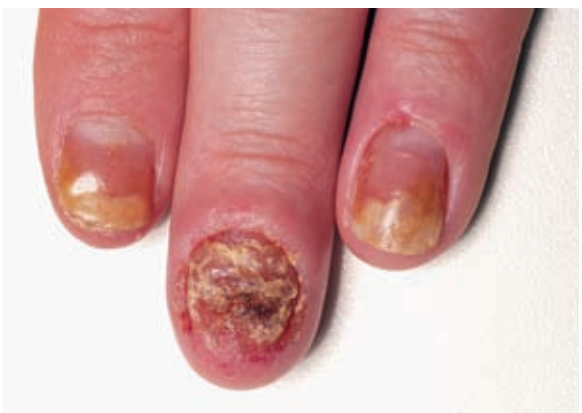


Figure 4.4
Psoriasis of nails. Note the onycholysis and nail pitting.

Acrodermatitis of Hallopeau

There are painful pustules on the tips of the fingers and under the nail bed, often with shedding of the nail plate.

Psoriatic arthritis

It is reported that 5–30% of patients with psoriasis also suffer from a form of arthritis. This can be:

- Mono/asymmetrical arthritis.
- Distal interphalangeal joint involvement — associated with nail involvement.
- Rheumatoid arthritis-like pattern.
- Arthritis mutilans.
- Spondylitis/sacroiliitis — increased in HLA B27 haplotypes.

Management of chronic plaque psoriasis

All dermatology textbooks list the various options for treating psoriasis, but few address the reality of the decision-making process. This is a complicated matter involving education of and negotiation with the patient. Flow charts are usually inadequate to describe the process, which is heavily influenced by the individual patient's previous experience of different therapies, their attitudes towards risk, the practicalities of using topical therapy and the current impact that the disease is having on the patient's life.

Table 4.1 shows the main topical and systemic treatments used for this condition. Management of psoriasis variants is covered under the individual sections. The Psoriasis Association is a useful point of contact and information for patients.[5]

ECZEMA

Eczema, or dermatitis (these are interchangeable terms), is an inflammatory skin reaction, featuring itching, redness, scaling and clustered papulovesicles. Eczema can be endogenous (from within the body) or exogenous (from an external trigger). Boxes 4.3 and 4.4 show the main subtypes of this.

ATOPIC DERMATITIS

Epidemiology

Atopic dermatitis has a prevalence of 10–20%, the highest prevalence being in the most developed Westernized countries. Immigrant populations, e.g. black Afro-Caribbean children residing in London, have twice the prevalence of atopic eczema of their Caucasian

counterparts. Ninety percent of cases begin before the age of 5 years. The prevalence of atopic diseases in general, and atopic eczema in particular, has been increasing over the last four decades.

Diagnosis

This is made according to the UK Working Party's refinement of Hanifin and Rajka's diagnostic criteria for atopic dermatitis (Box 4.5).[6] Unlike most disease criteria, this set has been validated.

Aetiology

Atopic eczema is thought to arise from an interaction of genetic and environmental factors.

Box 4.3: Types/causes of exogenous eczema

- Irritant contact dermatitis
- Allergic contact dermatitis
- Photoallergic/photoaggravated dermatitis
- Infective (secondary to bacterial/viral/fungal infection)
- Post-traumatic (rare, and NOT Koebner phenomenon)

Box 4.4: Types of endogenous eczema

- Atopic dermatitis
- Seborrhoeic dermatitis
- Asteatotic eczema
- Discoid eczema
- Hand eczema
- Gravitational/varicose eczema
- Eczematous drug eruptions
- Lichen simplex

Box 4.5: Criteria for diagnosis of atopic dermatitis[6]

The child must have an itchy skin condition (or parental report of scratching or rubbing in a child).

Plus three or more of the following:

1. Onset below age 2 years (not used if child is under 4 years)
2. History of skin crease involvement (including cheeks in children under 10 years)
3. History of generally dry skin
4. Personal history of other atopic disease (or history of any atopic disease in a first degree relative in children under 4 years)
5. Visible flexural dermatitis (or dermatitis of cheeks/forehead and outer limbs in children under 4 years)

Genetic and intrauterine factors

Parental (particularly maternal) history of atopy is one of the strongest risk factors for the development of atopy. Also, a higher birth weight correlates with increasing prevalence of atopic eczema.

Environmental factors

- *Pollution* — indoor (e.g. cigarette smoke) and outdoor (e.g. industrial) pollutants may increase the prevalence of atopic eczema.
- *The hygiene hypothesis* — children from large families, and those living in the developing world, have lower prevalence of atopic eczema. This may be due to early exposure to microbes, particularly those causing faeco-oral infection, thus driving the immune system to a protective response.
- *The home environment* — in moderate to severe eczema, reduction of house dust mite levels in the home may be of benefit. The main advice to give would be:
  - Frequent vacuuming of carpets or avoidance of carpets if possible.
  - Frequent dusting and ventilation of bedroom, and vacuuming of mattress every week.
  - Covering bedding with dust tight mattress and pillow covers.
  - Frequent washing of soft toys, or putting them in the freezer for 24 hours.

Other points of advice for the home would be:

- Avoidance of animal dander.
- Wearing of cotton clothes rather than wool.
- Washing clothes in non-fragranced, non-bio detergents, at higher temperatures (> 50°C).

Food

Food allergy can potentially aggravate atopic eczema in children less than one year old. Over the age of one its role is much less clear, and more unlikely. The best advice, if parents insist on following the dietary route, is to eliminate a certain food from the diet, singly, for 6 weeks only, to determine the effect of its avoidance (in the case of milk avoidance ensure other sources of calcium are given). The involvement of a dietician may be helpful to advise on safe and appropriate dietary manipulation. RAST (radioallergosorbent test) blood tests are available to diagnose food allergy, but the relationship between these antibodies in the blood and the effect on the skin is not predictable, thus the test is not a reliable basis for practical advice, and is best avoided.

Immunology

Patients with eczema have dry skin, with disruption of the epidermal barrier, increased transepidermal water loss, and increased entry of environmental allergens, so inducing the Th2-dominant immune response.

The Th1/Th2 response

T-helper cells, in their development, differentiate into Th1 cells (secrete cytokines IL-2 and IFN-α), or Th2 cells (secrete cytokines IL-4, IL-5 and IL-13). Which helper cell they

become depends on what signals they receive externally. In eczema, Th2 cells are mainly produced, secreting IL-4, and IL-5, which stimulate B-cells to produce more IgE, the main immunoglobulin involved in the pathogenesis of atopic disease.

Clinical features (Figure 4.5)

These include:

- Itching.
- Dry skin.
- Erythematous macules, papules or papulovesicles.
- Crusting.
- Excoriation and lichenification.
- Secondary infection.

Distribution

This often varies with age.

Infantile — usually most severe on the face (especially if excessive drooling is present). When crawling, extensor surfaces can become rubbed and affected by eczema.

Childhood (from 18 months to 2 years) — mainly affecting elbow and knee flexures, neck, wrists and ankles. The neck can show fine pigmentation, a 'dirty neck'. In Asian or Black skin, extensor distribution of the eczema is more common.

Adult — the eczema has a similar distribution to that of children, often with lichenified areas.

The course of atopic eczema

In 90% of affected children, the eczema starts before the age of 5 years. It tends to run a course of remissions and exacerbations. There is a general tendency towards spontaneous improvement throughout childhood. Clearance occurs in 50% by the age of 13 years. Severe persistent adult atopic eczema is seen, but is much less common than childhood eczema.

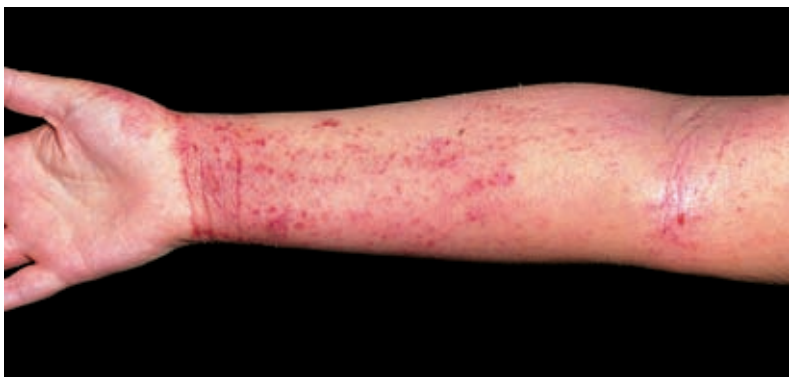


Figure 4.5
Atopic eczema. Note the flexural erythema, lichenification and secondary infection of the skin.

Complications

Bacterial infection: this is secondary, and is often streptococcal or staphylococcal, mainly *Staphylococcus aureus*.

Viral infection:

a) secondary infection with herpes simplex virus can cause 'eczema herpeticum' (Figures 4.6 and 4.7). This is a *dermatological emergency*. There is sudden onset of numerous painful small fluid-filled vesicles. This can become secondarily impetiginized, can cause systemic upset, and can also affect the conjunctivae. Systemic antivirals are indicated (oral is usually adequate), and topical corticosteroids or immunosuppressants should be stopped;

b) there is increased spread of viral warts and molluscum contagiosum. However, varicella zoster virus affects eczema sufferers in the same way as it would those with normal skin.

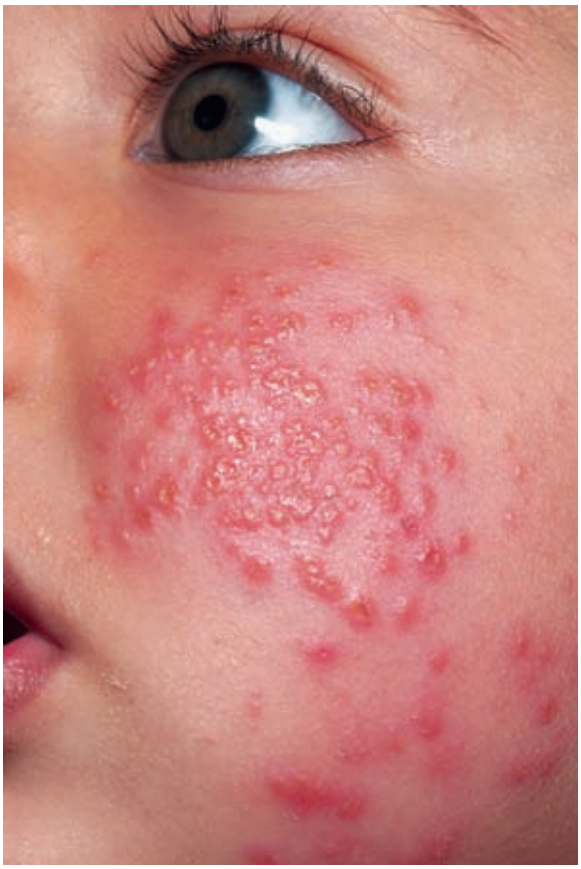


Figure 4.6
Eczema herpeticum (early). Note the tiny numerous fluid-filled blisters on the cheek.

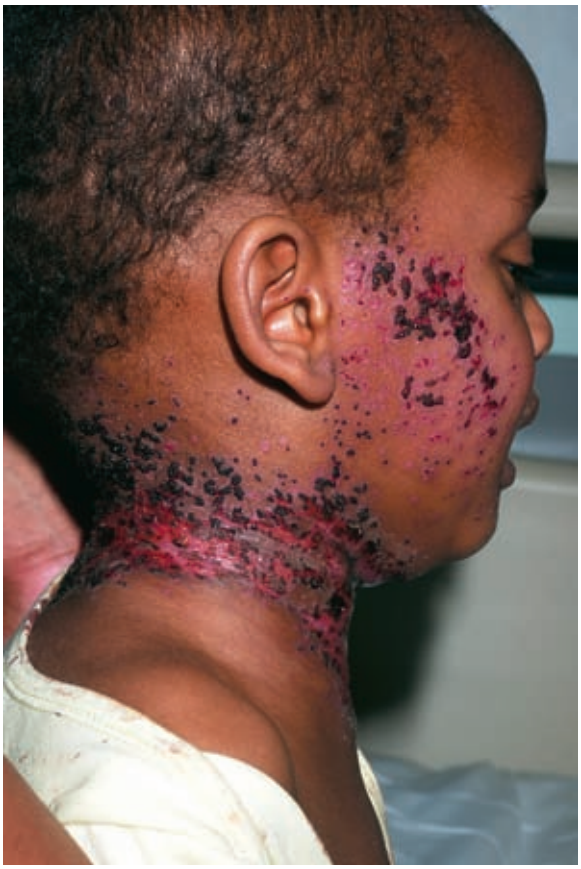


Figure 4.7
Eczema herpeticum (late). No blisters remain but there are tiny discrete erosions and secondary bacterial infection and crusting on the cheek and neck.

Ocular abnormalities: These include conjunctival irritation, keratoconus (a conical cornea leading to marked visual disturbance which is rare), and cataract (mainly if severe facial eczema, or use of strong topical or systemic corticosteroids).

Measurement of severity of eczema

This can be measured physically, for example, by the Eczema Assessment and Severity Index[7] or SCORAD.[8] It is also important to ask about the effect of eczema on quality of life, either with specific measures, such as the Dermatology Life Quality Index[3,4] or Children's Dermatology Life Quality Index,[4,9] or by general enquiry about itch, sleep loss, and loss of time at work. In children, their growth and progress at school should be particularly noted. All of these factors should influence decisions regarding management.

Treatment

As with any chronic inflammatory condition of the skin, time should be taken to develop a good relationship between the dermatologist and the patient, particularly in increasing understanding about the nature and course of the disease. Management should be based on a specific overall regimen, including bath additives, soap substitutes, emollients, and topical steroids or topical immunosuppressants.

This maintenance regimen should be *written down* for the patient. A second regimen specifically for flare-ups should also be *written down* for them, also specifying when they can go back to their usual treatments. Quantity of topical treatments required should be discussed and, if possible, demonstrated during the consultation. Treatment concordance is the biggest problem to tackle, and any reluctance to use the prescribed medication should be discussed (e.g. treatments which sting, fear about side effects of topical steroids, reluctance to ask GP for repeat prescriptions). This all takes time but is well worth it in the long term. Always inform the patient or parents about the National Eczema Society which is an excellent source of information.[10]

A summary of specific treatments is included in Table 4.3.

My patient is not improving with conventional eczema treatment

If eczema fails to improve with correct treatment, or worsens, the following should be considered:

Is the diagnosis correct?

Other differential diagnoses

- Scabies: Always look for scabies burrows, particularly on the finger webs, abdomen and genital area.
- Seborrhoeic dermatitis: This mainly affects the scalp, eyebrows and creases on the face. Greasy scales are clinically visible.

Table 4.3: Management of atopic dermatitis

Therapy	Top tips
Bath and shower additives	All patients should have one of these and be advised to avoid soaps, bubble bath and shower gels. Some contain antiseptic, important if the patient has recurrent infections. Care must be taken as some make the bath or shower very slippery.
Soap substitutes	Most emollients can also be used as soap substitutes.
Emollients	These are essential and should be applied liberally. They vary in intensity. Stick with one that the patient likes and tolerates, and is willing to use, to improve concordance.
Topical corticosteroids	These come in a range of potencies, and a 'step-up' and 'step-down' regimen can be used according to severity of eczema. More potent corticosteroids should be used for palms and soles, and less potent drugs for the face and neck. Some contain antibiotics and/or antifungals. These are useful in flexural areas, but antibiotic resistance can develop.
Topical immunomodulators Tacrolimus Pimecrolimus	These are steroid sparing, so useful particularly on the face or neck, or where the patient required potent topical steroids for long periods. These should be applied intermittently, beginning at the first signs of a new flare. They may feel 'burning' for the first few days of application. Due to lack of long term data on skin cancer risk, sun protection information should be given for patients specifically on these drugs.
UVB	As for Table 4.1.
Systemic treatments: Ciclosporin Azathioprine	See Chapter 7.

Is there an element of irritant contact dermatitis?

Atopic dermatitis patients are more prone to this, particularly on the hands.

Is there an allergic contact dermatitis?

Eczema in localized sites, e.g. the face or hands, or eczema which is unresponsive or worsening, may indicate an allergic contact dermatitis. Patients with atopic dermatitis are more prone to contact allergy. Also they are more likely to become sensitized to fragrances, topical steroids or preservatives in their treatments. Patch testing is indicated if this is suspected (see Chapter 6).

ACNE

Acne is a chronic inflammatory disorder of the pilosebaceous units. A pilosebaceous unit consists of a hair follicle, erector pili muscle, sebaceous gland, and associated apocrine and eccrine sweat glands.

Epidemiology of acne

Acne usually starts in adolescence and mainly resolves by the mid-twenties, although 10–20% of cases persist into adulthood, particularly females. Almost half of male and female adolescents develop acne to varying degrees, 10% of whom have severe acne. The peak prevalence is 14–16 years for females, and 16–19 years in males, reflecting earlier onset of puberty in females.

What if my patient has atypical features?

In patients who present at a younger age, or have more severe, refractory acne, the following should be considered and investigated as necessary:

- Precocious puberty.
- Polycystic ovarian syndrome.
- Hyperandrogenism.
- Hypercortisolism (including Cushing's syndrome).
- XYY chromosomal phenotype.

Acne can have some additional external causes which should be considered and enquired about in patients with atypical or refractory acne:

- Premenstrual flaring of acne: This type of acne responds best to hormonal modulation (see Table 4.4).
- Occupation: Patients dealing with heavy-duty oils and crude tars in their work are more susceptible. Those working with chlorinated hydrocarbons, if accidentally released, may develop chloracne which is relatively resistant to treatment and may take several years to resolve.
- Physical factors: Certain cosmetics, particularly those with an oily base, are comedogenic. Pomades, which are used to defrizz curly Afro-Caribbean hair, also have a comedogenic effect.
- Drugs: The commonest acne-inducing drugs are anabolic steroids, corticosteroids, phenytoin, lithium, isoniazid and iodides. It is important to ask about prescription and non-prescription drugs.

Pathogenesis

Acne appears to occur due to:

- Increased sebum production: this is mainly dependent on androgenic sex hormones of gonadal or adrenal origin.
- Genetically inherited distribution of sebaceous glands: increased numbers and size of glands appear to have a strong familial tendency, particularly in severe acne. Genetics are thought to be multifactorial.
- Hypercornification of the pilosebaceous duct, forming micro-comedones: comedones are due to abnormalities in proliferation and differentiation of ductal keratinocytes. Several

Table 4.4: Management of acne

Therapy	Top tips
Topical benzoyl peroxide Topical azelaic acid	All topical treatments for acne can irritate or dry the skin. Benzoyl peroxide can bleach clothes/bedclothes. Antimicrobial.
Topical retinoids	For oily skin, gels are often better to dry the skin. Topical retinoids contraindicated in pregnancy. Anticomedonal.
Topical antibiotics in combination with benzoyl peroxide/zinc	Some preparations can glow under ultraviolet strobe lights. Antibiotic resistance can occur.
Oral antibiotics Tetracyclines	At least 6 months of treatment should be given. Contraindicated in pregnancy and young children. Minocycline can cause blue-black pigmentation, more likely if higher dose for long duration of therapy; also avoid if history/family history of SLE as can cause a lupus-like syndrome.
Erythromycin Trimethoprim	Dose 500 mg BD. High dose 300 mg BD as second line treatment.
Hormonal treatments Cyproterone acetate Spironolactone	 Oral contraceptive, suppresses sebum production. Particularly useful for premenstrual flare of acne, or for acne related to polycystic ovarian syndrome.
Isotretinoin	Most common side effects are dryness of lips, skin and mucous membranes. Hair thinning and nosebleeds are also not uncommon. Depression and suicide risk is still unclear — ask about personal or family history of depression before starting treatment.
Blue light/blue-red light treatments	Small trials have shown moderate improvement.
Laser treatment	Small trials have shown moderate improvement with NLite laser treatment. This is not usually available on the NHS, and is contraindicated in patients on photosensitizing drugs, or on isotretinoin, due to risk of scarring.
Physical treatments Cryotherapy Intralesional triamcinolone Cautery	 This can be used for old acne nodules. This can be helpful for acne keloid scars, and for early acne nodules. Closed comedones respond well to this.
Treatments of acne scarring	These are usually not available on the NHS. They comprise of: Excision of scars Dermabrasion Laser resurfacing Chemical peeling Collagen injection

factors are involved in this, including sebaceous lipid composition, bacteria, local cytokine production and androgens.

- Abnormality of microbial flora, especially *Propionibacterium acnes*: patients with acne have more *P. acnes* on their skin, but levels do not correspond to clinical severity. The bacteria may induce inflammation.
- Production of inflammation: this is partly due to duct rupture, bacterial colonization and hormonal factors.

Clinical features (Figures 4.8 and 4.9)

The main features are:

- Seborrhoea.
- Open and closed comedones — 'blackheads' and 'whiteheads'.
- Erythematous papules.
- Nodules.
- Deep pustules.
- Pseudocysts.
- Scarring.

How to assess the severity of acne

Acne should be assessed both in physical terms, and in terms of its effect on the individual, in order to decide on the best management options for the patient. The most frequently used measure of physical severity for research purposes is the Leeds acne grading system.[11]

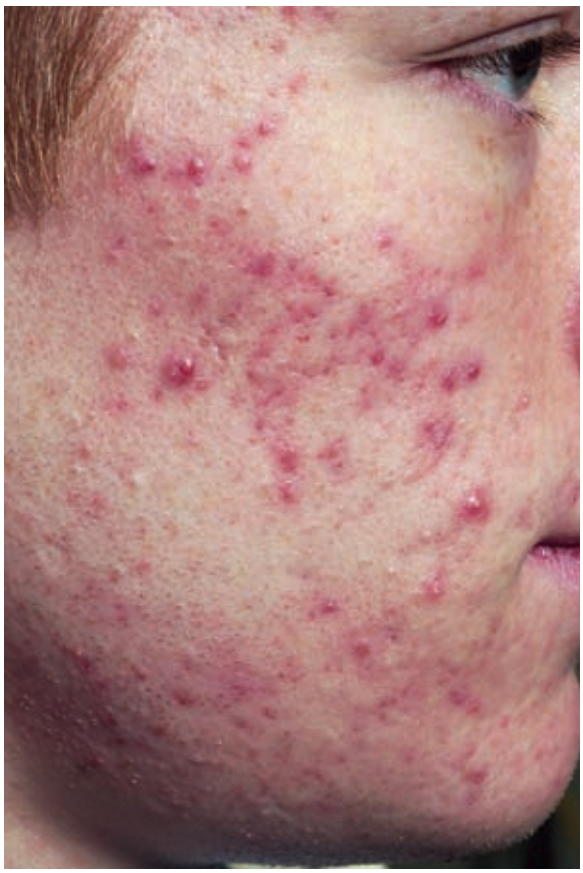


Figure 4.8
Moderate/severe acne. Note the papules, pustules, comedones and mild scarring on the cheek.

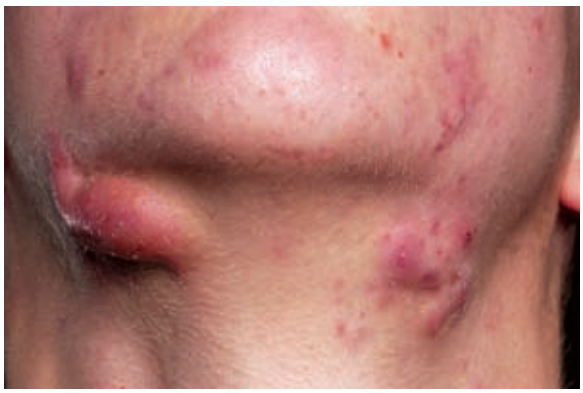


Figure 4.9
Severe nodulocystic acne. Note the open and closed comedones, cysts and keloid scarring under the chin (this should not be surgically excised).

However, this scale was developed before the introduction of isotretinoin and is biased towards extremely severe acne. It is useful to have a descriptive record of areas involved and presence/absence of cysts/scars/pustules/papules.

The psychological and social effects of acne cannot be underestimated. Often it comes on in adolescence, a time where embarrassment and lack of confidence are highest. Social contact may become limited, bullying may occur at school, and it may even have an effect on employment prospects. It is important to have some of idea of what the patient is going through, even in an outpatient consultation. More formal measures of quality of life can be used, such as the Dermatology Life Quality Index,[3,4] or an acne specific measure such as the Cardiff Acne Disability Index or the Acne Quality of Life Scale.[4]

Differential diagnosis

The main alternative diagnoses to consider would be:

- Rosacea. Typically, there are *no comedones* in rosacea.
- Perioral dermatitis. There is often a history of topical steroid use in the perioral area.
- Folliculitis. Gram-negative organisms, *Pityrosporum* and *Demodex* mite can cause a folliculitis, which may present as acne refractory to treatment. A trial of topical antibiotic, anti-yeast preparation, or permethrin, can help to differentiate between these.

Management

When managing a patient with acne, it is firstly important to address any misconceptions about what has caused it, for example:

- Diet: Many patients still believe that eating fats or chocolate can cause acne. There is no convincing evidence to suggest that diet plays any part in acne development.
- Lack of hygiene: Again, patients believe that 'blackheads' are due to dirt, and use abrasive or irritating preparations to cleanse their skin excessively. It is important to explain that the 'black' in a 'blackhead' is pigment, not dirt, and that excessive cleansing of the skin with these chemicals can make acne worse, as well as irritating the skin, causing dryness and soreness. A bland, non-irritating preparation, or just water, should be used to wash the skin.
- Make-up: As mentioned previously, there is some truth that greasy make-ups can cause acne. It is important to recommend a non-comedogenic formulation of make-up, and also recommend that it is completely removed before going to sleep at night. It is unrealistic to expect adolescent girls to go without make-up so a compromise should be reached on this.

Table 4.4 outlines the specific treatments used for acne.

How to treat a patient safely with isotretinoin

Isotretinoin is a very effective drug for severe, scarring, or non-responsive acne. However, it has many side effects, some of which are serious, and the benefits and risks of this treatment should be carefully weighed up before commencing the course. The following section describes current guidelines for the use of isotretinoin, but always consult the British Association of Dermatologists website for the most up-to-date guidelines.[12]

At first consultation, a written Medicines and Healthcare products Regulatory Agency (MHRA) approved patient information booklet should be given to the patient, and the main side effects (particularly the possible link with depression), indications and course of treatment discussed. It is useful to record any personal or family history of depression at this stage. Isotretinoin is *teratogenic* and any female considered for treatment with this drug should be assessed for their potential risk of pregnancy. All should be issued with a contraception information booklet, and sign to acknowledge their receipt of this. Baseline screening blood tests (including liver function tests and fasting lipids) should also be performed at this stage.

At a second consultation, provided the patient would like to go ahead with treatment, and all baseline blood tests are normal, the male patient can receive their full course of isotretinoin. All other topical acne treatments and systemic antibiotics should be stopped. Any female considered at risk of pregnancy will then be part of the pregnancy prevention plan.

Pregnancy prevention plan

Prescriber, pharmacist and patients must follow these rules:

- Pregnancy test just before starting therapy. Pregnancy tests can be from blood or urine but must be medically supervised. Isotretinoin should be started on the second day of the next period.
- One and preferably two forms of contraception to be used from at least 1 month before until at least 1 month after course of isotretinoin.
- Monthly pregnancy tests throughout therapy.
- Pregnancy test 5 weeks after stopping course of therapy.
- Isotretinoin prescriptions — for only 1 month of therapy at a time. Prescriptions are valid for 7 days only.
- Complete the checklist for prescribing to female patients at each stage, i.e. pre-treatment, each in-treatment visit and post-treatment visit.

If the patient is not regarded as at risk of pregnancy, and does not enter the pregnancy prevention plan, the reason for this should be recorded in the notes.

What if my patient becomes pregnant while on isotretinoin?

If pregnancy occurs or is suspected in any female patient during treatment or in the 5 weeks after therapy:

Patient should stop isotretinoin treatment immediately.
Patient should receive advice from a physician specialized or experienced in birth defects.
Patient should inform the primary prescriber of isotretinoin and the GP.
The supplier and the MHRA should be informed if pregnancy is confirmed.

How much isotretinoin can I give?

The standard dose of isotretinoin in the UK is up to 1 mg/kg/day for 16 weeks, and a single treatment course is sufficient for the majority of patients. A further improvement of acne can

be observed up to 8 weeks after discontinuation of treatment, so a further course should not be considered until this time has elapsed. Patients are able to have longer courses of treatment (up to 24 weeks) or a repeat course as necessary, but it has been shown that no substantial additional benefit is expected beyond a cumulative treatment dose of 120–150 mg/kg.

What if my patient has a flare of their acne when starting isotretinoin?

All patients should be warned that this may happen in the first few weeks of their treatment. In very severe acne, this can be minimized by starting on a half dose (0.5 mg/kg/day), or by the use of topical or oral corticosteroids to manage a severe flare, should it occur.

What if my patient is slow to respond, or fails to respond to isotretinoin?

Check if your patient is taking the tablets! If so, ensure that the patient is on the full dose according to weight. Some patients will be slower to respond, and a prolonged course (up to 24 weeks) can be given, provided side effects are tolerable. Note that acne cysts and large nodules will often require physical treatments to improve their appearance.

ROSACEA

This is a disorder characterized by frequent flushing, persistent erythema and telangiectasia, with episodes of inflammation, papules and pustules, but *no comedones*.

Epidemiology

Rosacea is very common, affecting 10% of the population. It is mainly seen in fair-skinned individuals who easily blush, or have a 'high colour'. It is more common in women in their third and fourth decades.

Aetiology and pathogenesis

This is unclear, and probably due to many factors with the most likely being a vascular abnormality.

- Vascular abnormality — this has been proposed as possible vascular hyper-reactivity, or long-standing vascular damage from solar radiation.
- *Demodex* mite — the *Demodex* mite is present on everyone, but some studies have found higher concentrations on the skin of patients with rosacea. Treatment directed at the mite has, in some cases, led to clinical improvement, especially in HIV infected patients. However, it may be that a separate entity, *Demodex* folliculitis, has clinically resembled rosacea in HIV infection, thus confusing the clinical outcomes.
- *Helicobacter pylori* — it has been noticed that many patients treated with *H. pylori* eradication for peptic ulcer have co-incidental improvement in their rosacea. The role of *H. pylori* in rosacea is still unproven.

Clinical features (Figure 4.10)

The cheeks, nose, forehead and chin are most commonly affected, with occasional spread to scalp and torso.

It often progresses in a stepwise fashion:

- Transient erythema.
- Persistent erythema and telangiectasia.
- Papules and pustules.
- Chronic thickening and induration of skin.
- Rhinophyma.

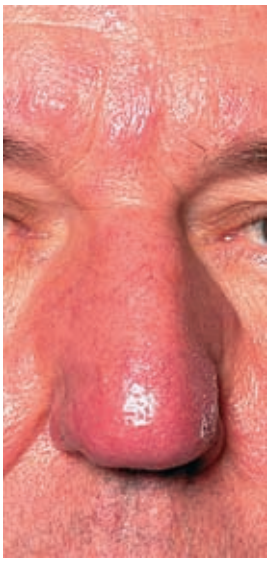


Figure 4.10
Rosacea. Note the erythematous papules and telangiectasia on the forehead, and rhinophyma on the nose.

Ocular rosacea

In ocular rosacea there may be irritation and redness of the conjunctiva, blepharitis, styes and, occasionally, keratitis. First line treatment is usually with artificial tears and systemic tetracyclines (Table 4.5).

Rhinophyma

Rhinophyma describes distortion of normal skin surface of the nose, which can lead to great cosmetic disfigurement. Once the active rosacea has been treated, surgical remodelling, with electrosurgery, CO_2 or Nd:Yag laser can be performed.

Differential diagnosis

- Acne vulgaris — comedones are also present.
- Systemic/discoid lupus erythematosus — no pustules occur. Scarring, scaling and follicular plugging are the prominent features of discoid lupus.
- Seborrhoeic dermatitis — the major feature is scaling, which occurs on the scalp, eyebrows and external ear canals.

Management

The management of rosacea is summarized in Table 4.5. In particular, the cosmetic appearance of this condition, and its effect on the patient, should be considered when deciding on management options.

Variants of rosacea

Steroid-induced rosacea

Prolonged facial application of potent topical steroid can induce rosacea. The steroid needs to be withdrawn (often with intermediate potency steroid initially). Concomitant use of

Table 4.5: Management of rosacea

Therapy	Top tips
Sunscreen	Avoiding alcohol, spicy foods and hot drinks may also reduce flushing
Topical metronidazole	Can irritate the skin
Oral antibiotics: Tetracyclines Erythromycin	See Acne Table 4.4
Topical sulphur/ Ketoconazole/ Demodex eradication	All may have some benefit as second/third line therapy
Isotretinoin	See Acne Table 4.4 and main text for acne
Cosmetic treatments: Cosmetic camouflage Pulsed dye laser	Both treatments used to conceal or cosmetically treat erythema on face

topical or systemic antibiotics, or topical tacrolimus, reduces the likelihood of the condition flaring on stopping steroid creams.

Rosacea fulminans ('pyoderma faciale')

This is a very severe variant of rosacea, mainly of adult females, with marked erythema, pustules and oedema, which can lead to severe scarring. It has been linked with use of the oral contraceptive pill and pregnancy, suggesting a hormonal trigger. Patients require treatment with systemic corticosteroids and isotretinoin (see Acne section for further information).

Perioral dermatitis

Small papules and pustules appear around the mouth, sparing the lip margins. There is also a peri-ocular variant (peri-ocular dermatitis). It is exacerbated by topical steroid use. Management consists of stopping any topical steroids (an initial flare may occur), and starting topical or systemic antibiotics, as one would in standard rosacea treatment (Table 4.5).

LICHENOID DISORDERS

Lichenoid describes the clinical appearance of a flat-topped, shiny, papular rash. It also describes the histological appearance of a band-like inflammatory infiltrate in the superficial dermis, with liquefaction of the basal layer. Its distinct histology usually makes a biopsy of such a rash helpful in its diagnosis. A lichenoid eruption can occur due to a number of causes (Box 4.6), and again histology can be helpful in distinguishing between the various causes. This section will discuss lichen planus only.

Box 4.6: Commoner causes of 'lichenoid' eruptions

- Lichen planus
- Drug eruption — particularly gold, mepacrine, quinine, tetracyclines, thiazide diuretics, amlodipine
- Graft versus host disease
- Pityriasis lichenoides
- Keratosis lichenoides chronica ('Nekam's disease')
- Lichen nitidus
- Lichen striatus
- Mycosis fungoides (cutaneous T-cell lymphoma)

LICHEN PLANUS

Epidemiology

Seventy five percent of patients with cutaneous lichen planus have oral involvement, so *looking in the mouth is essential* and helpful in diagnosing the condition. Ten to twenty percent of patients develop oral lichen planus first, so often present to their dentist or the oral surgeons.

Pathogenesis

Lichen planus is a T-cell mediated autoimmune inflammatory condition. Its cause is unknown, although small studies have suggested a familial tendency, and also a possible association with hepatitis C. Oral lichen planus may be related to amalgam fillings.

Clinical features (Figure 4.11)

Shiny, flat-topped violaceous papules occur on the skin, in a variety of configurations. These can be small papules, linear or annular lesions. They are often itchy. Lichen planus can also display the Koebner phenomenon (Box 4.1). On the surface, a lace-like, white pattern is often seen — Wickham's striae. The papules can also become hyperpigmented, especially in darker skin types, and can become hypertrophic, particularly on the ankles and shins.

Differential diagnosis

A skin biopsy is very helpful in confirming a lichenoid eruption, and also in distinguishing its cause. Other conditions which should be considered are plane warts, lichenified eczema, lichen simplex chronicus, lupus erythematosus, psoriasis and secondary syphilis.

Lichen planus of mucous membranes

The mouth

In the mouth, lichen planus has the appearance of white lace-like patches, often symmetrically distributed. If the patient has co-existing lichen planus of the skin, it is

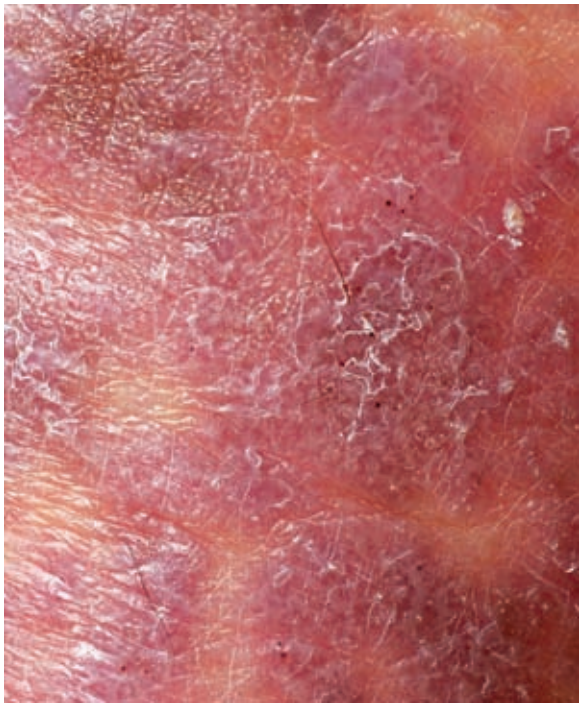


Figure 4.11
Lichen planus. A close up view showing the violaceous plaque topped by Wickham's striae.

reasonable to treat them in the first instance with topical corticosteroids to the mouth. A strong corticosteroid in a base designed for oral administration (e.g. triamcinolone in oral paste) is usually helpful. A patient with non-responding, atypical or asymmetrical lesions, particularly if they are a smoker, should be referred to the oral surgeons for consideration of biopsy. Remember that squamous cell carcinoma can occasionally arise in these lesions, so again atypical ulceration or new lumps in the mouth should be investigated.

Genital area

This can affect both sexes, but is more common on the vulva, and can be difficult to treat. At worst, the lesions on the vulva can ulcerate, causing painful scarring. A biopsy should be taken to differentiate it from lichen sclerosis, which can have a similar appearance.

Other sites

- Nails: In 10% of cases there is nail involvement, particularly of the finger nails, with ridging and thinning of the nail plate. The nail can be completely lost, or can form a 'pterygium' (severe narrowing of the nail resulting from partial destruction).
- Scalp: Lichen planus of the scalp can cause scarring alopecia and skin atrophy, and should be looked for (again a biopsy is very helpful) and managed early to try to avoid such permanent scarring.

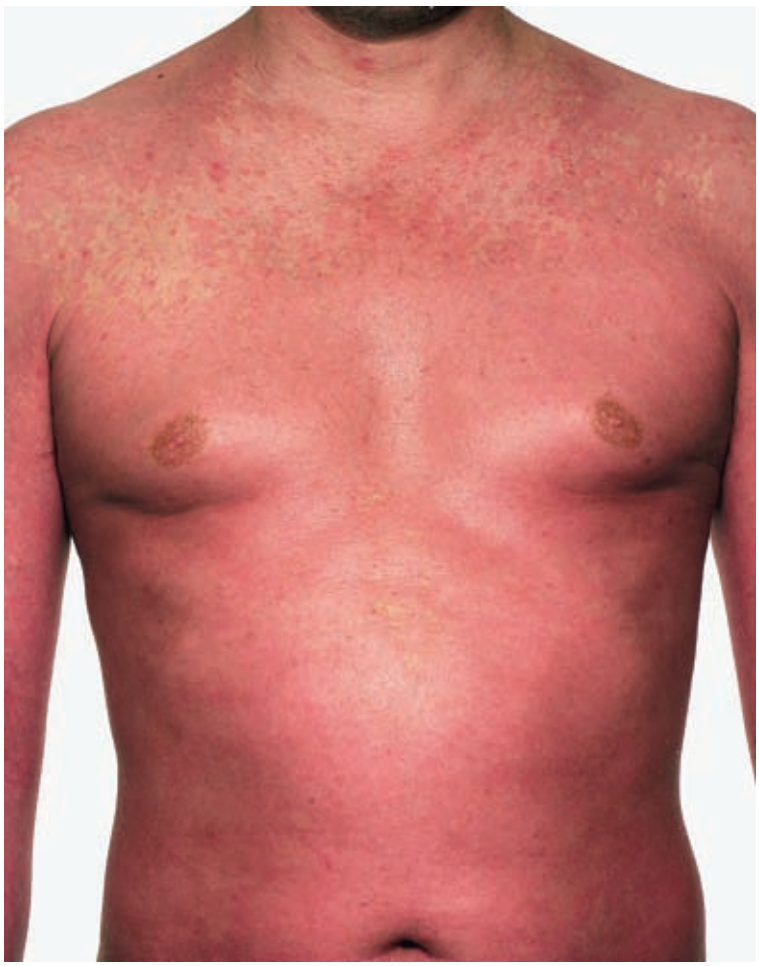
Treatment of lichen planus

The first line treatment of localized areas of lichen planus is topical steroids, which can be occluded to increase potency and also to reduce rubbing of the affected area. Use of potent corticosteroids, especially under occlusion, carries the risk of skin atrophy, and topical immunosuppressants may be a useful alternative. More widespread or non-responsive lesions require systemic treatment, with oral corticosteroids in the first instance (unless contraindicated), or with retinoids, ciclosporin or PUVA as second line therapy.

ERYTHRODERMA

Erythroderma is defined as more than 90% involvement of the body surface by an inflammatory skin disease (Figure 4.12). It can occur, for example, in patients with chronic

Figure 4.12
Erythroderma.



plaque psoriasis, who experience a trigger (e.g. infection/stress/withdrawal of topical or systemic corticosteroids or immunosuppressants). However, there are a number of other causes, summarized in Table 4.6.

It is important that the underlying cause is identified although in 8% of cases it is not found. Questions to ask in the history include previous and family history of skin disease, drug history (including over-the-counter medications) and systemic symptoms. General examination of the patient is essential (including lymph nodes) and a skin biopsy can be helpful if the cause is not obvious.

Management

Erythroderma is a *dermatological emergency*. The skin function has failed, and management is mainly supportive. The most important complications are:

- Loss of body heat — keep the patient warm. Try to get the patient nursed in a single cubicle as it is easier to keep the ambient temperature higher.
- Dehydration — plentiful oral fluids should be encouraged. Intravenous fluids should be considered if the patient is not drinking enough or is pyrexial. Liberal use of emollients is essential.
- Infection — weeping skin should be swabbed and treated with oral antibiotics. If the patient becomes pyrexial, a full septic screen should be performed (blood cultures/urine culture/throat swab/other depending on symptoms), but remember that just having the erythroderma can cause a pyrexia too.
- Loss of protein and increased energy requirements — increased nutrition, particularly protein supplements, should be given.
- Increased risk of deep vein thrombosis — if the patient is dehydrated and immobile, deep vein thrombosis prophylaxis should be considered.
- Find and treat underlying cause — this may involve stopping the offending drug, or starting immunosuppressive drugs, depending on the underlying condition.

Table 4.6: Commonest causes of erythroderma

	% of overall prevalence
Eczema (any type)	40
Psoriasis	25
Lymphoma and leukaemias	15
Drug reactions — particularly allopurinol, anticonvulsants, gold, penicillin, sulphonamides	10
Idiopathic	8
Pityriasis rubra pilaris/paraneoplastic (often late stage)/pemphigus foliaceous/ congenital ichthyoses	< 1

STEVENS–JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS

These are the more severe end of the 'erythema multiforme' spectrum, and are the most serious of *dermatological emergencies*. Patients usually present with macular, papular or urticarial lesions on the skin, sometimes with erosions affecting the mucous membranes. As you go further down the list (Box 4.7), the conditions become more severe, with more widespread skin erosions and skin loss, and more severe involvement of the mucous membranes. The mortality rate also increases, to a level of about 30–40% in toxic epidermal necrolysis (TEN). Stevens–Johnson syndrome (SJS) and TEN are usually due to drug reactions, and are often considered separately.

The most common drugs which can cause SJS or TEN are summarized in Box 4.8. There is an overlap between drugs which cause SJS and those which cause TEN, indeed SJS can evolve into TEN (so these patients should be monitored carefully).

Clinical features (Figure 4.13)

The patient is usually systemically unwell, often with a prodrome of fever, malaise and arthralgia. The most striking feature will be erosions of the lips and the inside of the

Box 4.7: Spectrum of erythema multiforme

Erythema multiforme	Mild
Stevens–Johnson syndrome (SJS)	↓
Toxic epidermal necrolysis (TEN)	Severe

Box 4.8

Commonest drugs which can cause Stevens–Johnson syndrome

- Sulphonamides
- Tetracyclines
- Penicillin
- Malaria prophylaxis drugs

Commonest drugs which can cause toxic epidermal necrolysis

- Sulphonamides
- NSAIDs
- Allopurinol
- Anticonvulsants
  - Barbiturates
  - Phenytoin
  - Carbamazepine
  - Lamotrigine
- Antiretroviral drugs
  - Nevirapine

Figure 4.13
Stevens–Johnson syndrome. Note the conjunctival and oral erosions, and a typical erythema multiforme-like 'target lesion' on the left of the mouth.

mouth. The conjunctiva and genital areas can also be severely affected, so the patient should be specifically asked about symptoms in these areas.

As the skin begins to blister, it is useful to test it with 'Nikolsky's sign'. A positive result describes firm sliding pressure with a finger, which then separates normal-looking epidermis from the dermis producing an erosion. The presence of Nikolsky's sign indicates weakness and loss of cohesion within the epidermis at the dermo-epidermal junction. Nikolsky's sign is useful to assess any blistering condition, including the immunobullous diseases. A positive result indicates that the patient is more at risk of complications.

The most important steps would be:

- *Seek senior help*.
- Stop the offending drug.
- Supportive care of the patient's skin — this is the same as in the Erythroderma section. Correct fluid balance is of the utmost importance for these patients.
- Correct placement — patients with TEN should be managed in an intensive care setting, preferably in a burns unit.
- Care of mucous membranes — this may involve the patient being nil by mouth, requiring catheterization, or needing referral to ophthalmology.
- An excellent review is recommended by Chave et al.[13]

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