Skin disease

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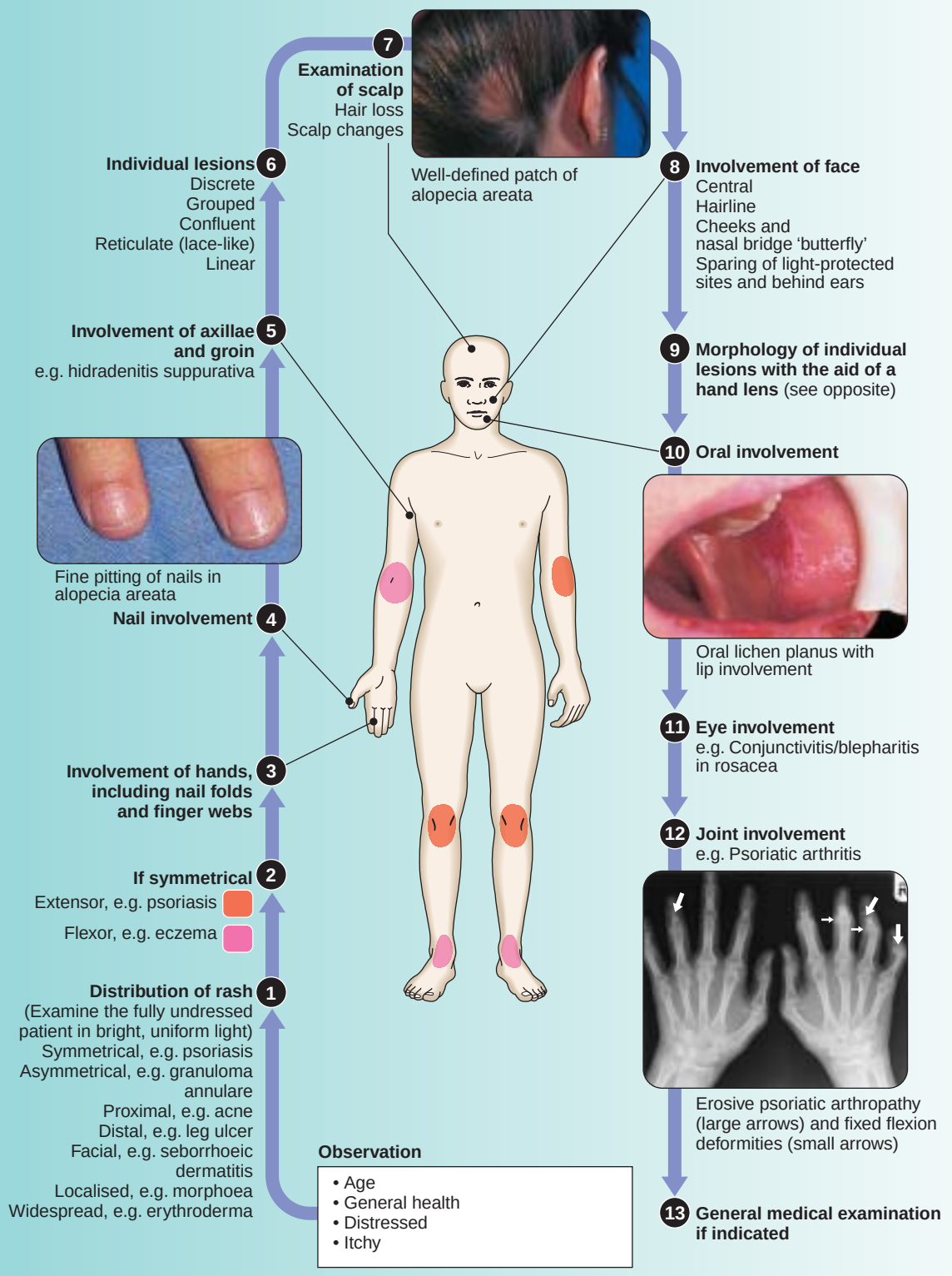
CLINICAL EXAMINATION IN SKIN DISEASE



TERMS USED TO DESCRIBE SKIN LESIONS

Term	Definition
PRIMARY LESIONS	
Macule	Small flat area of altered colour or texture
Papule	Small solid elevation of skin, less than 0.5 cm in diameter
Nodule	A solid mass in the skin, usually greater than 0.5 cm in diameter
Plaque	Elevated area of skin greater than 2 cm in diameter but without substantial depth
Vesicle	Circumscribed elevation of skin, less than 0.5 cm in diameter, and containing fluid
Bulla	Circumscribed elevation of skin, over 0.5 cm in diameter, and containing fluid
Pustule	A visible accumulation of pus in the skin
Abscess	A localised collection of pus in a cavity, more than 1 cm in diameter
Weal	An elevated, white, compressible, evanescent area produced by dermal oedema
Papilloma	A nipple-like mass projecting from the skin
Petechiae	Pinhead-sized macules of blood in the skin
Purpura	A larger macule or papule of blood in the skin
Ecchymosis	A larger extravasation of blood into the skin
Haematoma	A swelling from gross bleeding
Burrow	A linear or curvilinear papule, caused by a burrowing scabies mite
Comedo	A plug of keratin and sebum wedged in a dilated pilosebaceous orifice
Telangiectasia	The visible dilatation of small cutaneous blood vessels
SECONDARY LESIONS (which evolve from primary lesions)	
Scale	A flake arising from the horny layer
Crust	Looks like a scale, but is composed of dried blood or tissue fluid
Ulcer	An area of skin from which the whole of the epidermis and at least the upper part of the dermis have been lost
Excoriation	An ulcer or erosion produced by scratching
Erosion	An area of skin denuded by a complete or partial loss of the epidermis
Fissure	A slit in the skin
Sinus	A cavity or channel that permits the escape of pus or fluid
Scar	The result of healing, in which normal structures are permanently replaced by fibrous tissue
Atrophy	Thinning of skin due to diminution of the epidermis, dermis, subcutaneous fat
Stria	A streak-like, linear, atrophic, pink, purple or white lesion of the skin due to changes in the connective tissue

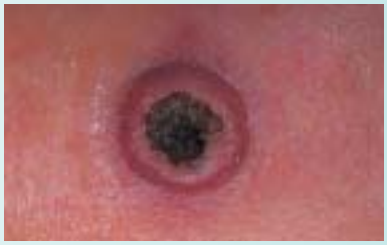
HISTORY

It is often sensible to introduce yourself to the patient, ask a few questions and then examine the skin before further cross-questioning of the patient. Ask about the onset of the skin lesions and the progression of the disease. A careful enquiry into drugs administered, particularly those bought without a prescription, a past or family history of skin disorders, comorbidity, and details of occupation and any hobbies are also potentially important. The relative contribution of history, elicitation of symptoms and physical signs differs for particular diagnoses.

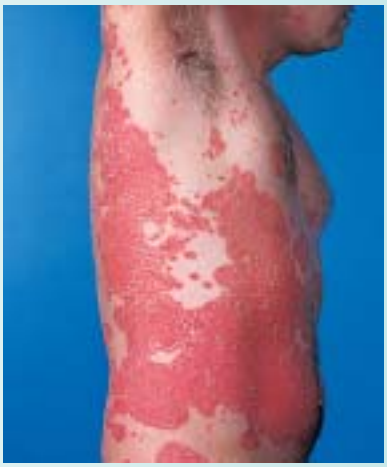
EXAMINATION

The patient needs to be undressed, and make-up and dressings should be removed. A frequent mistake is failure to undress the patient appropriately to allow the correct diagnosis to be made.

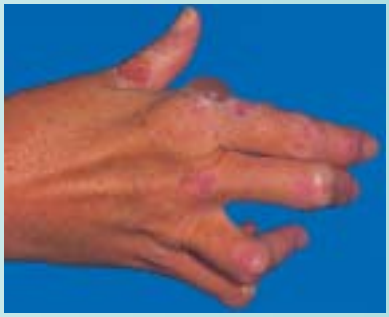
A magnifying lens is often helpful. Feeling the skin provides diagnostic clues and may also be therapeutic as many patients with skin disease, whatever their apparent level of sophistication, may feel like lepers. Skin diseases cannot usually be correctly diagnosed at arm's length.



Nodule. A keratoacanthoma.



Plaque. Erythematous plaques in psoriasis.



Bullae and scarring. Acquired epidermolysis bullosa in rheumatoid arthritis.

Comedo. Solar comedones occurring around the eyes in an elderly individual.

Skin disease is common. Surveys in Europe suggest that approximately 1 in 7 to 1 in 10 of all visits to a primary care physician is for a skin problem and that for many hospitals the number of patients attending for dermatological diagnosis and treatment exceeds the total number of visits for the whole of internal medicine. Population prevalence studies are in keeping with these figures, revealing an enormous burden of undiagnosed, untreated skin disease. Skin disease appears to be becoming more common for at least three reasons. Firstly, there is a lowered threshold for seeking medical attention. Secondly, the absolute incidence of many diseases such as skin cancer and atopic dermatitis has increased steeply. Thirdly, and often neglected, the therapeutic options for a number of diseases previously viewed as untreatable have increased and awareness of these therapies is belatedly spreading.

Skin complaints affect all ages from the neonate to the elderly and cause harm in a number of ways as shown in Box 21.1. Every clinician has the opportunity to look at the skin when listening to or examining a patient and should be able to identify important and common skin disorders. This chapter emphasises those skin conditions that are frequently seen in general practice and in general medical clinics. Those skin infections not covered here, including human immunodeficiency virus (HIV) disease, are dealt with in Chapter 1, and connective tissue diseases which often involve the skin, in Chapter 20.

The aim of this chapter is to give the reader:

- an idea of how to assess the patient with a rash or lesion
- advice on appropriate initial management and therapy
- theory underlying the mechanisms of some skin diseases and their therapies.

21.1 THE FOUR Ds

Discomfort

- Most often itching or pain (e.g. eczema, post-herpetic neuralgia)

Disfigurement

- Leading to embarrassment and withdrawal from society (e.g. birth marks, acne vulgaris and psoriasis)

Disability

- Leading to loss of work and wages (e.g. dermatitis of the hands and feet)

Death

- Rare but still seen (e.g. metastatic melanoma and widespread blistering drug reactions)

FUNCTIONAL ANATOMY, PHYSIOLOGY AND INVESTIGATIONS

ANATOMY AND PHYSIOLOGY

The skin of an average adult covers an area of just under 2 m^2. The epidermis, a stratified squamous epithelium, is the outermost layer and is predominantly composed of keratinocytes. The epidermis is attached to the underlying dermis by the basement membrane. The dermis contains and supports blood vessels, nerves and appendageal structures such as hair follicles and sweat glands. The predominant cell of the dermis is the fibroblast. It is important to remember that the appendageal structures such as hair follicles and sweat glands, whilst embedded within the dermis, are epidermal in origin. Below the dermis is the subcutis.

EPIDERMIS

Keratinocytes comprise 95% of epidermal cells (see Fig. 21.1). The proliferative compartment of epidermis resides in the basal layer and in the layer immediately adjacent to the basal layer where mitotic figures are also not uncommon. The site of the keratinocyte stem cell is not certain but is likely to be in a specialised region of the hair follicle analogous to the 'bulge' region in the mouse. In areas of skin without hair follicles (glabrous skin) stem cells may be present within the epidermis.

Keratinocytes synthesise a range of structural proteins including keratins and loricrin. There are over 20 different types of keratin, classed into two broad groups: basic (type I) and acidic (type II). Specific keratins form dimers made up of one acidic and one basic molecule that are aggregated to form larger macromolecular structures called intermediate filaments. Intermediate filaments play a key structural role in skin physiology and the expression patterns of the various gene products is highly complex. Genetic diseases that result in mutations of keratins (e.g. simple epidermolysis bullosa, some types of ichthyosis) are characterised by either epidermal fragility (i.e. blistering) or grossly disordered differentiation. As keratinocytes move out of the basal layer they differentiate, producing a variety of different protein and lipid products. Keratinocytes undergo a form of programmed cell death in the granular layer before becoming the flattened anucleate cells that make up the stratum corneum. The epidermis is a site of great lipid production, and the ability of the stratum corneum to act as a hydrophobic barrier is in large part due to the structure of highly proteinaceous dead corneocytes; these have a highly cross-linked protein membrane ('bricks') in a metabolically active layer of lipid ('mortar') also secreted by the corneocytes ('bricks and mortar' model).

Skin is required to have considerable physical resilience as well as being highly active metabolically. Whereas keratins provide structural support for individual keratinocytes, attachments between cells need to be able to transmit and dissipate stress, a function performed by desmosomes. Diseases that target desmosomes, such as pemphigus, result in blistering as the individual keratinocytes separate.

Three other cell types make up most of the remaining 5% of epidermal cells:

- *Langerhans cells* are dendritic, bone marrow-derived cells that circulate between the epidermis and the local lymph nodes. Their prime function is effective

presentation of foreign antigens to lymphocytes, as is seen, for example, in an allergic contact dermatitis reaction. They may also play a part in presentation of tumour antigens, a fact on which researchers have tried to capitalise in the production of anti-melanoma vaccines. Other dendritic cells which are effective at presenting antigen are also present in skin but are in the dermis rather than the epidermis.

- *Melanocytes*, of neural crest origin, are found predominantly in the basal layer; they synthesise the pigment melanin from tyrosine, package it in melanosomes and transfer it to surrounding keratinocytes via their dendritic processes.
- *Merkel cells* are found in the basal layer. They are thought to play a role in signal transduction of fine touch. Their embryological origin is not certain.

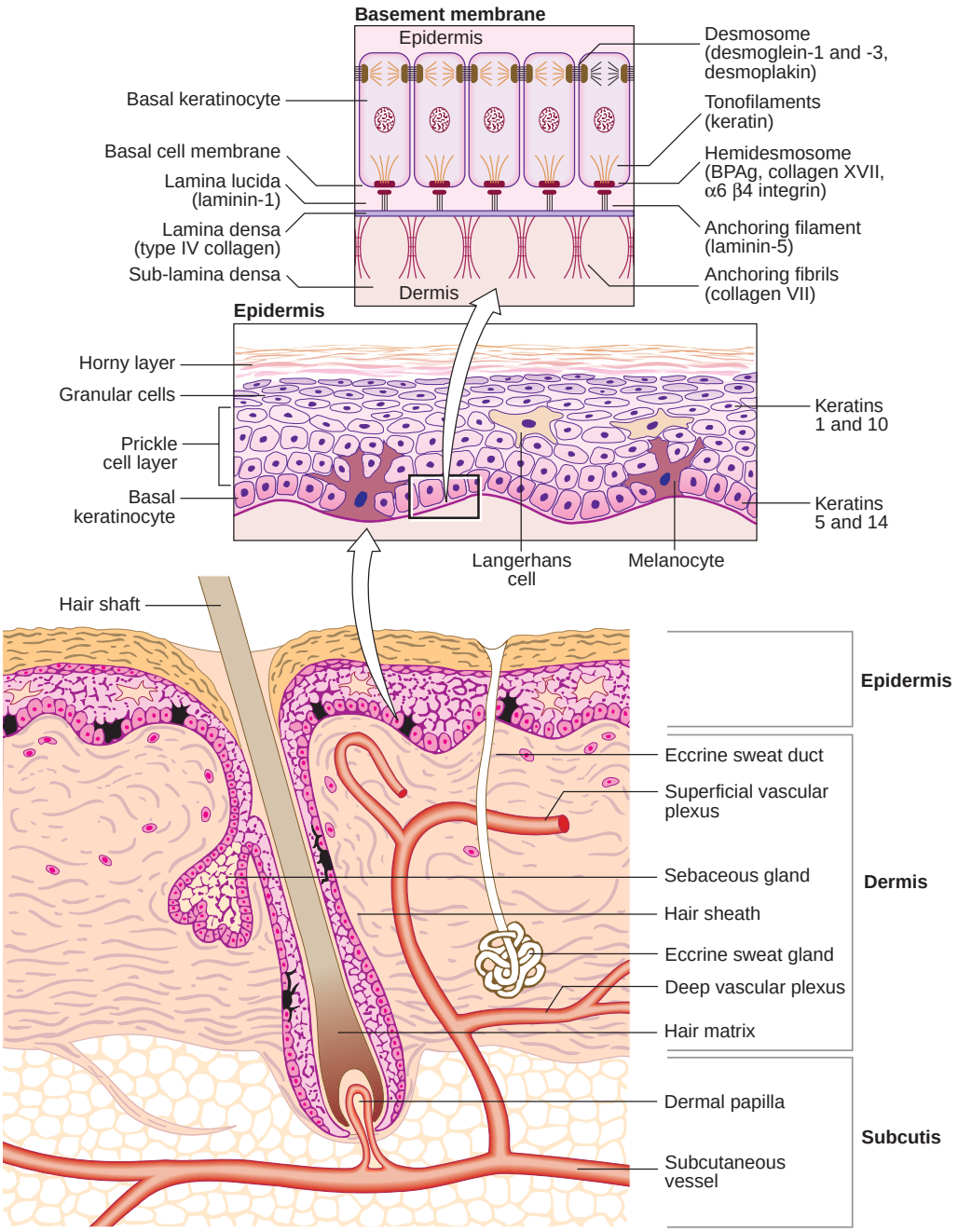


Fig. 21.1 Structure of normal skin.

BASEMENT MEMBRANE

The basement membrane (see Fig. 21.1) acts as an anchor for the epidermis but allows movement of cells and nutrients between the dermis and epidermis. It consists of several well-defined layers that are identifiable ultrastructurally and at the molecular level. The cell membrane of the epidermal basal cell is attached to the basement membrane via hemidesmosomes. The lamina lucida is the zone immediately subjacent to the cell membrane of the basal cell which is composed predominantly of laminin. Anchoring filaments extend through the lamina lucida to attach to the lamina densa. This electron-dense layer consists predominantly of type IV collagen; from it extend loops of type VII collagen forming anchoring fibrils that fasten the basement membrane to the dermis.

DERMIS

The dermis is vascular and supports the epidermis structurally and nutritionally. It varies in thickness from just over 1 mm on the inner forearm to 4 mm on the back. (By contrast, the epidermis on most sites is only 0.1–0.2 mm thick, except on the palms or soles where it can be several millimetres in thickness.) The acellular part of the dermis consists predominantly of fibres, mostly collagens I and III but also elastin and reticulin, synthesised by the major cell type, fibroblasts. Support is provided by an amorphous ground substance (mostly the glycosaminoglycans, hyaluronic acid and dermatan sulphate), whose production and catabolism may be influenced by hormonal changes and damage from ultraviolet radiation. Apart from fibroblasts, there is a large number of other cell types within the dermis including mast cells, mononuclear phagocytes, T lymphocytes, dendritic cells, nerves and vessels.

EPIDERMAL APPENDAGES: HAIR AND SWEAT GLANDS

Hair, sweat and apocrine glands (found mainly in the axillae) are epidermal structures which invaginate into the dermis. They are formed during the second trimester. Coarse, medullated hair accounts for the terminal hair of the scalp and pubic areas. Short, fine unmedullated hairs make up the remaining body hair. Sebaceous glands usually arise from hair follicles, with their ducts discharging sebum into the upper part of the follicle. Sebum excretion is under hormonal control; androgens and progestogen increase sebum excretion whereas oestrogens have an inhibitory effect. Apocrine glands are those sweat glands found in the axillae, perineum, genitalia and areolae which become functional after puberty under the influence of hormonal changes, particularly androgens. Eccrine sweat glands are found all over the body and their ducts open directly on to the skin surface. They play a major role in humans in thermoregulation and, unusually, are innervated by cholinergic fibres of the sympathetic (rather than parasympathetic) nervous system.

BLOOD VESSELS AND NERVES

There is an abundant blood supply in the skin arranged in superficial and deep plexi. The skin is well supplied with

21.2 FUNCTIONS OF THE SKIN

Function	Structure/cell involved
Protection against:	
Chemicals, particles	Horny layer
Ultraviolet radiation	Melanocytes
Antigens, haptens	Langerhans cells, lymphocytes, mononuclear phagocytes, mast cells
Microbes	Horny layer, Langerhans cells, mononuclear phagocytes, mast cells
Preservation of a balanced internal environment Prevents loss of water, electrolytes and macromolecules	Horny layer
Shock absorber Strong, yet elastic and compliant covering	Dermis and subcutaneous fat
Sensation	Specialist nerve endings
Calorie reserve	Subcutaneous fat
Vitamin D synthesis	Keratinocytes
Temperature regulation	Blood vessels, eccrine sweat glands
Lubrication and waterproofing	Stratum corneum
Protection and prising	Nails
Hormonal Testosterone synthesis from inactive precursors and testosterone conversion to other androgenic steroids	Hair follicles Sebaceous glands
Body odour (more important in animals)	Apocrine sweat glands
Psychosocial	Hair, nails, appearance and tactile quality of skin

nerves to both dermis and epidermis. It used to be thought that nerves did not penetrate into the epidermis but this is now known to be false and there are indeed a large number of nerves that appear to interact with Langerhans cells, melanocytes and other components of the epidermis. Blood vessels are supplied by sympathetic autonomic nerves and peptinergic nerves that take part in the axon reflex. The functions of the skin are summarised in Box 21.2.

ISSUES IN OLDER PEOPLE
SKIN CHANGES

- Skin changes in the elderly include atrophy, laxity, wrinkling, dryness, irregular pigmentation and sparse grey hair.
- There are also alterations in immune surveillance and antigen presentation, and reduced cutaneous vascular supply which lead to decreases in the inflammatory response, absorption and cutaneous clearance of topical medications.
- These changes make the skin less durable, slower to heal, and more susceptible to damage and disease.
- They are brought about by:
  —age-related alterations in structure and function of the skin
  —cumulative effects of environmental insults, especially ultraviolet radiation
  —cutaneous consequences of disease in other organ systems.

DIAGNOSIS AND INVESTIGATION OF SKIN DISORDERS

The key to successful treatment is accurate diagnosis. This requires an appropriate history, thorough examination of the skin including hair and nails (see p. 1088), and occasional use of ancillary investigations such as histopathology.

Some investigative tests can be performed in the clinic with immediate results, but as a general rule clinical skills, especially visual recognition, are perhaps of greater importance than in any other branch of general medicine.

DIASCOPY

In diascopy a glass slide is pressed firmly on the skin lesion. If a red lesion blanches, it implies that the red colour is secondary to blood within the vessels. By contrast, blood outside the vessels, such as that from a bruise or from vasculitis, will not blanch. In some vascular lesions with a convoluted vessel structure, however, blunt pressure from a flat surface will not empty the vessels and the corner of a glass slide needs to be gently placed on the lesion. Even then, it will not always blanch completely. Therefore, success in blanching is a more useful physical sign than failure to blanch. When pressed on to some granulomatous lesions a glass slide reveals an appearance commonly referred to as ‘apple jelly nodule’.

EPILUMINESCENCE MICROSCOPY (DERMATOSCOPY)

This refers to surface microscopy using an illuminated magnifying lens or microscope with oil immersion directly on to the skin’s surface. It has found most clinical use in the assessment of pigmented lesions. A number of patterns not visible to the naked eye are often revealed, which can support a clinical diagnosis of malignancy in experienced hands.

WOOD’S LIGHT

This involves ultraviolet radiation (wavelength 360 nm) from a light source which has a nickel oxide filter (Wood’s filter) to eliminate visible light. Green fluorescence is seen in scalp ringworm due to *Microsporum canis*, a sporadic ectothrix infection. It evokes coral pink fluorescence of flexural skin in erythrasma, caused by the bacterium *Corynebacterium minutissimum*. Wood’s light also enhances the examination of cutaneous pigmentary abnormalities.

MYCOLOGY SAMPLES

Cutaneous scale, nail clippings and plucked hairs can be examined by light microscopy when mounted in 20% potassium hydroxide. This allows the keratin to be dissolved and fungal hyphae can be identified. If the potassium hydroxide solution contains Indian ink, the typical ‘spaghetti and meatballs’ hyphae and spores of the yeast *Pityrosporum orbiculare* can be readily identified in pityriasis versicolor. In addition, samples are sent for identification by culture.

SWABS

Bacterial swabs

Bacterial swabs taken in an appropriate culture medium are sometimes useful. Some caveats do, however, remain. Organisms that grow on the swabs may not be causally implicated in the underlying disease and the growth of many organisms simply reflects the abnormal architecture of the skin and is not necessarily an indication for either systemic or even local antibacterial therapy. Conversely, in some obvious infections of the skin, such as cellulitis, swabs do not reveal the causative agent.

Viral swabs

Blister or pustule samples for herpes simplex and varicella zoster can be visualised within a few hours, either by electron microscopy or by indirect immunofluorescence. Samples are also cultured for identification when conserved in viral culture medium.

PRICK TESTS

Prick tests are a way of detecting cutaneous type I (immediate) hypersensitivity to various antigens such as pollen, house dust mite or dander. The skin is pricked with commercially available stylets through a dilution of the appropriate antigen solution. After 10 minutes a positive response is indicated by a weal and a flare. The weal is due to a local increase in capillary permeability and the flare a result of activation of the axon reflex. A positive control (histamine) and a negative control (antigen diluent) should be performed. Systemic antihistamines inhibit the magnitude of the reaction. In

individuals with a clear history of particular type I hypersensitivity a systemic reaction may follow a prick test and resuscitation facilities should be available. As an alternative, specific IgE levels to antigens can be measured in serum by a specific radioallergosorbent test (RAST).

PATCH TESTS

Patch tests detect type IV (delayed or cell-mediated) hypersensitivity. It is common practice for a 'battery' of around 20 common antigens, including common sensitisers such as nickel, rubber and fragrance mix, to be applied to the skin of the back under aluminium discs for 48 hours. The sites are then examined for a positive reaction 24 hours later and possibly again a further 24 hours later. An eczematous reaction, in the absence of an irritant reaction, suggests a type IV hypersensitivity to that particular allergen. The relevant antigens for a particular clinical case may not be represented in the standard battery of tests and expert advice may be needed. A negative patch test does not exclude a pathogenic role for a particular antigen nor does the presence of a particular response to an antigen mean that this antigen is causing the clinical disease.

HISTOLOGY

Skin biopsies for routine histological examination are usually fixed in 10% formalin and stained with haematoxylin and eosin. Immunocytochemistry may also be performed on formalin-fixed sections but may require frozen sections (see below). Immunocytochemistry is particularly useful for tumour diagnosis and for identification of particular T cell subsets.

IMMUNOFLUORESCENCE

A portion of the skin biopsy can be frozen in liquid nitrogen for direct immunofluorescence (IF). This involves visualising antigens that are present in skin by identifying them with fluorescein-labelled antibodies. Similarly, indirect immunofluorescence can identify circulating antibodies in the serum by an additional step of adding the serum to a section of normal skin or other substrate. Immunofluorescence plays a major role in the diagnosis of the autoimmune bullous disorders.

ELECTRON MICROSCOPY

This investigation has played an important role in the diagnosis of some of the rare blistering disorders such as epidermolysis bullosa, although the availability of a range of antibodies to basement membrane zone antigens has in part replaced it.

PHOTOTESTING

Phototesting involves exposing skin (often on the back) to a graded series of doses of ultraviolet radiation (UVR) of known wavelength, either on one occasion or repeatedly. In many photodermatoses erythema will occur at a lower dose of UVR than occurs in the normal population (e.g. drug-induced photosensitivity), or the time course of erythema may be prolonged (as in xeroderma pigmentosum). Alternatively, UVR will provoke lesions with the morphology of the underlying photodermatosis, such as may occur in lupus erythematosus or solar urticaria. Diagnostic phototesting is an essential component of the investigation of patients with presumed photosensitive drug reactions and idiopathic photodermatoses such as solar urticaria.

MAJOR MANIFESTATIONS OF SKIN DISEASE

THE CHANGING MOLE

The largest change in dermatological practice over the last 30 years has been the major increase in patients referred or requesting advice about particular lesions ('is it cancer, doctor?') as compared with rashes. Thirty years ago perhaps 90% of dermatology outpatients had rashes and 10% lesions whereas now the proportion of lesions often exceeds 50%. This reflects the fact that human skin cancer becomes more common as people grow older, and there is an increase in the elderly in many societies, and also the fact that there is an increase in the age-specific incidence rates for most skin cancers. Furthermore, there is greatly increased public awareness and concern about skin cancer, often in response to 'health campaigns'.

The principal clinical concern is to distinguish correctly between benign lesions and melanoma. Melanoma in most of Western Europe remains an uncommon tumour with a cumulative lifetime incidence of less than 1%. Nevertheless, the case fatality remains about 20% with there being no curative therapy if the primary tumour has metastasised. Metastasis occurs early in the development of melanoma, and therefore in the absence of highly effective therapies attention has naturally focused on primary prevention and recognition of early lesions. Far more early or thin melanomas are now diagnosed than was the case 30 or 40 years ago, reflecting increased awareness and the greater provision of medical services. The downside of this increased awareness is greater patient anxiety and a negative impact on other services provided by dermatologists. These themes are common to other debates about screening and early detection of disease.

The situation is complicated by the fact that whilst any one of a number of changes in a pigmented lesion (see Box 21.3) is highly sensitive as a marker of melanoma, its specificity is low. Even in the hands of experts diagnostic certainty is low for many pigmented lesions in the absence of a biopsy. As excision of suspicious lesions is relatively easy, any screening test or screening procedure will

21.3 ABCDE FEATURES OF MALIGNANT MELANOMA

- **A**symmetry
- **B**order irregular
- **C**olour irregular
- **D**iameter often greater than 0.5 cm
- **E**levation irregular
  (+ Loss of skin markings)

require high levels of negative predictive value before it can be adopted in routine clinical practice. For the present there is no evidence to suggest that population screening for melanoma in Northern Europe is indicated.

History

- Determine the precise nature of the change (see p. 1090). Is it due to the development of itch, inflammation, bleeding or ulceration, or changes in the colour, size, shape or surface of the lesion?
- Subtle changes should not be ignored, as many patients are good observers and get to know their own moles well. If the change has settled, could it have been due to a common insult such as nicking a facial naevus when shaving, plucking hairs from a naevus or the irritant effect of a depilatory?
- Is the patient worried about change in one or many moles? Paradoxically, concern about many moles should not alert the doctor so much as anxiety over a solitary lesion.
- Is there a positive family history of melanoma? Fewer than 10% of melanomas occur in individuals with a strong family history but in some of these families the history of melanoma is quite striking, with up to 50% of individuals developing melanoma. A suspicious mole on a patient with a first-degree relative with a melanoma probably warrants specialist opinion.

Examination

Examine the pigmented lesion carefully. Look at the morphology of the melanocytic naevi at other sites. Examination with a magnifying glass may help. Some dermatologists are keen on dermatoscopes to help define the nature of the lesion. Usually the key clinical question is whether the lesion is a benign melanocytic naevus (see p. 1089) or a malignant melanoma (see p. 1094). Before trying to answer this, the clinician needs to exclude the possibility that it is another type of pigmented lesion:

- *Lentigo* (a benign proliferation of melanocytes; see p. 1087).
- *Freckle* (ephelis; see p. 1087).
- *Seborrhoeic wart* (basal cell papilloma; see p. 1090).
- *Dermatofibroma*. This lightly pigmented firm dermal nodule is common on extremities in young adults. It feels larger than it looks. There is dimpling when the skin is squeezed on both sides (positive Fitzpatrick sign).
- *Pigmented basal cell carcinoma* (see p. 1092). This lesion is usually found on the face of the elderly and is slow-growing. It has a blue-brown hue with an opalescent look. There may be a rolled edge around an ulcer.
- *Subungual haematoma* (see Fig. 21.27, p. 1088).

Melanocytic naevus versus malignant melanoma

The ABCDE 'rule' is better viewed as a guide and reminder of what to consider (see Fig. 21.2). Loss of normal skin markings is not diagnostic but is suggestive of melanoma. Conversely, normal skin markings and the presence of fine hairs dispersed evenly over a lesion, though reassuring, are not certain signs of a lesion's benign nature.

Does the patient have other pigmented lesions?

Ask and examine the patient fully. Some patients (rarely) present with more than one primary melanoma and morphology of other melanocytic naevi may provide useful diagnostic information. Remember that seborrhoeic warts are usually multiple. If a naevus, especially a changing one, appears significantly different (in colour, shape, size etc.) from others, then it should be treated with suspicion.

Management

- Any changing lesion which is suspected of being a malignant melanoma should be excised without delay, with a clear margin. Depending on the thickness of the tumour further excision may be required.
- Some authors argue that if there is any doubt about the diagnosis the patient should be reviewed, or the individual lesion photographed and the patient reviewed in a couple of months and rephotographed.

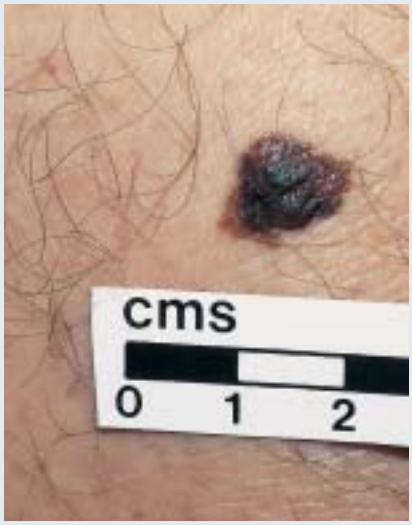


Fig. 21.2 Malignant melanoma. A changing mole which fails the ABCDE test.

Not all would agree with this management plan, given that melanomas may show only slow or intermittent progression in their early course. A 'wait and see' policy may increase anxiety.
- In this clinical context a positive diagnosis is essential. If you are uncertain whether the lesion is a melanocytic naevus or some other pigmented lesion, then it must be excised or specialist help obtained.
- Malignant melanoma can break most rules. Listen, look and think. If in doubt, cut out and then check the histology, or seek advice urgently.

ITCH (PRURITUS)

Pruritus is defined as an unpleasant sensation that provokes the desire to scratch. Despite being the major symptom of skin disease apart from disturbance of body image, it remains poorly studied and poorly understood. Although central nervous system lesions can cause itch, the majority of patients seen in clinical practice itch due to a primary disease of the skin.

The nerve endings that signal itch are believed to lie either within the epidermis or very close to the dermo-epidermal junction. Such sensory information is transmitted via C fibres, which have slow conduction speeds via the spinothalamic tract to the thalamus and on to a cortical representation. It was thought for a long time that itch was conducted along the same fibres that conduct pain and that itch may have been a subliminal form of pain. This hypothesis seems increasingly untenable as candidate fibres for itch have recently been identified. There does, however, seem to be an antagonistic or inhibitory relation between pain and itch. Scratching may either cause inhibition of the itch receptors by stimulating ascending sensory pathways which inhibit itch at the spinal cord (Wall's 'gate' mechanism), or interfere with itch fibres lying superficially in skin which may be damaged directly by scratching. Which of these hypotheses is correct is unknown.

As well as primary diseases of the skin, itch may be a result of various systemic diseases such as primary biliary cirrhosis or renal failure. The mechanisms of induction of itch in these cases are unknown but for liver disease there is some experimental evidence that abnormal circulating opioids stimulate itch centrally.

History

Assessment of the itchy patient, particularly in the absence of widespread skin damage secondary to scratching, is one of the most difficult clinical problems in dermatology. Helpful hints from the history include:

- *The time course* of the itching. This should be carefully defined as to whether it is sudden, as in infestations and urticaria, or chronic, as in chronic skin diseases such as eczema.
- *Localisation* of the pruritus, including the site of onset. For example, in an infant with atopic eczema the cheeks are usually the first site to be affected, whereas scabies almost never affects the face or scalp. Is the itch confined to certain sites, as in localised skin disease such as lichen planus and lichen simplex, or generalised, as in eczema and scabies?
- *Exacerbating factors*, such as heat and exercise in cholinergic urticaria, water in aquagenic pruritus and creams in some forms of eczema. In practice heat or warm water will exacerbate a number of different causes of pruritus and may be less useful diagnostic aids than often stated.
- *Alleviating factors*, which are worth noting but are seldom of great diagnostic help. Some patients discover that cooling below 18 degrees inhibits itch (but not pain). Similarly, other patients discover that a scalding hot bath replaces itch with pain which they find preferable. In the short term most patients seem to prefer cutaneous pain to itch.
- *Involvement of other family members*, as in a scabietic infestation. Insect bites usually only affect one member of the family.
- *General health* of the patient. Has it changed, suggesting an underlying medical disorder?

Examination

Attempt to determine whether there is a primary skin condition or whether the only visible clinical features are due to excoriation with some secondary degree of eczema or infection. Try to classify the patient into one of the three following groups (see Box 21.4):

1. *Generalised pruritus associated with skin disease*. The most common causes of a widespread itchy rash are eczema, usually atopic, and scabies infestation. These can be difficult to distinguish clinically, particularly in children. Secondary eczematisation occurs in scabies, giving rise to eczema-like lesions all over the body. Examine carefully for scabietic burrows, particularly in the finger and toe webs, along the borders of both the hands and the feet and at the wrists, and extract the mite (see p. 1085) to make a definite diagnosis. After treatment pruritus may continue for several weeks. Pruritus is a common skin complaint in pregnancy and may be due to several causes (see Box 21.5).
2. *Local pruritus associated with skin disease*. In these cases careful examination may reveal the underlying primary cutaneous disorder such as lichen planus or psoriasis.
3. *Pruritus with no evidence of skin disease*. The medical conditions that are sometimes associated with pruritus are listed in Box 21.6. In the absence of clues pointing to a primary skin disease detailed physical examination and investigations, including a careful search for lymphadenopathy, may be required. Investigations

21.4 PRURITUS

Skin diseases associated with generalised pruritus	
• Eczema	• Urticaria/dermographism
• Scabies	• Pruritus of old age and xeroderma
Skin diseases associated with localised pruritus	
• Eczema	• Dermatitis herpetiformis
• Lichen planus	• Pediculosis
Pruritus with no evidence of skin disease	

21.5 CAUSES OF PRURITUS IN PREGNANCY

Condition	Gestation and features	Treatment
Obstetric cholestasis	3rd trimester Associated with abnormal liver function tests	Emollients Chlorphenamine (chlorpheniramine) Colestyramine Early delivery
Pemphigoid gestationis	3rd trimester Pruritus followed by blistering Starts around the umbilicus	Topical or oral steroids
Polymorphic eruption (urticarial papules) of pregnancy	3rd trimester, after delivery Polymorphic lesions with urticaria	Chlorphenamine (chlorpheniramine)
Prurigo gestationis	2nd trimester Excoriated papules	Emollients Topical steroids Chlorphenamine (chlorpheniramine)
Pruritic folliculitis	3rd trimester Aseptic pustules on trunk	Topical steroids

should include a full blood count, iron status, urea and electrolytes, liver function tests, thyroid function and possibly a chest radiograph.

Many patients are incorrectly labelled as having itch due to a systemic cause when in reality they have a mild degree of xerosis with perhaps irritation from repeated use of soaps, or another cutaneous primary disorder such as dermographism or aquagenic pruritus.

Management

There are no specific anti-itch drugs. Effective remedies for the conditions that lead to itch do exist, however, such as potent H1 blockade for patients with chronic idiopathic urticaria or corticosteroids for individuals with atopic eczema. Nevertheless, in some instances it is not possible either to define the primary condition or to treat it effectively.

A large number of agents can be used to reduce pruritus including emollients, topical menthol, capsaicin, ultraviolet B and long-wavelength ultraviolet A (PUVA) phototherapy (see p. 1079), as well as opioid antagonists such as naltrexone. Their effects are variable, poorly characterised and require further study. Although frequently the subject of ridicule, significant itch may incapacitate, cause embarrassment, disrupt sleep and ruin the patient's self-image. It is easily under-estimated and trivialised as a symptom.

21.6 MEDICAL CONDITIONS THAT CAUSE PRURITUS

Medical condition	Cause of pruritus	Treatment*
Liver disease		
Cholestasis	Elevated bile salts	Colestyramine Rifampicin Antihistamines UVB
	Central opioid effect	Naloxone
Hepatitis C	Unknown	
Chronic renal disease	Multifactorial: including secondary hyperparathyroidism Elevated plasma histamine	UVB Oral activated charcoal Capsaicin
Blood disease		
Anaemia	Iron deficiency	Iron replacement
Polycythaemia rubra vera	Unknown	
Lymphoma Leukaemia Myeloma	Unknown	
Thyroid disease		
Thyrotoxicosis Hypothyroidism	Generalised due to dry skin Localised may be due to *Candida*	Emollients
HIV infection	Infection, infestation	Treatment of opportunistic infection
	Eosinophilic folliculitis	Local steroids, UVB
	Unknown	UVB
Malignancy	Unknown	
Psychogenic	Unknown	Psychotherapy Anxiolytics Antidepressives

* Added to that of primary condition.

THE SCALY RASH (PAPULOSQUAMOUS ERUPTIONS)

A common presenting complaint in general practice is an eruptive scaly rash sometimes associated with itching. The main causes are listed in Box 21.7. These can usually be distinguished by a discriminating history and examination. Secondary syphilis is an extremely rare cause of an eruptive scaly rash in current medical practice in the UK.

21.7 SUDDEN SCALY RASHES

- Eczema (see p. 1072)
- Psoriasis (see p. 1075)
- Pityriasis rosea
- Lichen planus (see p. 1080)
- Drug eruption (see p. 1099)
- Pityriasis versicolor
- Tinea corporis

History

How long has the rash been present?

Atopic eczema often starts within the first 2 years of life and subsequently fluctuates in extent and severity. Psoriasis can start at any age but usually does so between the ages of 15 and 40 years. Pityriasis rosea affects a similar age group and tends to occur in the autumn and spring. Both pityriasis rosea and drug eruptions have an acute onset, drug eruptions starting within a few days or weeks of taking the drugs. Pityriasis versicolor is a common yeast infection of the body and scalp. It can be acute in onset or persist for many years in the same individual.

Where on the body did it start?

Atopic eczema starts most commonly on the face in infants and then spreads to involve the flexures. However, it can sometimes just affect the extensor surfaces or may be present in coin-like lesions (discoid eczema). Psoriasis is classically present on the extensor surfaces—that is, the elbows and knees. Psoriasis can appear anywhere on the body in small (guttate), medium and large plaques all over the torso and limbs. Lichen planus usually presents as an intensely itchy, localised papular eruption with a characteristic colour and morphology (see p. 1080). Less commonly, it can be widespread and often exhibits the Köbner phenomenon with lichen planus lesions being induced in sites of non-specific trauma (see Fig. 21.17, p. 1080). Pityriasis rosea starts as a single herald patch that can occur anywhere on the body but usually is present on the trunk. This is a solitary erythematous lesion which starts as a papule and enlarges rapidly over a few days. Pityriasis versicolor usually affects the trunk and outer upper arms. Tinea corporis (dermatophyte infection) can occur anywhere on the body and is usually asymmetrical.

How has the rash evolved?

In pityriasis rosea the herald patch is followed in a few days by the appearance of many smaller plaques present mostly on the torso in a 'fir tree' distribution but it can also occur on the neck, extremities and flexures (inverse pityriasis rosea). The herald patch tends to persist throughout the eruption and the whole eruption can last for up to 3 months. Atopic eczema can, at varying stages, be localised or generalised but is a chronic disorder that fluctuates in severity throughout childhood. Psoriasis in the classical form tends to involve the elbows, knees, lower back and scalp. In the guttate (small plaque) variety many small, red, scaly plaques appear on the trunk and may persist for several months. Many cases subsequently develop chronic plaque psoriasis. Tinea corporis is usually a chronic, slowly evolving, often isolated annular lesion. Macular-papular drug eruptions evolve with exfoliation (a shedding of the most superficial portion of the skin) and may leave post-inflammatory hyperpigmentation. Pityriasis versicolor can be very chronic and is often exacerbated by sun exposure; it also becomes more obvious in the tanned individual because of its hypopigmentation and therefore patients often present after their summer holidays. On the other hand, it appears as light brown scaly patches on untanned Caucasoid skin.

Is it itchy?

Atopic eczema is extremely itchy and this is invariably the presenting complaint. Itching is exacerbated by changes in temperature, e.g. on undressing, and contact with irritants such as wool. It is not known why atopic eczema is so itchy and antihistamines have little effect. Drug eruptions and tinea corporis are usually pruritic. Psoriasis and pityriasis rosea are not usually so itchy. The rash of pityriasis versicolor is asymptomatic.

Was there a preceding illness?

Guttate psoriasis is often preceded by a β-haemolytic streptococcal sore throat. A small percentage of people with pityriasis rosea have a prodromal illness with malaise, headache and arthralgia. A patient who develops a morbilliform drug eruption will usually have the same reaction to that specific drug or to chemically related ones on each challenge. Rashes in response to drugs are not common; however, most patients with infectious mononucleosis treated with amoxicillin will develop an erythematous macular-papular rash. It is essential therefore to take a careful history of medications and preceding illnesses at least 4 weeks prior to the onset of the rash.

Is it associated with any systemic symptoms?

Certain drug eruptions can cause systemic upset with fever, malaise and joint pains and are associated with an eosinophilia. In eczema, superinfection can be associated with systemic symptoms of fever and malaise. *Staphylococcus aureus* causing secondary impetiginisation is the most common, but a streptococcus can cause similar features. Herpes simplex virus type 1 causes a widespread, severe, painful, erosive skin eruption in patients with atopic eczema (eczema herpeticum), which is a medical emergency requiring inpatient treatment with intravenous antiviral therapy and medical support. Arthritis occurs in 7% of patients with psoriasis (see p. 1011).

Examination

The distribution of the rash can be very useful in discriminating between the various causes of a scaly rash: flexural, extensor surfaces, truncal, palms and soles, or scalp involvement. Morphologically, these conditions are distinguishable by careful assessment with the use of a magnifying lens. Associated skin features that give useful diagnostic clues can be found by complete skin examination (see Box 21.8).

21.8 CLINICAL FEATURES OF COMMON SCALY RASHES

Type of rash	Distribution	Morphology	Associated clinical signs
Eczema	Face/flexures	Poorly defined erythema and scaling Lichenification	Shiny nails Infraorbital crease 'Dirty neck'
Psoriasis	Extensor surfaces	Well-defined plaques with a silvery scale	Nail pitting and onycholysis Scalp involvement Axillae and genital areas often affected
Pityriasis rosea	'Fir tree' pattern on torso	Well-defined erythematous papules and plaques with collarette of scale	
Drug eruption	Widespread	Macular-papular erythematous scaly areas which merge and are followed by exfoliation	
Pityriasis versicolor	Upper torso and upper shoulders	Hypo- and hyperpigmented scaly patches	
Lichen planus	Distal limbs, esp. volar aspect of wrists Lower back	Shiny, flat-topped violaceous papules with Wickham's striae	White lacy network buccal mucosa Rarely, nail changes
Tinea corporis	Asymmetrical, often isolated, red scaly lesions	Scaly plaques which expand with central healing	Nail involvement (see Fig. 21.29, p. 1089)

ERYTHRODERMA

Eczema, psoriasis, drug eruptions and lichen planus rarely progress to erythroderma, defined as erythema with or without scaling of almost all the body surface. Other causes include cutaneous T cell lymphoma (Sézary's syndrome), the psoriasis-like condition pityriasis rubra pilaris, and rare types of ichthyosis. Erythroderma may occur at any age and is associated with extreme morbidity and rarely mortality. It may appear suddenly or evolve slowly.

Erythrodermic patients may be systemically unwell with shivering, due to loss of temperature control, and pyrexia. The pulse rate may be elevated and the blood pressure low due to volume depletion; examination of the cardiovascular system is therefore essential. Peripheral oedema is a common finding consequent on the erythroderma, low albumin and high-output cardiac failure. Lymph nodes may be enlarged, either reactively, caused by the skin inflammation, or rarely due to lymphomatous infiltration.

URTICARIA (NETTLE RASH, HIVES)

Urticaria refers to an area of focal dermal oedema secondary to a transient increase in capillary permeability. On certain body sites such as the lips or hands the oedema spreads and is traditionally referred to as angio-oedema. By definition the swelling lasts less than 24 hours. Acute urticaria may be associated with angio-oedema of the lips, face, throat and, rarely, wheezing, abdominal pain, headaches and even anaphylaxis. Whilst severe angio-oedema can be life-threatening due to respiratory obstruction, this is exceedingly rare in a dermatological context.

The symptoms and signs of urticaria are due in large part to mast cell degranulation with release of histamine and a variety of other vasoactive mediators. That more than histamine is involved is reflected by the fact that potent histamine blockers, whilst frequently improving the itch of urticaria and the number of weals, do not abolish all the symptoms or signs in many patients (see Fig. 21.3).

Causes of urticaria are listed in Box 21.9. Recently, evidence for an autoimmune pathogenesis for one of the most common forms of urticaria, chronic idiopathic

21.9 CAUSES OF URTICARIA

Acute and chronic urticaria

- Allergens (in foods, inhalants and injections)
- Drugs (see Box 21.33, p. 1100)
- Contact (e.g. animal saliva, latex)
- Physical (e.g. heat, cold, pressure, sun, water)
- Infection (e.g. viral hepatitis, infectious mononucleosis, HIV infection during seroconversion)
- Other conditions (e.g. systemic lupus erythematosus, autoimmunity, pregnancy, intestinal parasites)
- Idiopathic

Urticarial vasculitis

- Hepatitis B
- Systemic lupus erythematosus
- Idiopathic

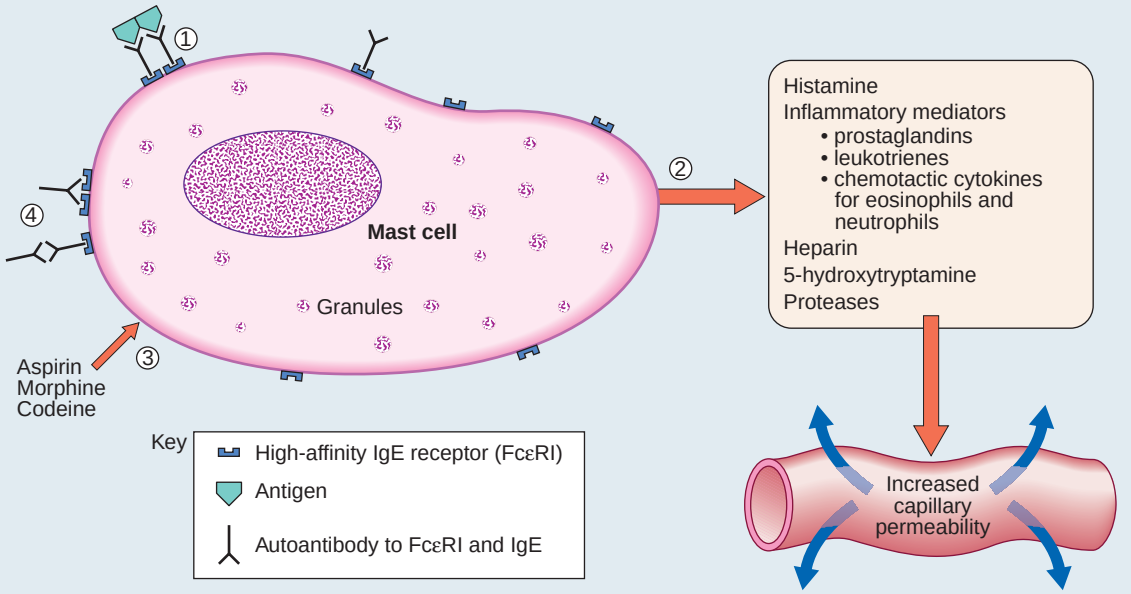


Fig. 21.3 Pathogenesis of urticaria. Mast cell degranulation occurs in a variety of ways. (1) Type I hypersensitivity causing massive degranulation and sometimes anaphylaxis. (2) Spontaneous mast cell degranulation in chronic urticaria. (3) Chemical mast cell degranulation. (4) Autoimmunity, which accounts for 30% of chronic urticaria.

urticaria, has been identified. In this condition, which is defined by the presence of urticarial episodes for over 6 weeks, self-reacting antibodies appear to cause cross-linking of the IgE receptor with subsequent degranulation of the mast cells.

Clinical features

Two questions may be asked:

1. How long does the individual lesion last?
   - < 24 hours (urticaria)
   - > 24 hours (urticarial vasculitis)
2. How long has the condition been present?
   - < 6 weeks (acute urticaria)
   - > 6 weeks (chronic urticaria)

In practice the above questions may be less helpful than is sometimes implied. There may be little mechanistic difference between urticaria of a month's duration and that of 6 months' duration. Both may be treated along similar lines. The length of time an individual weal lasts may also be of limited utility. Urticarial vasculitis is much less common than urticaria and many patients are unable to distinguish the development of new weals and disappearance of old ones from individual weals each of which persists for more than 1 day. It is sometimes helpful to draw around a weal with a pen and examine the patient 24 hours later to try to clarify this issue.

A directed history is still the best way to elicit any causes or precipitants of urticaria. A record of possible allergens, including drugs (see Box 21.33, p. 1100), should be determined. The physical urticarias can be identified by appropriate questions (see Box 21.9) and subsequent medically observed challenge. A family history must be sought in cases of angio-oedema. Examination may reveal nothing, as this is a transient eruption, or may uncover the classical weals, which can vary from papules to large extensive plaques (see Fig. 21.4).

Investigations

These need to be directed at the possible underlying cause as elicited from the clinical history:

- full blood count including eosinophil count in cases of underlying parasites
- erythrocyte sedimentation rate (ESR), which is elevated in cases of vasculitis
- urea and electrolytes, thyroid and liver function tests, which might reveal an underlying disorder

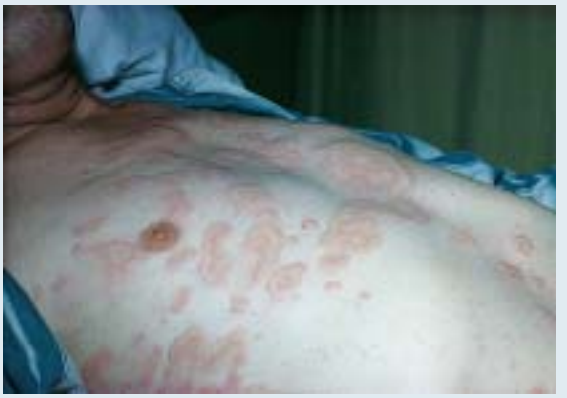


Fig. 21.4 Widespread acute urticaria. In this case urticaria was due to penicillin allergy.

- total IgE and specific IgE to possible allergens, e.g. foods such as shellfish and peanuts
- antinuclear factor in chronic urticaria or urticarial vasculitis
- CH50 as a general guide to complement activation and C_3 and C_4 levels as evidence of complement consumption via both the classical and the alternative pathways.

C_1 esterase inhibitor may be quantitatively reduced or more rarely functionally deficient as in hereditary angio-oedema. A skin biopsy may be helpful if urticarial vasculitis is suspected. Physical urticarias can be confirmed by the appropriate physical challenge. Frequently, no cause can be found for acute episodes, whereas in chronic urticaria the autoimmune pathogenesis will account for the majority of cases.

Management

The practical problem with management of urticaria is that whilst potent non-sedative histamine blockers are available they have little or no effect on the other mediators that also play a contributory role. Non-sedative antihistamines such as loratadine or fexofenadine are effective for perhaps one-third of patients with chronic urticaria, one-third show some moderate benefit whilst the results in the remaining third are minimal. If a patient fails to respond to one of these agents after 2 weeks of therapy, then it may be worth swapping to another non-sedative antihistamine and adding in an H_2-blocker such as cimetidine or ranitidine. A number of other agents have been used including mast cell stabilisers or protease and leukotriene inhibitors, although the evidence of efficacy is not clear. Systemic corticosteroids are widely prescribed for urticaria although surprisingly evidence of their benefit is still contestable. Patients with a history of life-threatening angio-oedema or anaphylaxis should carry a self-administered injection kit of adrenaline (epinephrine). The management of anaphylactic shock is described on page 201.

Urticaria may be precipitated by aspirin or non-steroidal anti-inflammatory drugs. If there is a clear history of these agents precipitating attacks, then they should be avoided. Even in the absence of a clear history it may be advisable to suggest alternatives such as paracetamol (codeine can also induce urticaria).

PHOTOSENSITIVITY

Ultraviolet radiation (UVR, 'sunlight') may improve some skin diseases such as psoriasis and eczema but confusingly may also exacerbate the same diseases and induce a number of specific dermatological conditions—the photosensitive dermatoses or photodermatoses. Usually this is attributable to particular parts of the electromagnetic radiation spectrum including ultraviolet B (UVB) and ultraviolet A (UVA) but rarely visible light may also cause some photodermatoses. The electromagnetic spectrum is shown in Figure 21.5. The causative wavelengths for some of the endpoints are provisional. For instance, UVB is thought to play a more major role in the induction of skin cancer but a role for UVA may also exist. Similarly, skin ageing is due not just to UVA, as is often stated, but also to UVB. Determination of the

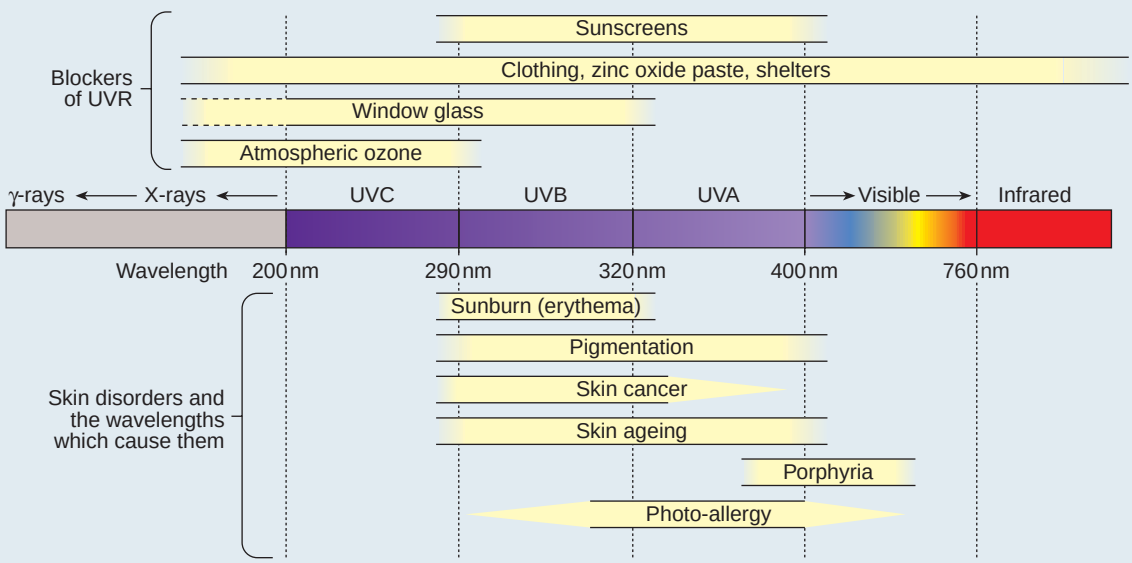


Fig. 21.5 The electromagnetic spectrum. For many conditions the action spectrum is approximate and may vary between patients. (LE = lupus erythematosus)

waveband or wavebands that contribute to sensitivity may be clinically important. For instance, UVB does not pass through window glass whereas UVA does. The practical corollary of this is that patients who are markedly UVA-sensitive need to wear sunblock and be protected even when inside a car or inside a building where there is strong natural light.

Clinical features

The clinical history may give a clear indication that the rash is temporally related to sun exposure, whereas in other cases there is no obvious indication of light aggravation.

When a rash is related to sunshine, then the sites affected tend to be light-exposed ones: the face, particularly the nose and the cheeks but excluding the eyelids, an area under the chin and an area in the shadow of the nose; the dorsa of the forearms and hands, with sparing of the finger webs and palms (see Fig. 21.6).

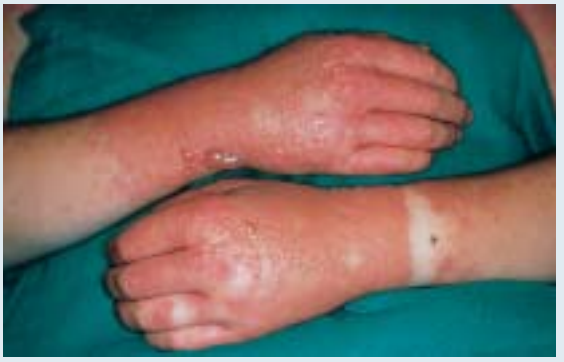


Fig. 21.6 Bullous photosensitive eruption. Note sharp cut-off at wrists, due to protection by shirt sleeves, and sparing of skin under watch and strap.

There are four main groups of photosensitive dermatoses and these are listed in Box 21.10. Confusingly, a photodermatosis that initially appears on some exposed sites may spread to sites which on history appear to have received no exposure to sunlight.

Management

Once a photosensitive eruption is identified on clinical grounds, an attempt should be made to provoke the lesion using phototesting. This may not always be possible. If a drug is suspected and clinical status allows, phototesting should be carried out whilst the individual is on the drug; this allows phototesting to be repeated once the drug has been stopped. Drug causes for photosensitivity are common and include compounds such as quinine, which are often neglected unless a careful and directed clinical history is taken. Treatment is with avoidance of the drug if appropriate, or with topical or occasionally systemic steroids. In chronic cases of photosensitivity, such as chronic actinic dermatitis, azathioprine 100–150 mg/day may be required as further immunosuppression. The main preventative treatment for the photosensitive dermatoses is avoidance of sun exposure and the use of sunscreens.

Sunscreens

Sunscreens act in two different ways: chemical or physical. Chemical sunscreens absorb specific wavelengths of UV radiation. Physical sunscreens reflect UV radiation and visible light. Most available products are a combination of UVA and UVB chemical sunscreens. If the individual is sensitive to visible light as well as ultraviolet radiation, then the agents that block visible light will be visible and often cosmetically undesirable.

Sunblocks are often graded in terms of the sun protection factor (SPF), the ratio of the time it takes to induce a

21.10 THE PHOTOSENSITIVE DERMATOSES

Cause	Condition	Clinical features
Drugs	Phototoxic drug eruption	Common; exaggerated sunburn occurs minutes after sun exposure Caused by phenothiazines, amiodarone, tetracyclines
	Photo-allergic drug eruption	Occurs more than 24 hours after sun exposure; causes a dermatitis or lichen planus-like reaction Caused by thiazides, enalapril, hydroxychloroquine, phenothiazines, or topical, e.g. fragrances Can become permanent (persistent light reactor)
Metabolic	Porphyrias	Particularly porphyria cutanea tarda (see p. 326)
	Pellagra	Diarrhoea, dementia, dermatitis due to dietary lack of tryptophan
Exacerbation of pre-existing conditions	Lupus erythematosus	See page 1034
	Erythema multiforme	See page 1098
	Herpes simplex	See page 30
Idiopathic	Polymorphic light eruption	Itchy papulo-vesicular eruption on exposed sites within hours of UV exposure
	Solar urticaria	Urticaria after 1-hour exposure
	Chronic actinic dermatitis	Disabling, itchy dermatitis on exposed sites in elderly men

certain degree of redness with and without sunblock. A sunblock with an SPF of 2 therefore affords 50% reduction whereas a sun protection factor of 10 blocks 90% of the radiation. It follows that the additional value of sunblocks with a very high sun protection factor become trivial over, say, SPF 15.

BLISTERS

Loss of keratinocyte-keratinocyte adhesion or loss of adhesion of keratinocytes to the basement membrane or of the basement membrane to the dermis leads to a potential space which, because of negative extracellular pressure, fills with fluid: a blister. There is an artificial distinction made by some between small (vesicles, < 0.5 cm) and large blisters (bullae, > 0.5 cm). The site of blister formation within the skin therefore depends on the aetiology and underlying pathogenesis.

Blisters are an important physical sign with a limited differential diagnosis but they can be very difficult to see. If a blister occurs high up in the epidermis (intraepidermal) and is due to a defect in cohesion of the keratinocytes, then the blister may be so fragile that only an erosion is seen (e.g. pemphigus foliaceus). On the other hand, a blister at the level of the basement membrane, as occurs in dermatitis herpetiformis, might be missed because the roof of the blister is easily destroyed due to the itch and resulting scratch. Blisters in the skin can occur at any age and may be caused by common infections or rare genetic skin diseases that can continue throughout life.

21.11 CAUSES OF BLISTERING AT BIRTH

- Herpes simplex
- Impetigo
- Bullous ichthyosiform erythroderma
- Epidermolysis bullosa (see Box 21.12)
- Incontinentia pigmenti

The main causes of blistering presenting at birth are listed in Box 21.11.

Assessment

The history of the onset of blistering, any predisposing events such as drug ingestion, and family history are of paramount importance. In infants blistering at birth is usually due to infection and more rarely to genetic skin diseases such as epidermolysis bullosa. There are several types of epidermolysis bullosa, as seen in Box 21.12, and studies of these disorders over the last 10 years have contributed enormously to our understanding of the biology of keratins and basement membrane. Adults who present with a blistering skin condition need to be assessed according to Box 21.13. At all ages, it is important to exclude both viral and bacterial infection as a cause of blistering and this is easily done by taking a swab from the blister fluid for bacterial assessment by both microscopy and culture. A similar sterile swab can be placed in viral culture medium and, in the case of the herpes virus, immediate electron microscopy or immunofluorescence performed on a sample of the blister fluid smeared on to a slide.

Toxic epidermal necrolysis is a severe form of widespread blistering that can occur at any age and is often due

21.12 DIFFERENT TYPES OF EPIDERMOLYSIS BULLOSA

Type	Mode of inheritance	Level of blister	Abnormal protein	Clinical features
Simple	Autosomal dominant	Epidermal basal cell	Keratins 5 and 14	Usually just blisters on palms and soles No scarring; nails normal; no oral involvement Rare recessive type associated with muscular dystrophy (plectin mutation)
Junctional	Autosomal recessive	Lamina lucida	Laminin-5 and $\alpha_6\,\beta_4$ integrin	Large, raw areas and flaccid blisters at birth Common around mouth and anus; heal slowly Nails and oral mucosa involved Often lethal May be diagnosed prenatally by chorionic villus sampling
Dystrophic	Autosomal dominant	Dermis below lamina densa	Collagen VII	Blisters on knees, elbows and fingers Healing with scarring and milia Nails may be involved Mouth seldom affected
	Autosomal recessive	Dermis below lamina densa	Collagen VII	Blisters often present at birth; seen on hands, feet, elbows and knees Heal with scarring which is so severe that digits may be lost Milia present Oral and oesophageal blistering followed by scarring/stricture Abnormal teeth Increased incidence of cutaneous squamous cell carcinoma in early adulthood

to drugs. It is a life-threatening condition as the skin peels off in thin sheets causing severe problems with fluid balance and temperature control as well as pain and infection. Intensive care management is indicated, with careful haemodynamic monitoring and high suspicion of secondary infection. Once the causative agent is removed the skin can rapidly re-epithelialise but toxaemia often leads to death in extensive cases. There is no convincing evidence that systemic corticosteroids work in this condition but there is some recent and persuasive but uncontrolled evidence that intravenous immunoglobulin may be helpful.

If there is no evidence of infection and the diagnosis is not apparent from the more common conditions listed in Box 21.13, then a skin biopsy should be taken for histological assessment and a frozen sample for direct immunofluorescence. The clinical and immunopathological findings for the immunobullous disorders are documented in Box 21.14. In the case of the rare genetic skin

21.13 CAUSES OF ACQUIRED BLISTERS

		Generalised	
	Localised	**With mucosal involvement**	**With no mucosal involvement**
Vesicular	Herpes simplex Herpes zoster Impetigo Pompholyx	Eczema herpeticum	Eczema herpeticum Dermatitis herpetiformis Epidermolysis bullosa acquisita
Bullous	Impetigo Bullous cellulitis Bullous stasis oedema Acute eczema Insect bites Fixed drug eruptions	Pemphigus Bullous erythema multiforme/ Stevens–Johnson syndrome Toxic epidermal necrolysis	Acute eczema Erythema multiforme Bullous pemphigoid Epidermolysis bullosa acquisita Bullous lupus erythematosus Pseudoporphyria Porphyria cutanea tarda Drug eruptions, e.g. barbiturates

21.14 CLINICAL FEATURES AND SKIN BIOPSY FINDINGS IN SOME IMMUNE-MEDIATED BLISTERING SKIN CONDITIONS

Disease	Age	Site of blisters	Nature of blisters	Mucous membrane involvement	Antigen	Circulating antibody (indirect IF)	Fixed antibody (direct IF)	Treatment
Pemphigus vulgaris	40–60 yrs	Torso, head	Flaccid and fragile, many erosions	100%	Desmoglein-3 (120kD)	IgG	IgG, C_3 intercellular (epidermal)	Steroids Cyclo-phosphamide
Bullous pemphigoid (see Fig. 21.7)	60s and over	Trunk (esp. flexures) and limbs	Tense	Occasionally	BP-220 (part of hemidesmosome)	IgG (70%)	IgG, C_3 at BMZ	Steroids Azathioprine
Dermatitis herpetiformis	Young, associated with coeliac disease	Elbows, lower back, buttocks	Excoriated and often not present	No	Unknown	None	Granular IgA in papillary dermis	Dapsone Gluten-free diet
Pemphigoid gestationis	Young pregnant female	Periumbilical and limbs	Tense	Rare	Collagen XVII (part of hemidesmosome BP-180)	IgG	C_3 at BMZ	Steroids
Epidermolysis bullosa acquisita	All ages	Widespread	Tense, scarring	Common (50%)	Type VII collagen	IgG (anti-type VII collagen)	IgG at BMZ	Poor response to steroids Cyclo-phosphamide Methotrexate Azathioprine
Bullous lupus erythematosus	Young, black female	Widespread	Tense	Rare	Type VII collagen	Anti-type VII collagen	IgG, IgA, IgM at BMZ	Dapsone

Note Pemphigus is characterised by an intraepidermal level of blistering (superficial). All the other conditions above have a subepidermal level of blistering. (BMZ = basement membrane zone)

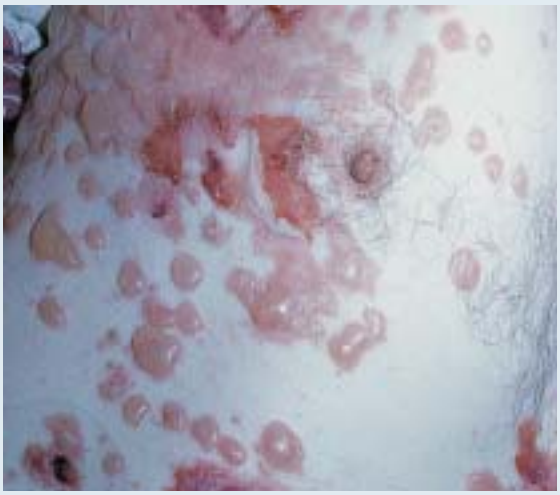


Fig. 21.7 Bullous pemphigoid. Large tense and unilocular blisters clustered in and around the axilla.

diseases a portion of the skin biopsy is processed for electron microscopy and immunofluorescence to enable a more accurate assessment to be made of the site of blistering. Further investigation is necessary for certain blistering conditions:

- *Pemphigus*. This is associated with underlying malignancy including lymphoma in a small proportion of patients ('paraneoplastic pemphigus'). Therefore a complete physical examination is mandatory and investigations including full blood count, erythrocyte sedimentation rate, urea and electrolytes, liver function tests, chest radiograph and any other directed scans should be performed.
- *Dermatitis herpetiformis*. This is associated with coeliac disease (see p. 792) and therefore all patients with this diagnosis should have blood taken for an anti-endomysial and antigliadin antibody screen, and a jejunal biopsy should be performed if indicated.
- *Epidermolysis bullosa acquisita (EBA)*. This is associated with inflammatory bowel disease, multiple myeloma and lymphoma (see pp. 808, 938 and 943), and these conditions should therefore be excluded.
- *Bullous lupus erythematosus*. It is important to follow patients with bullous lupus erythematosus for activity of their systemic disease (see p. 1034). There is a high incidence of clinically significant glomerulonephritis (> 90%).
- *Porphyria cutanea tarda and pseudoporphyria* (see pp. 1097–1098).

LEG ULCERS

Ulceration of the skin is the complete loss of the epidermis and part of the dermis. When present on the lower leg, it is usually due to vascular disease and the vast majority (75%) of cases are due in part to venous hypertension. The site of ulceration on the lower leg can give a good indication of the underlying cause (see Fig. 21.8), although this is not an absolute guide. For each cause of leg ulceration there are several different underlying pathologies that have to be considered (see Box 21.15).

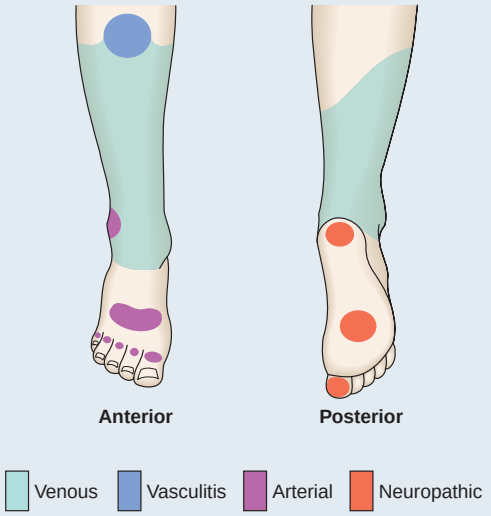


Fig. 21.8 Causes of lower leg ulceration.

21.15 MAIN CAUSES OF LEG ULCERATION

Venous hypertension	
• See text	
Arterial disease	
• Atherosclerosis • Vasculitis	• Buerger's disease
Small vessel disease	
• Diabetes mellitus	• Vasculitis
Abnormalities of blood	
• Sickle-cell disease • Cryoglobulinaemia	• Spherocytosis • Immune complex disease
Neuropathy	
• Diabetes mellitus • Leprosy	• Syphilis
Tumour	
• Squamous cell carcinoma • Basal cell carcinoma	• Malignant melanoma • Kaposi's sarcoma
Trauma	
• Injury	• Artefact

Assessment

The history of the onset of the leg ulceration and any underlying predisposing conditions should be sought. Then the site and surrounding skin should be carefully assessed. The appropriate investigations should include:

- *Urinalysis* for glycosuria.
- *Full blood count* to detect anaemia and blood dyscrasias.
- *Bacterial swab* to detect pathogens. Systemic antibiotics are only required if there is a purulent discharge, rapid extension, cellulitis, lymphangitis or septicaemia.
- *Doppler ultrasound* to assess arterial circulation if the peripheral pulses cannot be felt. If the ankle systolic pressure divided by the brachial systolic pressure is > 0.8, then there is insignificant arterial disease. (An exception to this rule occurs in some patients with peripheral vascular disease associated with diabetes, in whom arterial calcification of the lower limb vessels produces a spuriously high ankle/brachial index.)
- *Venography*, which is occasionally useful in detecting surgically remediable venous incompetence.
- *Duplex scanning*, if available.

The main conditions and the differences between them are discussed below.

EBM

LEG ULCER—assessment and management of chronic venous leg ulcers

'Peripheral arterial supply should be assessed in all patients by hand-held Doppler. Those individuals with an ankle/brachial pressure ratio (ABP) < 0.8 should be assumed to have arterial disease and therefore not able to tolerate compression bandaging. In those individuals with an ABP > 0.8, graduated compression bandaging is essential for effective treatment.'

- Moffat CJ, Oldroyd MI, Greenhalgh RM, Franks PJ. Palpating ankle pulses is insufficient in detecting arterial insufficiency in patients with leg ulceration. Phlebology 1994; 9:170–172.
- Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. BMJ 1997; 315:570–580.
- The care of patients with chronic leg ulcer. A National Clinical Guideline. Scottish Intercollegiate Guidelines Network, Royal College of Physicians of Edinburgh, July 1998.

Further information: www.sign.ac.uk

LEG ULCERATION DUE TO VENOUS DISEASE

Damage to the venous system of the leg results in oedema, haemosiderin deposition, eczema, fibrosis and ulceration.

Aetiology

In the normal leg there is a superficial low-pressure venous system connected to the deep, high-pressure veins by perforating veins. Muscular activity, aided by valves in the veins, pumps blood from the superficial to the deep system and towards the heart. Incompetent valves in the deep and perforating veins result in the retrograde flow of blood to the superficial system ('venous hypertension'), causing a rise in capillary hydrostatic pressure. Fibrinogen is forced out through the capillary walls and fibrin is deposited as a pericapillary cuff. One theory postulates that growth and repair factors are trapped in the macromolecular cuff so that minor trauma cannot be repaired and ulcers develop.

Incompetent veins leading to venous hypertension may be due to previous deep vein thrombosis (see pp. 908 and 953), congenital or familial valve incompetence, infection or deep venous obstruction (e.g. from a pelvic tumour).

Clinical features

The problem usually starts in middle age. Leg ulcers are more likely to occur and to persist in obese people. Varicose veins, although often present, are not inevitable. The first symptom is frequently heaviness of the legs, followed by the development of oedema. Haemosiderin pigmentation and ivory-coloured scarring may then be seen, sometimes associated with venous eczema (see p. 1074). The signs progress to lipodermatosclerosis, firm induration due to fibrosis of the dermis and subcutis, which may produce the well-known 'inverted champagne bottle' appearance. Ulceration, often precipitated by minor trauma or infection, soon occurs. Ulcers are seen typically around the medial malleolus but may encircle the ankle (see Fig. 21.9). If conditions are favourable, the ulcers will heal by granulation with small epithelial islands at the base and epithelial growth from the edges. Healing is often slow and may never be complete. Recurrent ulceration is common even after good healing.

Complications

Chronic venous ulcers are invariably colonised by bacteria. Only if infection becomes overt (see above) is systemic antibiotic treatment required. Contact dermatitis to an ointment, dressing or bandage is not uncommon. The usual culprits are preservatives, lanolin and neomycin.

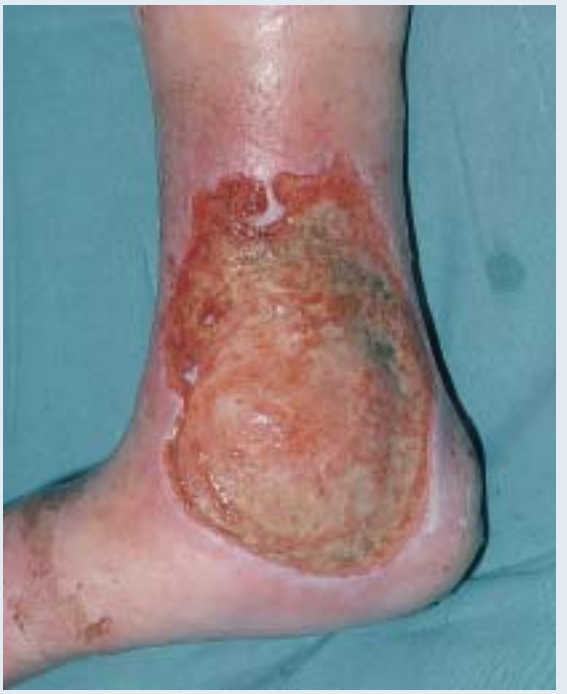


Fig. 21.9 A large venous ulcer overlying the medial malleolus.

Lipodermatosclerosis may cause lymphoedema, leading to hyperkeratosis and the so-called 'mossy foot'. A squamous cell carcinoma developing in a venous ulcer (Marjolin's ulcer) is rarely responsible for its failure to heal.

Management

- General management includes dietary advice for the obese and encouragement to take gentle exercise.
- Oedema should be reduced by the regular use of compression bandages, keeping the legs elevated when sitting and the judicious use of diuretics.
- The exudate and slough should be removed with normal saline solution, 0.5% aqueous silver nitrate or 5% aqueous hydrogen peroxide. If the ulcer is very purulent, soaking the leg for 15 minutes in 1:10 000 dilution of aqueous potassium permanganate may be helpful.
- Dressings commonly used for venous ulceration include antibiotic-impregnated tulle dressings, non-adhesive absorbent dressings (alginates, charcoals, hydrogels or hydrocolloids) and dry non-adherent dressings.
- The frequency of dressings depends on the state of the ulcer. Very purulent and exudative ulcers may need daily dressings whilst the dressing on a clean, healing ulcer may only require changing every week.
- Paste bandages, impregnated with zinc oxide or ichthammol, help to keep dressings in place and provide protection.
- Surrounding venous eczema is treated by a mild or moderately potent topical corticosteroid. The steroid should not be applied to the ulcer itself.
- Oral antibiotic therapy, given in short courses, is only necessary for the treatment of overt infection (see above). An anabolic steroid, stanozolol, may help lipodermatosclerosis but side-effects (fluid retention, hepatotoxicity) may limit its use.
- In the absence of any evidence of compromised arterial supply, graduated compression bandages applied from the toes to the knees enhance venous return and have been shown to be most beneficial in the healing of venous leg ulcers.
- Vein surgery may help some younger patients with persistent venous ulcers. Pinch grafts may hasten the healing of clean ulcers but do not influence their rate of recurrence.

LEG ULCERATION DUE TO ARTERIAL DISEASE

Deep, painful and punched-out ulcers on the lower leg, especially if they occur on the shin and foot and are preceded by a history of intermittent claudication, are likely to be due to arterial disease. Risk factors include smoking, hypertension, diabetes mellitus and hyperlipidaemia. The foot is cyanotic and cold, and the skin surrounding the ulcer is atrophic and hairless. The peripheral arterial pulses are absent or reduced. Doppler studies are required and then, if arterial insufficiency is confirmed, compression bandaging should be prohibited and advice from a vascular surgeon sought.

LEG ULCERATION DUE TO VASCULITIS

These ulcers start as painful, palpable, purpuric lesions turning into small punched-out ulcers. The involvement of larger vessels is heralded by painful nodules which may ulcerate. The intractable, deep, sharply demarcated ulcers of rheumatoid arthritis are due to an underlying vasculitis (see p. 1040). Management includes treatment of the underlying disorder as well as immunosuppression with, for example, steroids or cyclophosphamide.

LEG ULCERATION DUE TO NEUROPATHY

The most common cause of a neuropathic ulcer is diabetes. The ulcers occur over weight-bearing areas such as the heel. Microangiopathy also contributes to ulceration in diabetes. This is discussed in detail on page 677.

TOO LITTLE OR TOO MUCH HAIR

A patient who complains of too little or too much hair should be treated with sensitivity. These complaints may cause genuine morbidity. The causes are numerous and varied but a systematic approach to the history and examination can easily be used to elicit the correct diagnosis.

Hair undergoes a regular cycle of growth. Each cycle is independent of its neighbours in humans, whereas moulting animals, for instance, have hairs in a synchronous cycle. At any one time and depending on the age and sex of the person, up to 90% of hair follicles can be in anagen, the growing phase, and only 10% in telogen, the resting phase when hairs are normally shed. An alteration in this ratio can lead to an increased rate of hair loss and thus an impression of impending baldness.

ALOPECIA

The term means nothing more than loss of hair. There are many causes and patterns (see Box 21.16).

A detailed history, careful scalp examination and complete physical examination should enable a confident diagnosis to be made.

Tinea capitis

Fungal scalp infections are becoming increasingly common in urban areas in the UK. The clinical features can be variable but it usually affects children, causing patchy hair loss with some scaling. Any individual who develops

21.16 CLASSIFICATION OF ALOPECIA

Localised	Diffuse
Non-scarring	
Tinea capitis	Androgenetic alopecia
Alopecia areata	Telogen effluvium
Androgenetic alopecia	Metabolic
Traumatic (trichotillomania, traction, cosmetic)	Hypothyroidism
	Hyperthyroidism
Syphilis	Hypopituitarism
	Diabetes mellitus
	HIV disease
	Nutritional deficiency
	Liver disease
	Post-partum
	Alopecia areata
	Syphilis
Scarring	
Idiopathic	Discoid lupus erythematosus
Developmental defects	Radiotherapy
Discoid lupus erythematosus	Folliculitis decalvans
Herpes zoster	Lichen planus pilaris
Pseudopelade	
Tinea capitis/kerion	

an area of hair loss and scaling in the scalp should have the area scraped and affected hairs plucked for mycological microscopy and culture. Associated inflammation accounts for the variable presentation. Anthropophilic fungal infections (spread from child to child) account for the majority of cases in urban areas. Endothrix (within the hair shaft) infections, e.g. *Trichophyton tonsurans*, cause relatively uninflamed patchy baldness with breakage of the hairs at the skin surface ('black dot'). There is no fluorescence under Wood's light.

Ectothrix (outside the hair shaft) species of fungi, such as *Microsporum audouinii* (anthropophilic), show minimal inflammation; *Microsporum canis* (from dogs and cats) infections are more inflamed and can be identified by green fluorescence with Wood's light. Kerions are boggy, highly inflamed areas of tinea capitis and are usually caused by zoophilic (from animals, e.g. cattle ringworm) species of fungi (e.g. *Trichophyton verrucosum*).

Treatment is systemic, with either oral terbinafine, griseofulvin or itraconazole. Topical therapy, such as an antifungal shampoo, is recommended as an adjunct and arachis oil is used to remove crusting. Kerions sometimes require short courses of oral steroids in addition to systemic antifungal therapy to reduce the inflammation.

Accurate diagnosis and identification of the culprit fungus allows not only treatment but also control of the spread of infection.

Alopecia areata

This non-scarring condition appears as sharply defined non-inflamed bald patches, usually on the scalp (see p. 1050). During the active stage of hair loss pathognomonic 'exclamation mark' hairs are seen (broken-off hairs 3–4 mm long, which taper off towards the scalp—see Fig. 21.10). An uncommon diffuse pattern on the scalp is recognised. The condition may affect the eyebrows, eyelashes and beard. Pitting and longitudinal wrinkling of the nail may be seen. The hair usually regrows spontaneously in small bald patches, but the outlook is less good with larger patches and when the alopecia appears early in life or is associated with atopy. Alopecia totalis describes complete loss of scalp hair and alopecia universalis complete loss of all hair. There is an association of alopecia areata with autoimmune disorders, atopy and Down's syndrome.

Fig. 21.10 Alopecia areata. Marked hair loss with diagnostic exclamation mark hairs.

Androgenetic alopecia

Male-pattern baldness is physiological in men over 20 years old, though rarely it may be extensive and develop at an alarming pace in the late teens. It also occurs in females, most obviously after the menopause. The well-known distribution (bitemporal recession and then crown involvement) is described as 'male-pattern' but this type of hair loss in females is often diffuse.

Investigations

Laboratory tests, including a full blood count, erythrocyte sedimentation rate, urea and electrolytes, liver and thyroid function tests, an autoantibody profile and *Treponema pallidum* haemagglutination (TPHA) test, should help determine the cause of non-scarring alopecia. More specialised tests, including the hair pluck test where up to 50 hairs are removed with epilating forceps to determine the anagen:telogen ratio, are seldom necessary. Mycological assessment is advisable in cases of localised hair loss with scaling. A scalp biopsy, with direct immunofluorescence, may help to confirm a diagnosis of lichen planus of the scalp or discoid lupus erythematosus.

Management

Successful treatment of alopecia is difficult and management of these patients includes support and reassurance. Any underlying condition should be treated. Alopecia areata sometimes responds to topical or intralesional

steroids such as 0.3 ml triamcinolone (10 mg/ml). Some patients with androgenetic alopecia may be helped by systemic finasteride or topical 2% minoxidil solution. In females, anti-androgen therapy such as cyproterone acetate is used. A wig may be the most appropriate treatment for extensive alopecia. Scalp surgery and autologous hair transplants are expensive but sometimes effective in androgenetic alopecia.

HIRSUTISM

Hirsutism is the growth of terminal hair in a male pattern in a female. It should be distinguished from hypertrichosis, which describes the excessive growth of terminal hair in either sex in a non-androgenic distribution.

Hirsutism is often racial (e.g. Mediterranean Caucasians and Asians) and familial. Some degree of hirsutism is common after the menopause. The cause of most cases of hirsutism is unknown and only a small minority have a demonstrable hormonal abnormality.

Investigations

Full endocrinological investigations are required if hirsutism:

- occurs in childhood
- is of sudden onset
- is accompanied by signs of virilisation
- is associated with menstrual irregularity or cessation.

In addition to the screening tests for hyperandrogenism (see p. 709), Cushing's syndrome needs to be excluded (see p. 721).

Management

Depilatory creams, waxing, electrolysis, bleaching and shaving are often used for physiological hirsutism.

Any remediable cause should be corrected by medical and surgical methods, sometimes with the help of the endocrinologist or gynaecologist (see p. 710). Oral anti-androgens may be helpful.

VULVAL ITCH (PRURITUS VULVAE)

Pruritus vulvae is a distressing symptom that can occur at any age and can be difficult to diagnose. Chronic scratching of the vulval area leads to lichenification which, in this site, can be asymmetrical and associated with quite marked oedema and swelling. The history is important to give an indication of the underlying cause. Pre-existing skin disease, such as atopic eczema, psoriasis or fungal infections, needs to be sought and an autoimmune history might be associated with lichen sclerosus et atrophicus. It is important to determine if there is a previous history of sexually transmitted diseases, particularly genital warts or cervical dysplasia found on colposcopy. The main dermatological causes of itch in the vulval area are candidiasis (consider underlying diabetes), tinea cruris (dermatophyte infection), eczema (including contact dermatitis), psoriasis, lichen sclerosus and, less commonly, lichen planus. These can usually be differentiated by careful examination, bacteriological and mycological assessment and a search for evidence of similar skin disease elsewhere on the body. A well-defined, bright red plaque on the vulva can indicate psoriasis, particularly with skin, scalp or nail signs of this condition; oral lesions are often seen in lichen planus and this condition is often followed by marked post-inflammatory hyperpigmentation; lichen sclerosus is characterised by ivory papules that coalesce into pale plaques, with an atrophic surface (reminiscent of crinkly cigarette paper). There is sometimes associated haemorrhagic blistering. Lichen sclerosus often forms a 'figure of eight' around the vulva and perineal area and can cause scarring of the vulva with loss of normal contours culminating in stenosis of the introitus secondary to labial fusion. Biopsy for histology is occasionally needed to differentiate these conditions and in lichen sclerosus to assess any malignant change in, for example, non-healing areas.

Histology is always needed in the next group of itchy vulval lesions, neoplasia. Most tumours of the vulva can provoke the symptom of itch—in particular, vulval (squamous) intraepithelial neoplasia (VIN) and extramammary Paget's disease. Lesions of VIN can be solitary or multiple and may appear red, white, pigmented, warty, moist or eroded. As well as being itchy, VIN can be painful, particularly with superficial dyspareunia. There may be very little to see with the naked eye and then vulvoscopy is needed. In younger women there is a strong association of VIN with the papillomavirus, immunosuppression and possibly smoking. Extramammary Paget's disease is rare, is usually asymmetrical and can be painful. It presents as a moist, red, scaly patch often mistaken for eczema; hence the importance of biopsy in 'unresponsive eczema'.

Finally, it has been shown that a proportion of vulval itch is psychogenic; certainly vulval disease can be associated with psychological distress so careful consultation and an understanding doctor are essential to a correct diagnosis of this condition.

ISSUES IN OLDER PEOPLE
COMMON SKIN DISEASES

- About 40% of individuals over the age of 60 years have significant dermatological problems.
- The most common diseases in this age group are:
  - —skin cancers
  - —leg ulcers, a major cause of morbidity in the elderly
  - —blistering disorders
  - —herpes zoster (shingles) and post-herpetic neuralgia
  - —inflammatory skin diseases, e.g. asteatotic, varicose and seborrhoeic eczema, psoriasis
  - —lichen sclerosus
  - —scabies
  - —lymphoedema
  - —pruritus of old age
  - —drug-related rashes.

ECZEMA

The terms 'eczema' and 'dermatitis' are synonymous. They refer to distinctive reaction patterns in the skin, which can be either acute or chronic and are due to a number of causes.

Histopathology

In the acute stage oedema of the epidermis (spongiosis) progresses to the formation of intraepidermal vesicles, which may enlarge and rupture. In the chronic stage there is less oedema and vesiculation but more thickening of the epidermis (acanthosis); this is accompanied by a variable degree of vasodilatation and T-helper lymphocytic infiltration in the upper dermis.

Clinical features

There are several patterns of eczema (see Box 21.17); some of these have identifiable environmental causes whereas others are more complex. The clinical signs are similar in all types of eczema and vary according to the duration of the rash. The features of acute and chronic eczema are listed in Box 21.18.

Atopic eczema

Atopy is a genetic predisposition to form excessive IgE which leads to a generalised and prolonged hypersensitivity to common environmental antigens, including pollen and the house dust mite. Atopic individuals manifest one or more of a group of diseases that includes asthma, hay fever, urticaria, and food and other allergies, and this distinctive form of eczema. These atopic conditions tend to run true to type within each family. Atopic eczema has clear diagnostic criteria, which are listed in Box 21.19.

21.17 CLASSIFICATION OF ECZEMA

- Atopic
- Seborrhoeic
- Discoid
- Irritant
- Allergic
- Asteatotic
- Gravitational
- Lichen simplex
- Pompholyx

21.18 THE ECZEMA REACTION

Acute

- Redness and swelling, usually with ill-defined margins
- Papules, vesicles and, more rarely, large blisters
- Exudation and cracking
- Scaling

Chronic

- May show all of the above features, though it is usually less vesicular and exudative
- Lichenification, a dry leathery thickening with increased skin markings, is secondary to rubbing and scratching
- Fissures and scratch marks
- Pigmentation changes (hypo- and hyper-)

21.19 DIAGNOSTIC CRITERIA FOR ATOPIC ECZEMA

Itchy skin and at least three of the following:

- History of itch in skin creases (or cheeks if < 4 years)
- History of asthma/hay fever (or in a first-degree relative if < 4 years)
- Dry skin (xeroderma)
- Visible flexural eczema (cheeks, forehead, outer limbs if < 4 years)
- Onset in first 2 years of life

Aetiology. The inheritance of atopic eczema is controversial. The disorder is concordant in 86% of monozygotic twins but in only 21% of dizygotes. Atopic diseases show maternal imprinting—that is, they are inherited more often from the mother than from the father. A polygenic mode of inheritance is likely. More than one genetic locus has been identified that might play a role in the inheritance of atopy and more specifically atopic eczema.

The prevalence of atopic eczema is rising and has increased between twofold and fivefold over the last 30 years. It now affects 1 in 10 schoolchildren. Environmental factors, such as exposure to allergens either in utero or during childhood, have been shown to have a role in the aetiology of atopic eczema.

Pathogenesis. The pathogenesis of atopic eczema is complex and still incompletely understood. It is best considered as an interplay of genetic susceptibility that causes epidermal barrier dysfunction and abnormal immune responses, which are then stimulated by different environmental factors.

EBM

ATOPIC ECZEMA—are there intervention strategies that reduce the incidence of atopic eczema?

'Specific nutritional restrictions in maternal diet during pregnancy have no effect on the incidence of atopic eczema in an infant at hereditary risk and may adversely affect maternal and/or fetal nutrition. Breastfeeding, however, appears to reduce the prevalence of atopic eczema in early childhood.'

- Kramer MS. Maternal antigen avoidance during pregnancy for preventing atopic disease in infants of women at high risk (Cochrane Review). Cochrane Library, issue 1, 2001. Oxford: Update Software.
- Saarinen UM, Kajosaari M. Breastfeeding as prophylaxis against atopic disease: prospective follow-up study until 17 years old. Lancet 1995; 346:1065–1069.
- Chandra RK. Five year follow-up of high risk infants with family history of allergy who were exclusively breast-fed or fed partial whey hydrosylate, soy, and conventional cow's milk formulas. J Pediatr Gastroenterol Nutr 1997; 24:380–388.

Further information: www.cochranelibrary.com

21.20 ATOPIC ECZEMA: DISTRIBUTION AND CHARACTER OF RASH

Infancy

- The eczema is often acute and involves the face and trunk
- The napkin area is frequently spared

Childhood

- The rash settles on the backs of the knees, fronts of the elbows, wrists and ankles (see Fig. 21.11)

Adults

- The face and trunk are once more involved; lichenification is common

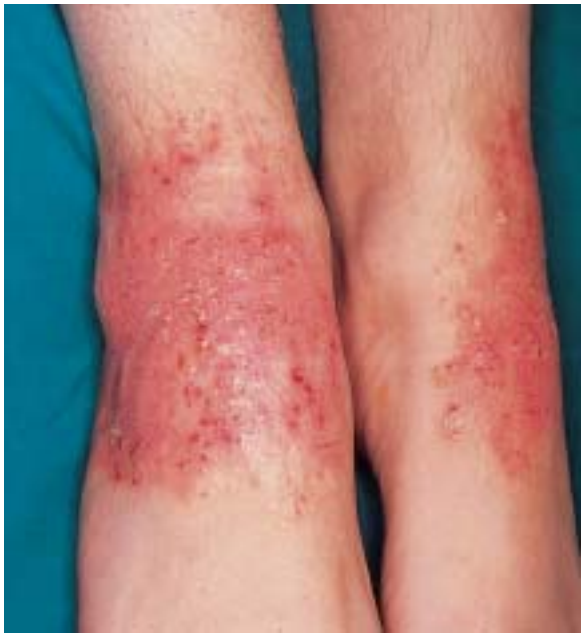


Fig. 21.11 Atopic subacute eczema on the fronts of the ankles of a teenager. These are sites of predilection, along with the cubital and popliteal fossae, in atopic eczema.

Clinical features. The cardinal feature of atopic eczema is itch, and scratching may account for many of the signs. Widespread dryness of the skin is another feature. The distribution and character of the rash vary with age, as shown in Box 21.20. Complications are listed in Box 21.21.

21.21 COMPLICATIONS OF ATOPIC ECZEMA

- Superinfection most often with bacteria *(Staphylococcus aureus)* but also importantly with viruses. Herpes simplex virus causes a widespread severe eruption—eczema herpeticum. Papillomavirus and molluscum contagiosum superinfections are also more common and are encouraged by use of local steroids
- Irritant reactions due to defective barrier function
- Sleep disturbance, loss of schooling and behavioural difficulties
- Children with atopic eczema have an increased incidence of food allergy, particularly to eggs, cow's milk, protein, fish, wheat and soya. These foods cause an immediate urticarial eruption rather than exacerbating their eczema

Seborrhoeic eczema

This condition which is characterised by a red scaly rash classically affects the scalp (dandruff), central face, nasolabial folds, eyebrows and central chest. It is due to *Pityrosporum ovale* infection of the skin. In its milder forms it is the same as dandruff, whereas when severe it may resemble psoriasis. Sebum may be permissive for the development of the rash but otherwise the name is a poor one. Treatment of *P. ovale* with anti-yeast agents improves the rash although the course may need to be repeated. Seborrhoeic eczema is a feature of AIDS and can be very severe in this condition.

Discoid eczema

This is a common form of eczema recognised by discrete coin-shaped lesions of eczema seen on the limbs of young men, associated with alcohol excess, and of elderly men. It can occur in children with atopic eczema and tends to be more stubborn to treat.

Irritant eczema

Detergents, alkalis, acids, solvents and abrasive dusts are common causes. There is a wide range of susceptibility to weak irritants. Irritant eczema accounts for the majority of industrial cases and work loss. The elderly, those with fair and dry skin, and those with an atopic background (personal or family history of asthma, hay fever or eczema) are especially vulnerable. Napkin eczema in babies is common and due to irritant ammoniacal urine and faeces.

Strong irritants elicit an acute reaction at the site of contact whereas weak irritants most often cause chronic eczema, especially of the hands, after prolonged exposure.

Allergic contact eczema

This is due to a delayed hypersensitivity reaction following contact with antigens or haptens. Previous exposure to the allergen is required for sensitisation and the reaction is specific to the allergen or closely related chemicals. Common allergens and their origin are listed in Box 21.22.

The eczema reaction occurs wherever the allergen is in contact with the skin and sensitisation persists indefinitely. It is important to determine the original site of the rash before secondary spread obscures the picture, as this often provides the best clue to the contactant. There are many easily recognisable patterns, e.g. eczema of the earlobes, wrists and back due to contact with nickel in costume jewellery, watches and bra clips; or eczema of the hands and wrists due to rubber gloves. Oedema of the lax skin of the eyelids and genitalia is a frequent concomitant of allergic contact eczema (see Fig. 21.12).

21.22 SOME COMMON ALLERGENS

Allergen	Present in
Nickel	Jewellery, jean studs, bra clips
Dichromate	Cement, leather, matches
Rubber chemicals	Clothing, shoes, tyres
Colophony	Sticking plaster, collodion
Paraphenylenediamine	Hair dye, clothing
Balsam of Peru	Perfumes, citrus fruits
Neomycin, benzocaine	Topical applications
Parabens	Preservative in cosmetics and creams
Wool alcohols	Lanolin, cosmetics, creams
Epoxy resin	Resin adhesives

Asteatotic eczema

This is frequently seen in the hospitalised elderly, especially when the skin is dry; low humidity caused by central heating, over-washing and diuretics are contributory factors. It occurs most often on the lower legs as a rippled or 'crazy paving' pattern of fine fissuring on an erythematous background.

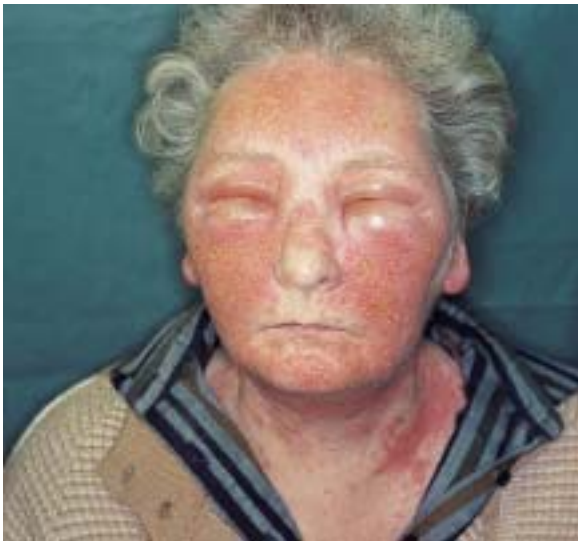


Fig. 21.12 Allergic contact eczema. This was caused by the application of an antihistamine cream. The acute eczematous reaction and bilateral periorbital oedema are typical.

Gravitational (stasis) eczema

This occurs on the lower legs and is often associated with signs of venous insufficiency (oedema, red or bluish discoloration, loss of hair, induration, haemosiderin pigmentation and ulceration).

Lichen simplex

This describes a plaque of lichenified eczema due to repeated rubbing or scratching, as a habit or in response to stress. Common sites include the nape of the neck, the lower legs and the anogenital area.

Pompholyx (dyshidrotic eczema)

Recurrent vesicles and bullae occur on the palms, palmar surface of the fingers and soles, and are excruciatingly itchy. This form of eczema can occur in atopic eczema and in irritant and contact allergic dermatitis. It can be provoked by heat, stress and nickel ingestion in a nickel-sensitive patient but is often idiopathic.

Investigation of eczema

(For details of tests see pp. 1055–1056.)

Patch tests

These are performed in suspected cases of contact allergic dermatitis (see p. 1073).

IgE and specific IgE

These are occasionally performed to support the diagnosis of atopic eczema and to determine specific environmental allergens, e.g. pet dander, horse hair, house dust mite, pollens and foods.

Prick tests

The indications are the same as for specific IgE but are less commonly performed.

Bacterial and viral swabs for microscopy and culture

These are useful tests in suspected secondary infection. Skin swabs for bacteriological assessment will invariably reveal the presence of bacteria, and antibacterial treatment should be reserved for those cases with evidence of clinical infection. In the case of recurrent impetigo in a child with atopic eczema, bacterial swabs should be taken from carrier sites (nares, axillae and groin) from both the affected individual and all household members.

General management of eczema

The main points are listed in Box 21.23.

21.23 GENERAL MANAGEMENT FOR ALL TYPES OF ECZEMA

- Explanation, reassurance and encouragement
- Avoidance of contact with irritants
- Regular use of greasy emollients
- Appropriate use of topical steroids

Topical steroids

Lotions (aqueous base) and creams (oil/water mixture) are preferable in acute eczema and ointments (in an oily base) in chronic cases; they are usually applied twice daily. Only 1% hydrocortisone should be used on the face and in infancy. Even in adults it is seldom necessary to prescribe more than 200 g of a low-potency steroid (e.g. 1% hydrocortisone), 50 g of a moderately potent steroid (e.g. 0.05% clobetasone butyrate) or 30 g of a potent steroid (e.g. 0.1% betamethasone valerate, 0.1% mometasone furoate) per week. Very potent topical steroids (e.g. 0.05% clobetasol propionate) should not be used long-term. The side-effects of strong or extensive local steroid therapy should be borne in mind when patients are applying these preparations for years on end. They include skin thinning (with striae, fragility and purpura), enhanced or disguised infections, and systemic absorption (causing suppression of the hypothalamic-pituitary-adrenal axis and even Cushingoid features). There are no absolute guidelines for the amount of topical steroid that should be used but care should be taken on certain sites such as the face and flexures. The best rule is to use the least potent steroid for the shortest possible time that is effective. Often one finds that topical steroids are being under-used and are therefore ineffective.

Other topical immunosuppressants, including tacrolimus and pimicrolimus, have just become available for use. Early reports of their efficacy are encouraging.

Bland emollients (e.g. emulsifying ointment) are used regularly, both directly on the skin and in the bath. They not only prevent excessive water loss from an already dry skin, but also help to reduce the amount of local steroid used. Emollient soap substitutes (e.g. aqueous cream) are also helpful. Sedative antihistamines (e.g. alimemazine tartrate (trimeprazine tartrate)) are of value if sleep is interrupted.

Specific measures

Atopic eczema

Explanation and patient support are increasingly provided for these patients through general practice, dermatology clinics, community liaison nurses and patient support groups such as the National Eczema Society in the UK. Treatment involves the regular use of emollients (moisturisers) and the least possible use of topical steroids. These topical treatments can be used with a variety of types of

bandaging such as 'wet wraps', tar and ichthammol paste bandages. Allergen avoidance has a role in selected patients. Routine inoculations are allowed during quiescent phases of eczema. An egg-free measles vaccine is available for children who have a severe egg allergy.

EBM

ATOPIC ECZEMA—are topical steroid/antimicrobial combinations better than topical steroids alone?

'RCTs show no evidence that combinations of topical antimicrobial agents and steroids are better than topical steroids alone in improving the clinical signs and symptoms of atopic eczema.'

- Ramsay CA, Savoie JM, Gilbert M, et al. The treatment of atopic dermatitis with topical fusidic acid and hydrocortisone acetate. J Eur Acad Dermatol Venereol 1996; 7:15–22.
- Wachs GN, Maibach HI. Co-operative double-blind trial of an antibiotic/corticoid combination in impetiginised atopic dermatitis. Br J Dermatol 1976; 95:323.

Seborrhoeic eczema

Antipityrosporal agents such as ketoconazole shampoo form the basis of treatment, supplemented with weak corticosteroids if needed. Treatments may need to be repeated at intervals.

Irritant eczema

This is best treated by the regular use of emollients, avoidance of irritants and protective clothing, e.g. gloves.

Contact allergic eczema

Avoidance of the culprit allergen is the most important treatment for this form of eczema and may involve lifestyle changes such as a new job or giving up hobbies. Measures used for irritant eczema are also helpful.

Gravitational eczema

Local steroids (see above) should only be applied to eczematous areas and ulcers should be avoided. Sensitisation to topical antibiotics (neomycin) and preservatives (e.g. chlorocresol) is common in this form of eczema. Associated peripheral oedema should be eliminated by elevation of the leg and graded compression bandages.

ISSUES IN OLDER PEOPLE
ECZEMA

- With advancing age, the skin becomes less pliable and drier. This increases the tendency for irritant dermatitis.
- Topical steroid usage causes more local side-effects, such as purpura or ecchymoses, in the elderly individual.
- Widespread eczema is potentially life-threatening in the elderly, particularly when combined with other illnesses.

PSORIASIS AND OTHER ERYTHEMATOUS SCALY ERUPTIONS

Psoriasis and lichen planus will be described here in detail; other scaly conditions were covered on pages 1059–1060.

PSORIASIS

Psoriasis is a non-infectious, chronic inflammatory disease of the skin, characterised by well-defined erythematous plaques with silvery scale which have a predilection for the extensor surfaces and scalp, and by a chronic fluctuating course.

The prevalence is approximately 2% in European populations. Accurate figures for many other parts of the world are not available but there seems to be consistent evidence that the prevalence of psoriasis is lower in people of African origin and lower still in some Asian communities such as the Japanese. Psoriasis may come on at any age but is unusual before the age of 5; the oldest recorded onset was in a patient aged 107. There appear to be two epidemiological patterns of psoriasis. The first shows an onset in the teenage and early adult years; such individuals frequently have a family history of psoriasis and there is an increased prevalence of HLA Cw6. In a second epidemiological grouping disease onset is in an individual's fifties or sixties, a family history is less common and the HLA group Cw6 is not so prominent. Some authors refer to these two groupings as type 1 and type 2 psoriatics.

The clinical course of psoriasis is very variable. As a general rule the earlier the age of onset and the more severe the initial presentation, the more severe the lifetime course of the disease.

Aetiology

Basic defect

There are two key pathophysiological aspects to the abnormalities in psoriatic plaques. Firstly, the keratinocytes hyperproliferate with a grossly increased mitotic index and an abnormal pattern of differentiation involving the retention of nuclei in the stratum corneum (in normal skin the dead stratum corneum cells do not have nuclei). Secondly, there is a large inflammatory cell infiltrate comprising polymorphs, T cells and other inflammatory cells. It is uncertain which of these characteristics is primary. Traditionally, psoriasis was viewed as a primary disorder of cell turnover but in recent years there has been increased support for the hypothesis that the hyperproliferation may be secondary to the inflammatory infiltrate and that the increase in keratinocyte proliferation is a consequence of inflammatory cell mediators or signalling.

There is a large familial component to psoriasis. Formal estimates from twin studies suggest a hereditability of around 80%. In monozygotic twins perhaps one-third of pairs will be concordant for psoriasis. Put another way, two-thirds of monozygotic twins will not be concordant despite an apparently identical or near-identical genetic background.

The mode of inheritance of psoriasis does not fit a clear Mendelian pattern and is therefore described as genetically complex. Empirical estimates suggest that if one parent has psoriasis, then the chance of a child being affected is in the order of 15–20%. If both parents have psoriasis the probability of a child being affected is 0.5. Both these estimates are increased if one sibling already has the disease. Genome scanning linkage and association studies have indicated various chromosomal areas of susceptibility including the HLA region.

Disordered cell proliferation in psoriasis is reflected by the increase in the number of mitoses visible in the psoriatic plaque. The transit time—that is, the time it takes for keratinocytes in the basal layer to leave the epidermis—is shortened in psoriasis from perhaps 28 to 5 days. Whilst it used to be thought that the cell cycle was actually reduced in psoriasis

more recent data suggest that it is just that the proportion of cycling cells (rather than cells that are in G_0) is increased. There are some data suggesting that the non-plaque skin also shows an elevated rate of proliferation, although any increase above background rate is modest. These data have not been confirmed in all studies. The nails of patients with psoriasis, even when clinically unaffected, do, however, grow more quickly than those of controls.

The importance of keratinocyte hyperproliferation initially received support from the demonstration that cytostatic drugs such as methotrexate were clinically useful. However, more recent data suggest that methotrexate may exert its effects primarily through an influence on the immune system.

The evidence implicating a key role for an immune pathogenesis relates to:

- the association with certain HLA groups (HLA Cw6)
- the success of certain immunosuppressive drugs (such as ciclosporin) in improving the clinical state of the disease
- reports of the development of psoriasis in recipients of bone marrow transplants from donors with a history of psoriasis.

The precise molecular mechanisms operating in psoriasis are, however, poorly understood. A large number of theories have been advanced over the last 30 or 40 years claiming that one particular mediator may be a key or rate-limiting factor in psoriasis. The majority of these explanations have not stood the test of time; nor have they provided useful therapeutic insight.

Precipitating factors

Psoriasis is a chronic disease characterised by variation in both temporal and spatial extent. Most of this variation cannot be explained. At any one time perhaps 10% of people who have received the diagnosis of psoriasis have no lesions and perhaps 15% may report remissions of up to 5 years or more. Some factors, however, are thought to precipitate an exacerbation of the disease and these are listed in Box 21.24.

21.24 FACTORS CAUSING FLARE-UPS OF PSORIASIS

Trauma
• When the condition is erupting lesions appear in areas of skin damage such as scratches or surgical wounds (Köbner phenomenon)
Infection
• β-haemolytic streptococcal throat infections often precede guttate psoriasis
Sunlight
• Rarely, ultraviolet radiation may worsen psoriasis
Drugs
• Antimalarials, β-blockers and lithium may worsen psoriasis and the rash may 'rebound' after stopping systemic corticosteroids or potent local corticosteroids
Emotion
• Anxiety precipitates some exacerbations

Pathology

The histology of psoriasis is depicted in Figure 21.13.

Clinical features

Stable plaque psoriasis

This is the most common type. Individual lesions are well demarcated and range from a few millimetres to several centimetres in diameter (see Fig. 21.14). The lesions are red with dry, silvery-white scaling, which may be obvious only after scraping the surface. The elbows, knees and lower back are commonly involved.

Other sites of predilection include:

- *Scalp*. Scalp is involved in approximately 60% of patients with psoriasis. The reason why the scalp is so commonly involved is not clear. One possibility relates it to Köbnerisation from *P. ovale* infection of the skin. (*P. ovale* is the cause or precipitant of dandruff or seborrhoeic dermatitis.) Psoriasis of the scalp typically

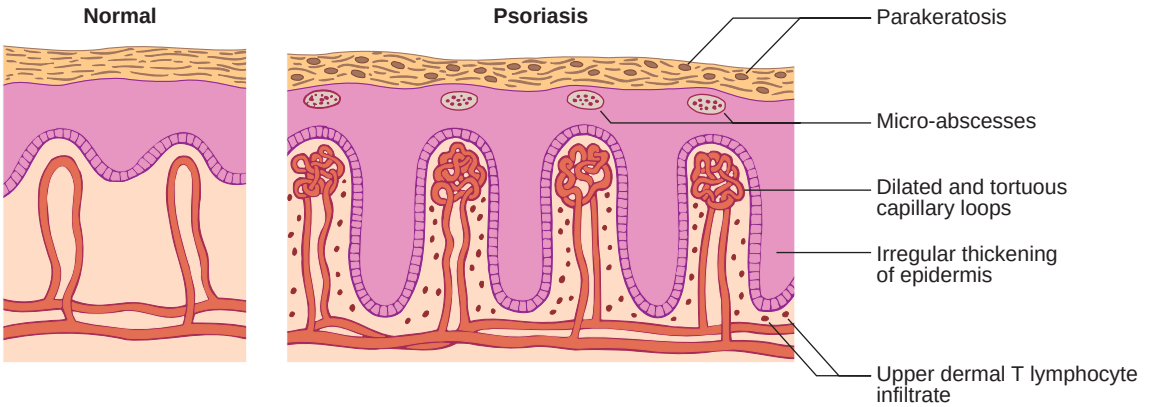


Fig. 21.13 The histology of psoriasis.

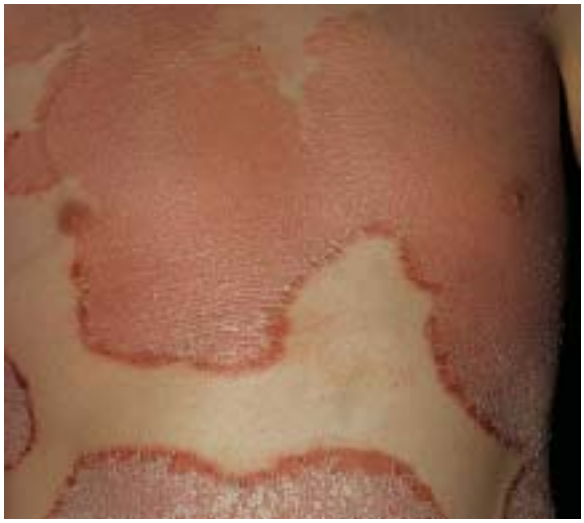


Fig. 21.14 Large, sharply circumscribed plaques of psoriasis. The silvery scaling of the lower (untreated) plaque is typical.

shows well-demarcated, easily palpable areas, but on occasion a diffuse, fine scaling difficult to distinguish from classical seborrhoeic dermatitis may be present. Temporary hair loss is not uncommon and rarely permanent focal hair loss may occur.

- *Nails*. Involvement of the nails is common, with 'thimble pitting', onycholysis (separation of the nail from the nail bed—see Fig. 21.15) and subungual hyperkeratosis.
- *Flexures*. Psoriasis involving the natal cleft, and submammary and axillary folds is not scaly but red, shiny and symmetrical (see Fig. 21.16).
- *Palms*. Psoriasis here is often difficult to recognise, as individual plaques may be poorly demarcated and barely erythematous. It is often impossible to differentiate between psoriasis and eczema of the palms.

Guttate psoriasis

This is most commonly seen in children and adolescents and may follow a streptococcal sore throat. In many patients this will be the first clinical indication of the disease. The rash often appears rapidly. Individual lesions are droplet-shaped, small (seldom greater than 1 cm in diameter) and scaly. Bouts of guttate psoriasis may clear in a few months but

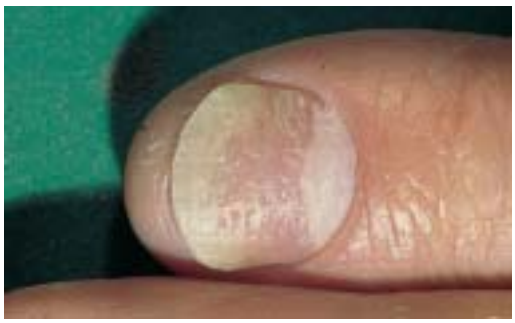


Fig. 21.15 Coarse pitting of the nail and separation of the nail from the nail bed (onycholysis). These are both classic features of psoriasis.

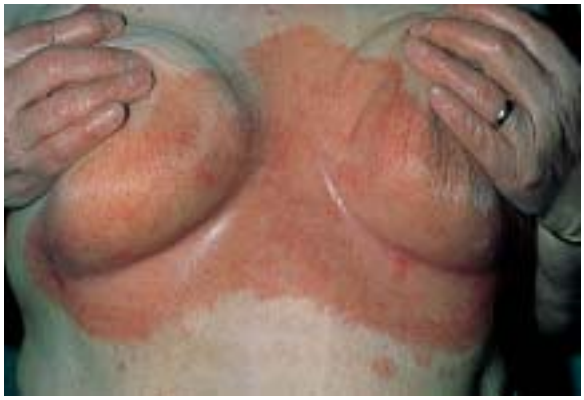


Fig. 21.16 Flexural psoriasis. Note the glistening but not scaly rash.

respond well to early treatment with phototherapy. The majority of these patients will develop plaque psoriasis later in life.

Erythrodermic psoriasis

The skin becomes universally red or scaly, or more rarely just red with very little scale present. As in other forms of erythroderma temperature regulation becomes problematic with a danger of either hypothermia or hyperthermia developing. Precipitants for erythroderma may not be evident but inappropriate use of dithranol, tar or phototherapy is a known factor.

Pustular psoriasis

There are two varieties of pustular psoriasis. The first is the generalised form which is rare but very serious. The onset is usually sudden with large numbers of small sterile pustules erupting on a red base. The patient may rapidly become ill with a swinging pyrexia coinciding with the appearance of new pustules. Such patients will usually require urgent assessment and hospital admission to a dermatology ward. More common is a localised form of pustular psoriasis which primarily affects the palms and soles. This eruption is chronic and comprises small sterile pustules which lie on a red base, and resolve to leave brown macules or scaling in their wake. The relation between pustular psoriasis of the palms and the soles (palmoplantar pustulosis) and psoriasis remains disputed by some, although the majority agree that they are indeed related.

Arthropathy

Between 5 and 10% of individuals with psoriasis appear to have a chronic inflammatory arthropathy (see p. 1011).

Investigations

Few are indicated. Biopsy is seldom necessary and often contributes little where there is clinical doubt (for example, in attempting to distinguish between psoriasis of the palms and eczema of the palms). Throat swabbing for streptococci or other evidence of recent infection may occasionally be useful. Skin scrapings and nail clippings may help to exclude dermatophyte infection where the clinical diagnosis is uncertain. Assessment of all but minor joint symptoms may require assessment by a rheumatologist.

Management

General measures

Explanation, reassurance and instruction are vital but easily neglected; they must be based on insight into the patient's state of mind. In the vast majority of cases psoriasis is not life-threatening and therefore if the treatment appears worse than the disease, then the treatment should be stopped. Often patients need encouragement to take many of the important decisions themselves, albeit with advice from the physician. Two patients, even with identical patterns of psoriasis, don't have the same experience of the disease.

There is little robust evidence to support the statement that stress exacerbates psoriasis or is causally involved. Certain studies suggest that alcohol consumption is greater amongst some psoriasis patients, but it is not clear whether this is a cause or a result of the disease. What is clear is that doctors need an awareness of the impact that this disease can have on many individuals. For instance, many fathers will, with embarrassment, admit that they cannot take their young children swimming because of the alarm their rash causes to other swimmers. Similarly, blood on the sheets and the ubiquitous scale on bedclothes and carpets may act against many personal relationships. It is said that 'Girls with scalp psoriasis don't wear navy clothes' (the scale being more prominent when viewed against a dark background).

Treatment

Treatment can be classed in four broad categories:

- easily applied topical agents such as emollients, corticosteroids, vitamin D agonists, or 'weak' tar or dithranol preparations
- ultraviolet therapies such as PUVA and ultraviolet B
- systemic agents such as retinoids or immunosuppressives such as ciclosporin
- intensive inpatient or day-patient care with topical agents and ultraviolet radiation under medical supervision.

Traditionally, therapies such as inpatient dithranol, when combined with ultraviolet radiation in the Ingram's regimen, were capable of inducing clearance of the disease, i.e. all or > 95% of the psoriasis disappeared. The patient remained clear of disease until relapse occurred. The duration of remission varied considerably from less than 1 month to over a year. By contrast, many more acceptable treatments such as calcipotriol do not clear psoriasis; rather they reduce the thickness, scaling and redness of individual plaques. Depending on the clinical context and extent of disease, patient and physician need to choose the appropriate endpoint of treatment. This is often a compromise between side-effects, practical considerations such as time available to attend hospital, and disease extent.

Topical agents

A large number of topical agents have been used to treat psoriasis. Emollients have a modest effect in terms of reducing scale and diminishing itch. Many patients feel more comfortable using emollients than not using them.

Dithranol. Traditionally, the gold standard of therapy was treatment with dithranol or crude tar. Dithranol originally came into use in the late 19th century and is now known to be a potent producer of free radicals. Unsurprisingly, when applied to normal skin dithranol is proinflammatory and stimulates hyperproliferation, but for reasons that remain unclear it normalises differentiation and inhibits proliferation when applied to psoriatic plaques.

Dithranol is used in two main regimens. The first is Ingram's regimen; the plaques are covered with low concentrations of dithranol in a zinc oxide paste following a tar bath and ultraviolet radiation exposure, and then covered in talcum powder and bandages and left in situ for 24 hours. More recently, short-contact dithranol therapy has been developed in which higher concentrations are applied for between 15 and 30 minutes and then washed off. The main clinical limitation of dithranol is its proinflammatory action on normal skin. This presents as 'burning' with pain and erythema, which peaks 72 hours after application. Dithranol also results in a brown staining of the skin and can cause a purple discoloration in individuals with light hair colour. In general, use of dithranol as an inpatient therapy has diminished over the last 20–30 years due to low patient acceptability, the invention of new phototherapy modalities and lack of inpatient beds. As with tar, attempts have been made to make dithranol easier to use and more patient-friendly but efficacy is reduced; these attempts have been largely unsuccessful.

Tar. Tar, particularly crude tar, has been shown to be effective in the treatment of psoriasis. There are certain similarities with dithranol in that tar is proinflammatory and has different effects on the plaque compared with normal skin. Unfortunately, as for dithranol, attempts to define the exact therapeutic mechanism and dissociate efficacy from side-effects have been unsuccessful. It remains true that the more cosmetically acceptable the preparation, the lower its efficacy.

Calcipotriol. More recently, a number of other topical preparations have been developed which have become clinically popular. Calcipotriol is a vitamin D agonist which is highly acceptable cosmetically; it seldom clears a plaque of psoriasis but tends to reduce the thickness of the plaque and diminish the scaling. It is applied twice daily and, providing no more than 100 g is used each week, does not cause hypercalcaemia or hypercalciuria. Patients like calcipotriol because it is odourless, colourless and does not stain. Irritation, which is usually transient, is the main side-effect.

Tazarotene. A vitamin A agonist (retinoid), this has also come into clinical use recently and has many properties in common with calcipotriol. It tends not to induce clearance and may cause irritation, but is easy to use and diminishes the induration, scaling and redness of plaques.

Corticosteroids. The frequency of use of corticosteroids varies considerably between different countries. In the UK they tend not to be used nearly as much as in many other European countries or North America. The hazards of corticosteroids are local skin atrophy and the fact that when they are stopped the psoriasis tends to return, i.e. they do not induce remission. Nevertheless, they are invaluable for many body sites, particularly the flexures where tar and dithranol may be too irritant, and short bursts of moderately potent corticosteroids can be invaluable in the management of

many patients. Use of potent topical corticosteroids on the face or hair margins should be under close and expert medical supervision.

Ultraviolet and PUVA therapy

Ultraviolet therapy. Ultraviolet radiation (UVR) forms the mainstay of management of patients with moderate to severe psoriasis. As could be predicted given the known biology of UVR, the main risk of ultraviolet therapies lies in burning in the short term and in the induction of skin cancers in the long term.

There are two main therapeutic modalities in use. It has been known for almost a century that ultraviolet B (UVB) administered therapeutically improves the condition of many patients with psoriasis. To some degree this mirrors the natural improvement that many patients with psoriasis notice in summer. In the past broadband UVB radiation given 3–7 times a week formed part of the Ingram's regimen using dithranol.

More recently, a particular type of UVB radiation produced by the Philips TL01 lamp (narrowband UVB) has become a very popular modality of treatment delivered 2–5 times a week on an outpatient basis. This lamp peaks at 311 nm and was developed specifically following work showing that shorter wavelength (< 311 nm) radiation, while inflammatory, had little therapeutic efficacy, whilst longer wavelengths (> 311 nm) were also relatively ineffective. The long-term safety of this lamp is, however, less clear. Some argue that it may be more carcinogenic than broadband UVB therapy while others believe it is less carcinogenic. The results of long-term observation are awaited.

PUVA therapy. Psoralens are natural photosensitisers found in a number of plants. In the early 1960s topical preparations of psoralen used in combination with ultraviolet A (UVA) were reported to have therapeutic effects on psoriasis. In the early 1970s a large randomised trial showed that oral psoralen together with long wavelength ultraviolet A (PUVA) was a dramatically effective treatment for individuals with chronic plaque psoriasis. Psoralen molecules intercalate between the two strands of DNA and upon excitation with UVA photons cross-link the DNA strands. In this sense PUVA therapy is not a 'light therapy'; rather, psoralen is a pro-drug that upon oral administration is distributed throughout the body but is only activated by ultraviolet radiation in those sites that are exposed to UVA (skin and eye—the latter should be protected).

PUVA treatment induces clearance to a greater degree than intensive dithranol therapy and has revolutionised the management of patients with psoriasis. The short-term side-effects are minimal. The therapy can be delivered between 2 and 5 times a week and clearance expected in the majority of individuals within 8 weeks. Clearance will occur in more than 75% of individuals. Some individuals may develop nausea in response to the psoralen, and because the psoralen is also present in the eye individuals need to wear UVR-resistant sunglasses for 24 hours after therapy. The long-term hazards of PUVA therapy give cause for concern but are not surprising because PUVA is by its mechanism of action known to be mutagenic. In patients who have received a large amount of PUVA therapy, particularly 'maintenance therapy' (continuous PUVA lasting for 6 months to a year), there is an elevated risk of squamous cell carcinoma and basal cell carcinoma. Recent work suggests that the risk of melanoma may also be increased although this single study requires confirmation. Instead of being used orally, psoralens can also be applied to the bath before irradiation with UVA (so-called bath PUVA). A few different psoralen photosensitisers are available that vary in their characteristics.

EBM

TREATMENT OF PSORIASIS—phototherapy

'RCTs show that oral PUVA therapy clears chronic plaque psoriasis in > 75% of patients. Clearance rates and the length of remission following PUVA are similar to those obtained with inpatient treatment with the Ingram's dithranol regimen. RCTs show that TL01 UVB phototherapy twice weekly is less effective at inducing clearance of psoriasis and produces a shorter remission than oral PUVA given twice weekly.'

- Gordon PM, Diffey BL, Matthews JN, Farr PM. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999; 41:728–732.
- Parrish JA, Fitzpatrick TB, Tanenbaum L, Pathak MA. Photochemotherapy of psoriasis with oral methoxsalen and longwave ultraviolet light. N Engl J Med 1974; 291:1207–1211.

Systemic treatment

Three main systemic agents are used for the management of patients with severe psoriasis: methotrexate, oral retinoids and ciclosporin.

Methotrexate. Methotrexate has been available for the last 40 years and can be very useful therapeutically. In dermatological practice it is administered once a week at much lower doses than those used in haematology. It seems likely that its mechanism of action involves a cytostatic effect on the immune system rather than a primary effect on keratinocyte or epidermal hyperproliferation. The main hazards of methotrexate are that it is an immunosuppressive, may dangerously depress the white cell count without careful monitoring, and in the long term is associated with hepatic fibrosis and potentially cirrhosis, particularly if individuals continue to drink alcohol. Liver biopsies are required in many if not all patients.

Oral retinoids. Oral retinoids such as acitretin are also effective in some patients with psoriasis. They tend to be particularly effective in pustular psoriasis of the palms and soles but are widely used to improve plaque psoriasis. The drugs do not appear to have a quick mode of action but are often combined with other therapies including PUVA treatment. There are some theoretical reasons for arguing that retinoids may diminish the chances of skin neoplasia and these are often employed to justify their use in individuals receiving PUVA. Systemic retinoids are potent teratogens and following use of acitretin pregnancy is not safe for at least 2 years.

Ciclosporin. Ciclosporin was the first of a number of potent immunosuppressives to find a role in the management of a minority of patients with psoriasis. Unfortunately, these agents are known not to be active topically in psoriasis (at least not in clinical practice) and therefore their oral use carries considerable risks in terms of nephrotoxicity and the

potential for elevated risks of neoplasia, particularly of the cervix and skin and lymphoma. Despite ciclosporin being effective in inducing and maintaining clearance of individuals with psoriasis continuous use of this drug will be difficult to justify in the vast majority of patients. Long-term surveillance data are not available in this particular patient group.

Intensive inpatient care

Intensive inpatient treatment with dithranol or tar is less common than previously. In many parts of the world this is because beds for management of patients with skin disease are not available to the same degree that they once were. Ingram's regimen will produce clearance in 80% of psoriatics in 3 weeks. Such a regimen still remains the gold standard in terms of both efficacy and safety. Set against this is the fact that many individuals are reluctant to come into hospital for such a period of time. The balancing of risk between known safe inpatient treatments and potentially more toxic outpatient treatments still gives cause for concern.

LICHEN PLANUS

Lichen planus is a rash characterised by intensely itchy polygonal papules with a violaceous hue involving the skin and less commonly the mucosae, hair and nails.

Aetiology

The cause is unknown but an immune pathogenesis is suspected as there is an association with some autoimmune diseases such as myasthenia gravis (see p. 1183), and with thymoma and graft-versus-host disease. Rashes with clinical and histological features of lichen planus can occur in chronic active hepatitis, hepatitis B and C infections, and in patients taking drugs, the most common culprits being gold and other heavy metals, sulphonamides, penicillamine, antimalarials, antituberculous drugs and thiazide diuretics. They also occur in those handling colour developers.

Pathology

There is hyperkeratosis, a prominent granular layer, basal cell degeneration and a heavy T lymphocyte infiltration in the upper dermis. Degenerating basal cells may form colloid (apoptotic) bodies. The T cell–basal cell interaction leaves a 'sawtooth' dermo-epidermal junction. The picture suggests an immune reaction to an unknown epidermal antigen.

Clinical features

Lichen planus tends to start on the distal limbs, most commonly the volar aspects of the wrists (see Fig. 21.17), and the lower back. Intensely itchy, flat-topped, pink-purplish papules appear and some develop a characteristic fine white network on their surface (Wickham's striae). New lesions may appear at the site of trauma (Köbner phenomenon) and the rash may spread rapidly to become generalised. Individual lesions may last for many months and the eruption as a whole tends to last about 1 year, often leaving marked post-inflammatory pigmentation. Mucous membrane involvement, comprising an asymptomatic fine white lacy network or pinhead-sized white papules, occurs in about two-thirds of patients (see p. 1050). The nails are usually normal but in 10% they may be affected, with changes ranging from longitudinal grooving to destruction of the nail fold and bed. Variants of the classic picture are rare but often challenging diagnostically. They include annular, atrophic, bullous, follicular, hypertrophic and ulcerative types.

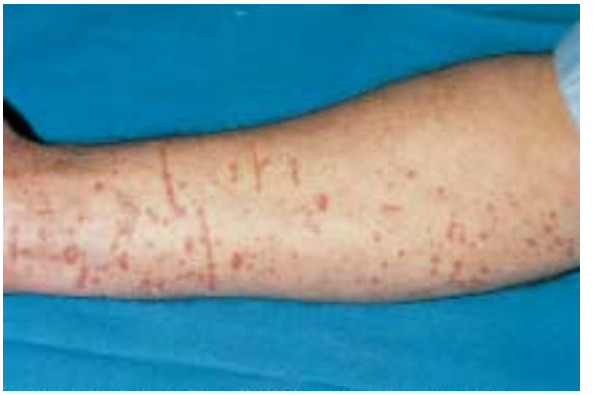


Fig. 21.17 Lichen planus. Glistening discrete papules involving the volar aspects of the forearm and wrist. Note the lesions along scratch marks (Köbner phenomenon).

Diagnosis

This is usually clear-cut clinically but a skin biopsy can be helpful. Other erythematous scaly conditions should be considered in the differential diagnosis, including guttate psoriasis, pityriasis rosea, pityriasis lichenoides and drug eruptions.

Management

The condition is usually self-limiting, although rarely, particularly with oral lichen planus, it may persist for more than 10 years. Potent local corticosteroids may help with intense itch but systemic corticosteroids may be indicated. Topical corticosteroids applied to the buccal mucosa may also be required. A variety of other therapies have been used including ciclosporin, retinoids and phototherapy.

ISSUES IN OLDER PEOPLE
PRACTICAL PROBLEMS OF INFLAMMATORY SKIN DISEASE

- Quality of life is affected due to distress and discomfort.
- Skin disease is potentially more life-endangering in the elderly: for example, erythroderma.
- Skin disease is cosmetically unattractive, causing depression and increased social isolation.
- Irritation, soreness and itching cause sleep disturbance and increasing confusion.
- Older people may be reluctant to seek help because they are anxious that they may be perceived as not coping.
- Older people may have difficulty administering topical treatments, e.g. opening jars and tubes and applying creams during bathing; there is an increased risk of slipping in an oily bath.
- They have less access to information on skin care.