

Skin disease

23

Structure and function of the skin 1315

Approach to the patient 1317

Infections 1318

Bacterial infections 1318

Mycobacterial infections 1320

Viral infections 1321 Fungal

infections 1322 Infestations

1325

Papulo-squamous/inflammatory rashes 1326

Eczema 1326

Psoriasis 1331

Urticaria 1334

Pityriasis rosea 1335

Lichen planus 1335

Granuloma annulare 1336

Lichen sclerosus et atrophicus 1336

Facial rashes 1337

Photodermatology 1339

Idiopathic photodermatoses 1340

Erythroderma 1340

Cutaneous signs of systemic disease 1341

Bullous disease 1346

Immunobullous disease 1347

Mechanobullous disease 1348

Skin tumours 1349

Benign cutaneous tumours 1349

Potentially pre-malignant cutaneous tumours 1350

Malignant cutaneous tumours 1351

Disorders of blood vessels/lymphatics 1353

Leg ulcers 1353

Pressure sores 1354

Vasculitis 1355

Lymphatics 1356

Disorders of collagen and elastic tissue 1356

Disorders of pigmentation 1357

Hypopigmentation 1357

Hyperpigmentation 1358

Drug-induced rashes 1358

Disorders of nails 1359

Disorders of hair 1360

Hair loss 1360

Increased hair growth 1361

Birth marks/neonatal rashes 1361

Human immunodeficiency virus and the skin 1362

Dermatoses of pregnancy 1363

Principles of topical therapy 1364

Introduction

Skin diseases have a high prevalence throughout the world. In developing countries infectious diseases such as tuberculosis, leprosy and onchocerciasis are common, whereas in developed countries inflammatory disorders such as eczema and acne are common. Skin disorders can be inherited, e.g. Ehlers-Danlos syndrome, a part of normal development, e.g. acne vulgaris, or may present as part of a systemic disorder, e.g. systemic lupus erythematosus (SLE).

Approximately 25% of the UK population will develop a skin problem and, although self-medication is common, skin disease still accounts for 10% of the workload of family doctors. The common reasons for this are itching or pain, which can interfere with people's ability to function normally or to sleep; rashes which cause anxiety, depression and lack of self-confidence and can lead to social isolation if obviously visible; and an inability to work, because certain dermatoses (such as allergic hand eczema in a builder or hairdresser) can interfere with or even prevent working.

Rarely skin disease can be fatal. Examples are malignant melanoma, toxic epidermal necrolysis and pemphigus. ■

STRUCTURE AND FUNCTION OF THE SKIN

The skin consists of four distinct layers: the epidermis, the basement membrane zone, the dermis and the subcutaneous layer (Fig. 23.1). The functions are summarized in Box 23.1.

The epidermis

The epidermis is a stratified epithelium of ectodermal origin that arises from dividing basal keratinocytes. The downward projections of the epidermis into the dermis are called the 'rete ridges'. The lower epidermal cells (basal layer) produce a variety of keratin filaments and desmosomal proteins (e.g. desmoglein and desmoplakin),

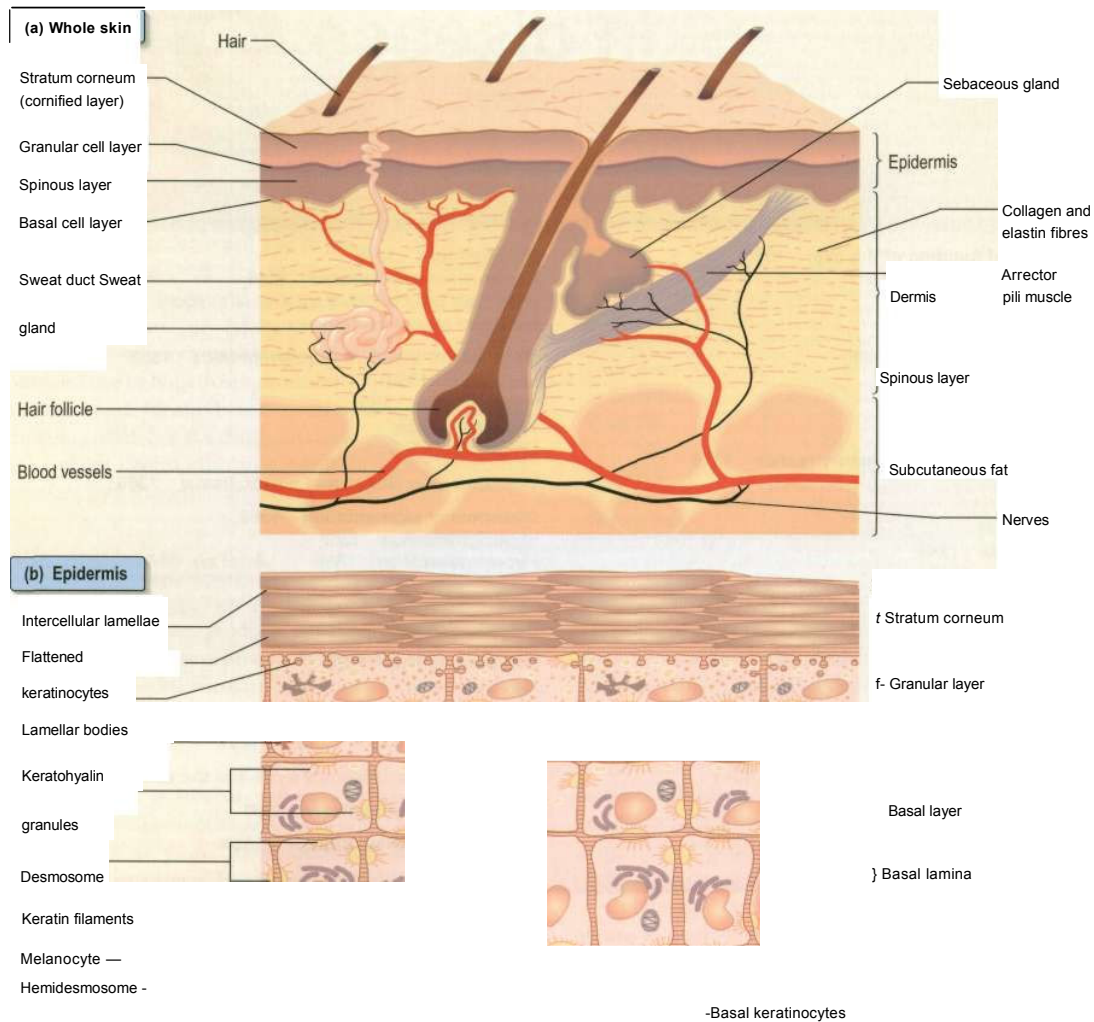


Fig. 23.1 The structure of the skin.

O

Box 23.1 Functions of the skin

- Physical barrier against friction and shearing forces
- Protection against infection (immune and innate), chemicals, ultraviolet irradiation
- Prevention of excessive water loss or absorption
- Ultraviolet-induced synthesis of vitamin D
- Temperature regulation
- * Sensation (pain, touch and temperature)
- Si Antigen presentation/immunological reactions/wound healing

which make up the 'cytoskeleton'. This confers strength to the epidermis and prevents it shedding off. Higher up in the granular layer, complex lipids are secreted by the keratinocytes and these form into intercellular lipid bilayers which act as a semipermeable skin barrier. The upper cells (stratum corneum) lose their nuclei and become surrounded by a tough impermeable 'envelope' of various proteins (loricrin, involucrin, filaggrin and keratin). Changes in lipid metabolism and protein

expression in the outer layers allow normal shedding of keratinocytes.

Keratinocytes can secrete a variety of cytokines (e.g. interleukins, gamma-interferon, tumour necrosis factor alpha) in response to tissue injury or in certain skin diseases. These play a role in specific immune function, cutaneous inflammation and tissue repair. There is a further layer of protection against microbial invasion, called the innate immune system of the skin. This includes neutrophils and macrophages as well as keratinocyte-produced antimicrobial peptides (called *fi*-defensins and cathelicidins). Expression of these peptides is both constitutive and induced by skin inflammation, and they are active against bacterial, viral and fungal pathogens. There is evidence to suggest a deficiency of these peptides may account for the susceptibility of patients with atopic eczema to skin infection.

Other cells in the epidermis

Melanocytes are found in the basal layer and secrete the pigment melanin. These protect against UV irradiation.

Racial differences are due to variation in melanin production not melanocyte numbers.

Merkel cells are also found in the basal layer and originate from either neural crest or epidermal keratinocytes. They are numerous on finger tips and in the oral cavity and play a role in sensation.

Langerhans' cells are dendritic cells found in the suprabasal layer. They derive from the bone-marrow and as they express the cytokine CCR6, they are guided to normal skin, which contains a CCR6 agonist called macrophage inflammatory protein 3a. Langerhans' cells endocytose extracellular antigens in the skin and then migrate to local lymph nodes for T cell presentation and thus act as antigen-presenting cells.

Basement membrane zone (see Fig. 23.27)

The basement membrane zone is a complex proteinaceous structure consisting of type IV and VII collagen, hemidesmosomal proteins, integrins and laminin. Collectively they hold the skin together keeping the epidermis firmly attached to the dermis. Inherited or autoimmune-induced deficiencies of these proteins can cause skin fragility and a variety of blistering diseases (see p. 1346).

The dermis

The dermis is of mesodermal origin and contains blood and lymphatic vessels, nerves, muscle, appendages (e.g. sweat glands, sebaceous glands and hair follicles) and a variety of immune cells such as mast cells and lymphocytes. It is a matrix of collagen and elastin in a ground substance.

The sweat glands

Eccrine sweat glands are found throughout the skin except the mucosal surfaces.

Apocrine sweat glands are found in the axillae, anogenital area and scalp and do not function until puberty.

The sweat glands and vasculature are involved in temperature control.

The sebaceous glands

These are inactive until puberty. They are responsible for secreting sebum or grease onto the skin surface (via the hair follicle) and are found in high number on the face and scalp.

Nerves

The skin is richly innervated. These fibres allow sensation of touch, pain, itch, vibration and change in temperature.

Hair

Hairs arise from a downgrowth of epidermal keratinocytes into the dermis. The hair shaft has an inner and outer root sheath, a cortex and sometimes a medulla. The lower portion of the hair follicle consists of an expanded

bulb (which also contains melanocytes) surrounding a richly innervated and vascularized dermal papilla. The hair regrows from the bulb after shedding. There are three types of hair:

- *terminal* - medullated coarse hair, e.g. scalp, beard, pubic
- *vellus* - non-medullated fine downy hairs seen on the face of women and in prepubertal children
- *lanugo* - non-medullated soft hair on newborns (most marked in premature babies) and occasionally in people with anorexia nervosa.

All hair follicles follow a growth cycle: anagen (growth phase), catagen (involution phase), telogen (shedding phase). At any one time most hairs (> 90%) will be in the anagen phase, which is typically 3-5 years for scalp hair. Grey hair is due to decreased tyrosinase activity in the hair bulb melanocytes. White hair is due to total loss of these melanocytes.

Nails

Nails are tough plates of hardened keratin which arise from the nail matrix (just visible as the moon-shaped lunula) under the nail fold. It takes 6 months for a fingernail to grow out fully and 1 year for a toe-nail.

The subcutaneous layer

The subcutaneous layer consists predominantly of adipose tissue as well as blood vessels and nerves. This layer provides insulation and acts as a lipid store.

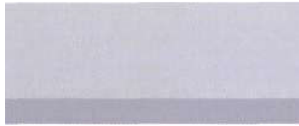
APPROACH TO THE PATIENT

The *history* should aim to elicit the following points:

- time course of rash
- distribution of lesions
- symptoms (e.g. itch or pain)
- family history (especially of atopy and psoriasis)
- drug/allergy history
- past medical history
- provocating factors (e.g. sunlight or diet)
- previous skin treatments.

Examination entails looking at and feeling a rash (for terminology, see Table 23.1). It should include an assessment of nails, hair, and mucosal surfaces, even if these are recorded as unaffected. The following terms are used to describe distribution: flexural, extensor, acral (hands and feet), symmetrical, localized, widespread, facial, unilateral, linear, centripetal (trunk more than limbs), annular and reticulate (lacy network or mesh like).

Investigation. With regard to investigation, clinical acumen remains the most useful tool in dermatology but a variety of tests are useful in confirming a diagnosis (Table 23.2).



FURTHER READING

Montagna W, Kligman AM, Carlisle KS (1992) *Atlas of normal human skin*. New York: Springer Verlag.
 Ong PY, Ohtake T, Brandt C et al. (2002) Endogenous antimicrobial peptides and skin infections in atopic dermatitis. *New England Journal of Medicine* **347**: 1151-1160 (and editorial, pp. 1199-1200).
 Paus R, Cotsarelis G (1999) The biology of hair follicles. *New England Journal of Medicine* **341**: 491-497.
 Rees J (1999) Understanding barrier function of the skin. *Lancet* **354**:1491-1492.
 Robert C, Kupper TS (1999) Inflammatory skin diseases, T cells, and immune surveillance. *New England Journal of Medicine* **341**:1817-1828.

Table 23.1 Morphological description of skin lesions

Atrophy	Thinning of the skin
Bulla	A large fluid-filled blister
Crusted	Dried serum or exudate on the skin
Ecchymosis	Large confluent area of purpura ('bruise')
Erosion	Denuded area of skin (partial epidermal loss)
Excoriation	Scratch mark
Fissure	Deep linear crack or crevice (often in thickened skin)
Lichenified	Thickened epidermis with prominent normal skin markings
Macule	Flat, circumscribed non-palpable lesion
Nodule	Large papule (> 0.5 cm)
Papule	Small palpable, circumscribed lesion (< 0.5 cm)
Petechia	Pinpoint-sized macule of blood in the skin
Plaque	Large flat-topped, elevated, palpable lesion
Purpura	Larger macule or papule of blood in the skin which does not blanch on pressure
Pustule	Yellowish white pus-filled lesion
Scaly	Visible flaking and shedding of surface skin
Telangiectasia	Abnormal visible dilatation of blood vessels
Ulcer	Deeper denuded area of skin (full epidermal and dermal loss)
Vesicle	A small fluid-filled blister
Weal	Itchy raised 'nettle rash'-like swelling due to dermal oedema

INFECTIONS

BACTERIAL INFECTIONS (see also p 62)

The skin's normal bacterial flora prevents colonization by pathogenic organisms. A break in epidermal integrity by trauma, leg ulcers, fungal infections (e.g. athlete's foot) or abnormal scaling of the skin (e.g. in eczema) can allow infection. If reinfection occurs this may be due to asymptomatic nasal carriage of bacteria or the presence of other infected close contacts.

Table 23.2 Investigations used in skin disorders

Test	Use	Clinical example
Skin swabs	Bacterial culture	Impetigo
Blister fluid	Electron microscopy and viral culture	Herpes simplex
Skin scrapes	Fungal culture Microscopy	Tinea pedis Scabies
Nail sampling	Fungal culture	Onychomycosis
Wood's light	Fungal fluorescence	Scalp ringworm Erythrasma
Blood tests	Serology Autoantibodies HLA typing DNA analysis	Streptococcal cellulitis Discoid lupus erythematosus Dermatitis herpetiformis Epidemolysis bullosa
Skin biopsy	Histology Immunohistochemistry Immunofluorescence Culture	General diagnosis Cutaneous lymphoma Immunobullous disease Mycobacteria/fungi
Patch tests	Allergic contact eczema	Hand eczema
Urine	Dipstick (glucose) Cytology (red cells)	Diabetes mellitus Vasculitis
Dermatoscopy (direct microscopy of skin)	Assessment of pigmented lesions	Malignancy

Impetigo

Impetigo is a highly infectious skin disease most common in children (Fig. 23.2). It presents as weeping, exudative areas with a typical honey-coloured crust on the surface. It is spread by direct contact. The term 'scrum pox' is impetigo spread between rugby players. Group A (3 haemolytic streptococci and staphylococci are the causative agents: skin swabs should be taken. *Bullous impetigo* is caused by bacterial toxins (exfoliation A and B) from *Staphylococcus aureus*.

Treatment

Localized disease is treated with topical fucidic acid and mupirocin is used for MRS A (three times daily). The antiseptic povidone iodine is used to soften crusts and exudates for 1 week. Extensive disease is treated with oral antibiotics for 7-10 days (flucloxacillin 500 mg four times daily for *Staphylococcus*; penicillin V 500 mg four times daily for *Streptococcus*). Other close contacts should be examined, and children should avoid school for 1 week after starting therapy. If impetigo appears resistant to treatment or is



Fig. 23.2 Impetigo - crusted blistering lesions on the chin.

recurrent, take nasal swabs and check other family members. Nasal mupirocin (three times daily for 1 week) is useful to eradicate nasal carriage in hospitals.

Cellulitis

Cellulitis presents as a hot, sometimes tender area of confluent erythema of the skin owing to infection of the deep subcutaneous layer. It often affects the lower leg, causing an upwards-spreading, hot erythema, and occasionally will blister, especially if oedema is prominent. It may also be seen affecting one side of the face. Patients are often unwell with a high temperature. It is usually caused by a streptococcus or a staphylococcus. In the immunosuppressed or diabetic patient, Gram-negative organisms or anaerobes should be suspected. There may be an obvious portal of entry for infection such as a recent abrasion or a venous leg ulcer. The web spaces of the toes should be examined for evidence of fungal infection. Skin swabs are usually unhelpful. Confirmation of infection is best done serologically by streptococcal titres (antistreptolysin O titre (ASOT) and ADB).

Erysipelas is the term used for a more superficial infection (often on the face) of the dermis and upper subcutaneous layer that clinically presents with a well-defined edge. However, both erysipelas and cellulitis overlap, so it is often impossible to make a meaningful distinction.

Necrotising fasciitis: (see p. 64).

Treatment

Treatment is with penicillin V (or erythromycin) and flucloxacillin (all 500 mg four times daily). If disease is advanced, treatment may need to be given intravenously for 3-5 days followed by 1-2 weeks of oral therapy. Treat any identifiable underlying cause. If cellulitis is recurrent, low-dose antibiotic prophylaxis (e.g. penicillin V 500 mg twice daily) should be given, as each episode will cause further lymphatic damage.

Ecthyma

Ecthyma is also an infection due to *Streptococcus* sp. or *Staphylococcus aureus* or occasionally both. It presents as

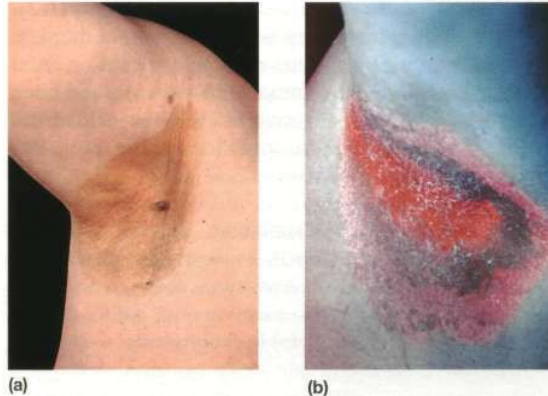


Fig. 23.3 Erythrasma of the axilla, showing pink fluorescence under a Wood's lamp.

chronic well-demarcated, deeply ulcerative lesions sometimes with an exudative crust. It is commoner in developing countries, being associated with poor nutrition and hygiene. It is rare in the UK but is seen more commonly in intravenous drug abusers and people with HIV.

Treatment is with penicillin V and flucloxacillin (both 500 mg four times daily) for 10-14 days.

Erythrasma

Erythrasma is caused by *Corynebacterium minutissimum*. It usually presents as an orange-brown flexural rash, and is often seen in the axillae or toe web spaces (Fig. 23.3). It is frequently misdiagnosed as a fungal infection. The rash shows a dramatic coral pink fluorescence under Wood's (ultraviolet) light.

Treatment is with topical fucidin three times daily for 7 days or oral erythromycin 500 mg four times daily for 7-10 days.

Folliculitis

Folliculitis is an inflammation of the hair follicle. It presents as itchy or tender papules and pustules. *Staphylococcus aureus* is frequently implicated. It is commoner in humid climates and when occlusive clothes are worn. A variant occurs in the beard area (called 'sycosis barbae') which is commoner in black Africans. This is probably caused by the ability of shaved hair to grow back into the skin, especially if the hair is naturally curly. Extensive, itchy folliculitis of the upper trunk and limbs should alert one to the possibility of underlying HIV infection. Folliculitis following exposure in hot tubs is due to *Pseudomonas* ovale.

Treatment is with topical antiseptics, topical antibiotics (e.g. fucidin) or oral antibiotics (e.g. flucloxacillin 500 mg or erythromycin 500 mg both four times daily for 2-4 weeks).

Skin disease

Boils (furuncles)

Boils are a rather more deep-seated infection of the skin, often caused by *Staphylococcus*. These can cause painful red swellings. They are commoner in teenagers and often recurrent. Recurrent boils may rarely occur in diabetes mellitus or in immunosuppression. Large boils are sometimes called 'carbuncles'.

Treatment is with oral antibiotics (e.g. erythromycin 500 mg four times daily for 10-14 days) and occasionally by incision and drainage. Antiseptics such as povidone iodine, chlorhexidine (as soap) and a bath oil (e.g. Oilatum plus™) can be useful in prophylaxis.

Hidradenitis suppurativa

This is a rare condition characterized by a painful, discharging, chronic inflammation of the skin at sites rich in apocrine glands (axillae, groins, natal cleft). The cause is unknown but it is commoner in females, and within some families it appears to be inherited in an autosomal dominant fashion. Clinically it presents after puberty with papules, nodules and abscesses which often progress to cysts and sinus formation. With time, scarring may arise. The condition follows a chronic relapsing/remitting course and is often worse in obese individuals.

Treatment is very difficult but weight loss, antibiotics, oral retinoids and co-cyprindiol ('2 mg cyproterone acetate + 35 ug ethinylestradiol' in females only) have been tried. They should be used as for acne vulgaris (p. 1338). Severe recalcitrant cases have been treated occasionally with surgery and skin grafting and more recently intravenous infliximab, a monoclonal antibody (p. 498).

This is a superficial infection of the horny layer of the skin caused by a *Corynebacterium*. It frequently involves the sole of the forefoot and appears as numerous small punched-out circular lesions of a rather macerated skin (e.g. as seen after prolonged immersion). There may be an associated hyperhidrosis of the feet and a prominent odour.

Treatment. Topical antibiotics (e.g. fucidin or clindamycin, applied three times daily for 2-4 weeks) and topical anti-sweating lotions are effective therapies.

Erysipeloid

This is a very rare infection due to *Erysipelothrix insidiosa*. It is seen in people who handle raw meat (especially pork) and fish. The organism gains entry through breaks in the skin. It presents as a spreading well-demarcated purplish red lesion, usually on the fingers, hands or forearms. There are no systemic symptoms.

Treatment is with penicillin V or oxytetracycline (both 500 mg four times daily for 7-10 days).

MYCOBACTERIAL INFECTIONS

Leprosy (Hansen's disease) (p. 80)

Leprosy usually involves the skin, and the clinical features depend on the body's immune response to the organism *Mycobacterium leprae*.

Indeterminate leprosy is the commonest clinical type, especially in children. This presents as hypopigmented or erythematous circular macules with occasional mild anaesthesia and scaling. This may resolve spontaneously or progress to one of the other types. Biopsy reveals a perineural granulomatous infiltrate and scant acid-fast bacilli.

Tuberculoid leprosy presents with a few hypopigmented or erythematous plaques with an active erythematous, raised rim. Lesions are usually markedly anaesthetic, dry and hairless reflecting the nerve damage. Nerves may be enlarged and palpable. Biopsy shows a granulomatous infiltrate centred on nerves, but no organisms.

Lepromatous leprosy presents with multiple inflammatory papules, plaques and nodules. Loss of the eyebrows ('madarosis') and nasal stuffiness are common. Skin thickening and severe disfigurement may follow. Anaesthesia is much less prominent. Biopsy shows numerous acid-fast bacilli.

Diagnosis and treatment are discussed on page 81.

Skin manifestations of tuberculosis

Tuberculosis can occasionally cause skin manifestations:

- **Lupus vulgaris** usually arises as a post-primary infection. It usually presents on the head or neck with red-brown nodules which look like apple jelly when pressed with a glass slide. They heal with scarring, and new lesions slowly spread out to form a chronic solitary erythematous plaque. Chronic lesions are at high risk of developing squamous cell carcinoma.
- **Tuberculosis verrucosa cutis** arises in people who are partially immune to tuberculosis but who suffer a further direct inoculation in the skin. It presents as warty lesions on a 'cold' erythematous base.
- **Scrofuloderma** arises when an infected lymph node spreads to the skin causing ulceration, scarring and discharge.
- **The tuberculides** are a group of rashes caused by an immune manifestation of tuberculosis rather than direct infection. Erythema nodosum is the commonest and is discussed on page 1341. Erythema induratum ('Bazin's disease') produces similar deep red nodules but these are usually found on the calves rather than the shins and they often ulcerate.

Atypical mycobacteria

Atypical (non-tuberculous) mycobacteria can occasionally infect the skin. *Mycobacterium marinum* is found in fish tanks and occasionally swimming pools. It can gain access via a break in the skin and then causes deep granulomatous nodules, often in a linear fashion.

VIRAL INFECTIONS

Viral exanthem

This, probably the commonest type of virally induced rash, presents clinically as a widespread non-specific erythematous maculopapular rash. It probably arises because of circulating immune complexes of antibody and viral antigen localizing to dermal blood vessels. The rash can be caused by many different viruses (e.g. echo-, parvo-, human herpes virus-6, Epstein-Barr virus; see p. 47) and so is rarely diagnostic. The rash will resolve spontaneously in 7-10 days.

Slapped cheek syndrome (erythema infectiosum, fifth disease)

This affects children and is caused by parvovirus B19 (see p. 48). It is a mild viral illness which is followed by an intense erythema on the cheeks ('slapped cheeks') and a reticulate erythema on the proximal limbs.

Herpes simplex virus (see also p. 43)

Herpes simplex virus (HSV) occurs as two genomic subtypes. HSV type 1 is spread by direct contact and droplet infection. Most people are affected in early childhood but the infection is usually subclinical. Occasionally it can cause a self-limiting pyrexial primary illness with either clusters of painful blisters on the face or a painful gingivostomatitis. Once infected, cell-mediated immunity develops. In some individuals this response is poor and they may get recurrent attacks of HSV, often manifest as cold sores. Immunosuppression can also cause a recrudescence of HSV. HSV can also autoinoculate into sites of trauma and present as painful blisters/pustules. For example they may be seen on the fingers of healthcare workers ('herpetic whitlow').

HSV type 2 infections occur mainly after puberty and usually affect the genital area. Infections are often symptomatic and transmitted sexually. However, HSV type 1 can also be found in the genital area due to orogenital contact.

Other rare complications of HSV infection include corneal ulceration, eczema herpeticum (p. 1327), chronic perianal ulceration in AIDS patients and erythema multiforme (p. 1342).

Treatment

Oral valaciclovir (500 mg twice daily for 5 days) is used for primary HSV and painful genital HSV. Recurrent cold sores are treated with aciclovir cream but this must be used early to be effective in shortening an attack. Attacks of genital herpes become less frequent with time. Intravenous aciclovir must be used in immunosuppressed patients.

Varicella zoster virus

Varicella zoster virus (VZV) causes the common child-



Fig. 23.4 Herpes zoster in an African (courtesy of Dr P Matondo, Lusaka, Zambia).

hood infection called chickenpox. It is discussed on page 45. It also causes herpes zoster.

Herpes zoster (shingles)

'Shingles' results from a reactivation of the VZV. It may be preceded by a prodromal phase of tingling or pain, which is then followed by a painful and tender blistering eruption in a dermatomal distribution (Fig. 23.4 and Fig. 2.15, p. 46). The blisters occur in crops, may become pustular and then crust over. The rash lasts 2-4 weeks and is usually more severe in the elderly. Occasionally more than one dermatome is involved.

Complications of shingles include severe, persistent pain (post-herpetic neuralgia), ocular disease (if ophthalmic nerve involved) and rarely motor neuropathy.

Treatment

Herpes zoster requires adequate analgesia and antibiotics (if secondary bacterial infection is present). Valaciclovir 1 g or famciclovir 500 mg three times daily for 7 days is used, or oral aciclovir 800 mg, five times daily for 7 days helps shorten the attack if given early in the illness. High-dose intravenous aciclovir is needed for immunosuppressed patients. It remains unclear how useful aciclovir therapy is in preventing prolonged post-herpetic neuralgia.

Human papilloma virus

Human papilloma virus (HPV) is responsible for the common cutaneous infection of 'viral warts'. There are more than 70 subtypes as detected by DNA hybridization. All can cause overgrowth of differentiated squamous epithelium.

Common warts are papular lesions with a coarse roughened surface, often seen on the hands and feet, but also on other sites. Small black dots (bleeding points) are often seen within the lesion (Fig. 23.5). Children and adolescents are usually affected. Spread is by direct contact and is also associated with trauma.

Plantar warts (verrucae) is the term used for lesions on the soles of the feet. They often appear flat ('inward

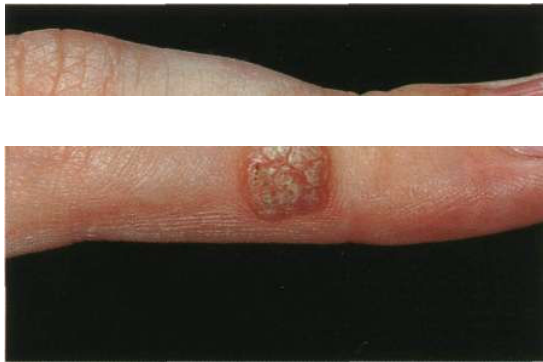


Fig. 23.5 Viral wart.

growing') although they have the same papillomatous surface change and black dots are often revealed if the skin is pared down (unlike callosities). Warts may be painful or tender if they are over pressure points or around nail folds.

Filiform warts occur on the face, at the nasal vestibule or around the mouth. They are elongated with a horny cap.

Plane warts are much less common and are caused by certain HPV subtypes. They are clinically different and appear as very small, flesh-coloured or pigmented, flat-topped lesions (best seen with side-on lighting) with little in the way of surface change and no black dots within them. They are usually multiple and are frequently found on the face or the backs of the hands.

Anogenital warts are usually seen in adults and are normally transmitted by sexual contact. They are rare in childhood and, whilst child sex abuse should always be considered, it should be remembered they may well have been transmitted through non-sexual contact. HPV subtypes 16 and 18 are potentially oncogenic and are associated with cervical and anal carcinomas.

Treatment

Common warts on the skin are surprisingly difficult to treat effectively but they almost always resolve spontaneously after months to years (with no scarring), presumably because of cell-mediated immune recognition. When they do resolve, they tend to do so rapidly within a few days.

Regular use of a topical keratolytic agent (e.g. 2-10% salicylic acid) over many months with weekly paring of the lesion helps speed up resolution in some patients and remains the mainstay of treatment. A course of cryotherapy (freezing) can also help. Cautery, surgery, carbon dioxide laser, alpha-interferon injection and bleomycin injection have all been used with variable success but are not recommended, as treatments may be very painful and can cause permanent scarring. Experimental usage of a complex of oc-lactalbumin and oleic acid (human cx-lactalbumin made lethal to tumour cells - HAMLET) is promising.

Genital warts (see p. 126) are usually treated with either cryotherapy, trichloroacetic acid, 5% imiquimod

cream or topical podophyllin. Patients with genital warts (and their sexual partners) must be screened for other sexually transmitted diseases.

Molluscum contagiosum ('water blisters')

Molluscum contagiosum is a common cutaneous infection of childhood caused by a pox virus. The virus can be seen in the fluid under EM. Clinically, lesions are multiple, small (1-3 mm) translucent papules which often look like fluid-filled vesicles but are in fact solid. Individual lesions may have a central depression called a punctum. They exhibit the Kobner phenomenon (p. 1332). They can occur at any body site including the genitalia. Transmission is by direct contact. Occasionally lesions may be up to 1 cm in diameter ('giant molluscum'). They are said to be more extensive in children with atopic eczema, which may just reflect that scratching aids their spread.

They usually continue to occur in crops over 6-12 months and rarely require treatment as they spontaneously resolve. Any form of localized trauma, including scratching, helps speed up resolution and cryotherapy may be considered in an older child. Molluscum in an adult, especially if giant, should raise the underlying possibility of immunosuppression, especially HIV infection.

Orf

Orf is a disease of sheep (and occasionally goats) due to a pox virus infection. It causes a vesicular and pustular rash around the mouths of young lambs. People who come into contact with the affected fluid may develop lesions on the hands. Clinically they appear as 1-2 cm reddish papules with a surrounding erythema which usually become pustular. The lesion(s) resolves spontaneously after 4-6 weeks and immunity lasts lifelong. Occasionally orf is complicated by erythema multiforme (p. 1342).

FUNGAL INFECTIONS

Fungi are primitive, saprophytic organisms found throughout our environment. Fungal skin disease (mycosis) has a high prevalence in humans, with 'thrush' and 'athlete's foot' being two of the commonest examples. In the immunosuppressed, mycoses can be widespread and life-threatening. There are three groups of pathogenic fungi that commonly affect the outer layer of skin or keratinizing epithelium: dermatophytes, *Candida albicans* and pityrosporum.

Dermatophyte infection

By definition, dermatophytes cause a 'ringworm' type of rash. The three main genera responsible are *Trichophyton*, *Microsporum* and *Epidermophyton*. These organisms are identified by microscopy and culture of skin, hair or nail samples. The clinical appearance of mycoses depends in



Fig. 23.6 Tinea cruris - ringworm of the groin.

part on the organism involved, the site affected and the host reaction. All are spread by direct contact from other humans or from infected animals. The use of communal showers and swimming baths and the sharing of towels or sportswear aids indirect fomite transmission.

Tinea corporis

Ringworm of the body usually presents with slightly itchy, asymmetrical, scaly patches which show central clearing and an advancing, scaly, raised edge. Occasionally vesicles or pustules may be seen in the edge. Central clearing is not a universal feature and it is recommended that all asymmetrical scaly lesions should be scraped for fungus. Ringworm of the face (*tinea faciei*) often arises after the use of topical steroids. It tends to be more erythematous and less scaly than trunk lesions and it may become itchy after sun exposure.

Tinea cruris

Ringworm of the groin is extremely common world-wide. Early on, the lesions appear as well-demarcated red plaques with an arc-like border extending down the upper thigh (Fig. 23.6). Central clearing may appear and a few pustules or vesicles may be seen if inflammation is intense. Satellite lesions, suggestive of *Candida*, are not present.

Tinea pedis

Athlete's foot may be confined to the toe clefts, where the skin looks white, macerated and fissured. It may also be more diffuse, usually causing a diffuse scaly erythema of the soles, spreading on to the sides of the foot. Annular lesions are rare and can be misdiagnosed. There may be an associated hyperhidrosis and fungal involvement of one or more toe-nails. In severe infection, a strong inflammatory reaction can occur causing pustules or blistering and this often leads to a misdiagnosis of pompholyx-type

Tinea manuum

Ringworm of the hands also presents with a diffuse erythematous scaling of the palms with variable skin peeling and skin thickening. Annular lesions are rare at this site.

Tinea capitis

The fungus is either within the hair shaft (endothrix) or spread out over the hair surface (ectothrix). The latter can cause fluorescence under a Wood's lamp (ultraviolet light). Scalp ringworm is spread by close contact (especially in schools and households) and may also be spread indirectly by hairdressers. The number of new cases has risen enormously in the large cities in developed countries. Increase in travel and immigration has allowed the spread of different pathogenic fungi (e.g. *Trichophyton tonsurans* from Central America, *Trichophyton violaceum* from India and Pakistan) into new countries where there is overcrowding and poor social conditions. The majority of UK cases are due to *T. tonsurans* (which does not show fluorescence).

Tinea capitis is much commoner in children, especially those of black African origin, whose scalp and hair seems more susceptible to fungal invasion. The clinical appearance of scalp ringworm is highly variable from a mild diffuse scaling with no hair loss (similar to dandruff) to the more typical appearance of circular scaly patches in the scalp with associated alopecia and broken hairs. As the hosts immune response increases, a few pustules may appear and an exudate may be present. At worst, a full-blown 'kerion' develops; a boggy swollen mass with copious quantities of discharging pus and exudate accompanied by severe alopecia. This is still poorly recognized and inappropriately treated with antibiotics and attempted surgical drainage.

Extensive infection is occasionally accompanied by a widespread papulopustular rash on the trunk. This is a so-called 'Id reaction' and probably relates to the host immune response to the fungus. It seems commoner in black African children. It resolves when the fungal infection is treated.

Tinea unguium

Ringworm of the nails is increasingly common with age and frequently ignored as it is often asymptomatic. Clinically this presents as asymmetrical whitening (or yellowish black discoloration) of one or more nails, which usually starts at the distal or lateral edge before spreading throughout the nail (Fig. 23.7). The nail plate appears



Fig. 23.7 Dermatophyte infection of the nail showing white crumbling dystrophy.

Skin disease

thickened. Crumbly white material appears under the nail plate and this is the best specimen to obtain for mycology sampling. The nail plate may become destroyed with advanced disease.

'Tinea incognito'

This is the term used to describe a fungal skin infection that has been modified by therapy with a topical steroid. The clinical appearance is variable but may show a non-specific erythema with little in the way of scaling or a few reddish nodules. The history of the rash improving with steroid treatment (owing to the suppression of inflammation) but worsening and spreading every time it is stopped is typical. Skin scrapings for mycology or even a biopsy should confirm the diagnosis.

Treatment

Localized ringworm of the body or flexures is treated with topical antifungal creams (clotrimazole, miconazole, terbinafine or amorolofine applied three times daily for 1-2 weeks). More widespread infection, including tinea pedis, tinea manuum and tinea capitis, requires oral antifungal therapy. Itraconazole (100 mg daily) and terbinafine (250 mg daily) are the most effective drugs used for periods of 1-2 months, but are not licensed for use in children. High-dose griseofulvin is still used in children for scalp ringworm (15-20 mg/kg per day for 8 weeks).

Tinea unguium of the toe-nails is the most resistant to treatment. Itraconazole (100 mg daily or 200 mg twice daily for 1 week per month 'pulsed therapy') or terbinafine (250 mg daily) given for 3 months will cure up to about 80% of cases.

Candida albicans (see also p. 91)

Candida albicans is a yeast that is sometimes found as part of the body's flora, especially in the gastrointestinal tract. It acts as an opportunist, taking hold in the skin when there is a suitable warm moist environment such as in nappy rash (p. 1362) or intertrigo in obese individuals (Fig. 23.8).

The flexural areas affected are red with a rather ragged peeling edge that may contain a few small pustules. Small circular areas of erythema or small papules and pustules may be seen in front of the advancing edge (satellite lesions). *Candida* may also affect the moist interdigital clefts of the toes and mimic tinea pedis. In people who have their hands immersed frequently in water (e.g. cleaners, nurses) *Candida* may cause infection in the macerated skin of the finger web spaces or the damaged skin around the nail folds ('chronic paronychia'). Nail infection may mimic tinea unguium. It can infect mucosal surfaces of the mouth or genital tract. This tends to occur in patients taking broad-spectrum antibiotics (due to suppression of protective bacterial flora) or in immunosuppressed patients. Clinically superficial white or creamy pseudomembranous plaques appear which can be scraped off leaving raw areas underneath.



Fig. 23.8 Intertrigo with satellite lesions typical of candidiasis.

Treatment

Treatment is aimed at removing any underlying predisposing factor and applying topical antifungal creams, e.g. clotrimazole or miconazole (or the equivalent as mouth lozenges/pessaries). *Candida* nail infections require systemic antifungal therapy with an imidazole such as itraconazole (100 mg daily for 3 months). Recurrent candidiasis is relatively common, especially in women. Diabetes mellitus should always be excluded. Repeated topical treatment or an oral imidazole may be needed.

Pityrosporum

This yeast occurs as part of the normal flora of human skin. Colonization is prominent in the scalp, flexures and upper trunk. There are two morphological variants called *Pityrosporum ovale* and *Pityrosporum orbiculare*, and the mycelial form of this yeast is called *Malassezia furfur*. *Pityrosporum* can overgrow in some individuals and has been implicated in three dermatoses:

- pityriasis versicolor
- seborrhoeic eczema (p. 1329)
- pityrosporum folliculitis.

Pityriasis versicolor

This is a relatively common condition of young adults caused by infection with *Pityrosporum*. In Caucasians it presents most commonly on the trunk with reddish brown scaly macules which are asymptomatic. In black-skinned individuals (or in whites who are sun-tanned) it more commonly presents as macular areas of hypopigmentation. Inappropriate use of topical steroids tends to spread the rash.

Diagnosis can be confirmed by skin scrapings or Wood's light examination (yellow fluorescence).

Treatment is with selenium sulphide shampoo (apply to body and remove after 30 minutes and repeat daily for 1 week) or a topical imidazole cream (twice daily for 10 days). Oral itraconazole (100 mg twice daily for 1 week) can be used for resistant cases. The pigmentation takes months to recover even after successful treatment. The condition may recur but can be retreated.

Pityrosporum folliculitis

This is common in young adult males and characterized by small itchy papules and pustules on the upper back which are centred on hair follicles. It is commoner in people with Down's syndrome. It responds well to ketoconazole shampoo or a topical imidazole cream (twice daily for 2 weeks).

JN^{AS}WIONS

Scabies

Scabies is an intensely itchy rash caused by the mite *Sarcoptes scabiei*. It can affect all races and people of any social class. It is most common in children and young adults but can affect any age group. There are 300 million cases of scabies in the world each year. It is commoner in poorer countries with social overcrowding.

Scabies is spread by prolonged close contact such as within households or institutions, and by sexual contact. It presents clinically with itchy red papules (or occasionally vesicles and pustules), which can occur anywhere in the skin but rarely on the face, except in neonates. The distribution of lesions is often suggestive of the diagnosis (Fig. 23.9). Sites of predilection are between the web spaces of the fingers and toes, on the palms and soles, around the wrists and axillae, on the male genitalia, and around the nipples and umbilicus.



Fig. 23.9 Scabies - itchy papules and pustules centred on the web spaces of the hand.

The pathognomonic sign is of linear or curved skin burrows but these are not always present. The pruritus is normally worse at night. Excoriations and secondary bacterial infection may complicate the rash. Scabies can be confirmed by taking skin scrapings of a lesion and examining a potassium hydroxide preparation for the mite and/or its eggs by microscopy.

Treatment

This involves application of a topical scabicide (e.g. 5% permethrin or malathion). For the treatment to be successful the following factors should be noted:

- All the skin below the neck should be treated, including the genitalia, palms and soles, and under the nails. Treat the head and neck regions in infants (up to age 2 years).
- All close contacts should be treated at the same time even if asymptomatic.
- Reapply scabicide to the hands if they are washed during the treatment period.
- Patients should be warned that the pruritus may persist for up to 4 weeks after successful treatment. Adjunct treatment with crotamiton cream, an emollient or a mild topical steroid is helpful.
- A patient information leaflet about therapy helps improve compliance.

Benzyl benzoate is still used occasionally but it can be very irritant. Lindane is a cheap therapy which is still used in many countries but there are concerns about resistance to this drug and possible neurotoxic side-effects.

Crusted scabies (Norwegian scabies)

Crusted scabies is a clinical variant that occurs in immunosuppressed individuals where huge numbers of mites are carried in the skin. Patients are not always itchy but they are extremely infectious after relatively minimal contact, which is unfortunate as the diagnosis is often delayed. Clinically this presents as hyperkeratotic crusted lesions, especially on the hands and feet. Lesions may progress such that the patient has a widespread erythema with irregular crusted plaques. It can therefore mimic infected eczema or psoriasis.

Treatment is with careful barrier nursing, repeated applications of a scabicide and, in resistant cases, oral ivermectin (100-200 (ig/kg - two doses 1 week apart) may be given but this is an unlicensed use.

Lice infection

Lice are blood-sucking ectoparasites that can affect man in three ways.

Head lice (pediculosis capitis)

Head lice is a common infection world-wide, afferring predominantly children and being commoner in females. Spread is by direct contact and encouraged by overcrowding. It usually presents with itch or scalp

Skin disease

excoriations. Occasionally, erythematous papules on the neck may be seen.

Diagnosis can be confirmed by the presence of eggs ('nits') seen tightly bound to the hair shaft. Adult lice may be seen rarely in heavy infection. School nurses and parents are usually adept at this.

Treatment. Eradication is difficult because of non-compliance as well as resistance patterns. Malathion, carbaryl or permethrin applications (two applications 7 days apart) are the most commonly used. Nit combing of wet hair is not as effective as chemical treatment. District policies of rotating insecticides are outmoded. If one treatment fails, a different insecticide is used for the next course in an individual. Treatment is usually repeated after 7 days and metal nit combs may help remove the eggs. Some areas in the UK have given up with specific anti-lice treatments but have a policy of treating schools and family members with regular nit-combing, shampooing and conditioning of the hair. However, a recent study showed that chemical therapies are more effective than physical treatments, but more studies are needed.

Body lice (pediculosis corporis)

Body lice is a disease of poverty and neglect. It is rarely seen in developed countries except in homeless individuals and vagrants. It is spread by direct contact or sharing infested clothing. The lice and eggs are rarely seen on the patient but are commonly found on the clothing. It presents with itch, excoriations and sometimes post-inflammatory hyperpigmentation of the skin.

Treatment consists of malathion or permethrin for the patient and high-temperature washing and drying of clothing.

Pubic lice (crabs, phthiriasis pubis)

Pubic lice are transmitted by direct contact, usually sexual. It presents with itching, especially at night. Lice can be seen near the base of the hair with eggs somewhat further up the shaft. Occasionally eyebrows, eyelashes and the beard area are affected.

Treatment is as for head lice but all sexual contacts should be treated and other sexually transmitted diseases should be screened for. Pubic lice of the eyelashes is treated with white soft paraffin three times daily for 1-2 weeks.

Arthropod-borne diseases ('insect bites' or papular urticaria)

These depend on contact with an animal (e.g. dog, cat, bird) that is infected with fleas (*Ctenocephalides*) or on bites from flying insects (e.g. midges, mosquitoes). In the case of flea bites the animal itself may be itchy with scaly and thickened skin. These fleas can also live in soft furnishings (e.g. carpets and beds) even after the animal

has been removed. Bites present as itchy urticated lesions which are often grouped in clusters. The legs are most commonly affected. It is not unusual for an individual to react badly to bites when other family members seem unaffected. Anti-flea treatment of the animal and furnishings is required. Insect repellents and appropriate clothing help reduce bites from flying insects.

FURTHER READING

- Chosidow O. (2000) Scabies and pediculosis. *Lancet* **355**: 819-826. Gnann JW, Whitley RJ (2002) Herpes zoster. *New England Journal of Medicine* **347**: 340-346 Ko CJ et al. (2004) Pediculosis. *Journal of the American Academy of Dermatology* **50**:1-12. Manders SM (1998) Toxin-mediated streptococcal and staphylococcal disease. *Journal of the American Academy of Dermatology* **39**: 383-398. Sterling JC et al. (2001) Guidelines for the management of cutaneous warts. *British Journal of Dermatology* **144**: 4-11. Swartz MN (2004) Cellulitis. *New England Journal of Medicine* **350**: 908-912.

PAPULO-SQUAMOUS/ INFLAMMATORY RASHES

ECZEMA

The term 'eczema' derives from the Greek word for 'boiling', which reflects that the skin can become so acutely inflamed that fluid weeps out or vesicles appear. It is synonymous with the term dermatitis and the two words are interchangeable. In the developed world eczema accounts for a large proportion of skin disease, both in hospital and community-based populations. It is estimated that 10% of people have some form of eczema at any one time, and up to 40% of the population will have an episode of eczema during their lifetime.

All eczemas (see Table 23.3) have some features in common and there is a spectrum of clinical presentation from acute through to chronic. Vesicles or bullae may appear in the acute stage if inflammation is intense. In subacute eczema the skin can be erythematous, dry and flaky, oedematous, and crusted (especially if secondarily infected). Chronic persistent eczema is characterized by thickened or lichenified skin. Eczema is nearly always itchy. Histologically 'eczematous change' refers to a col-

Table 23.3 Classification of eczema

Endogenous	Exogenous
Atopic eczema	Contact eczema - irritant
Discoid eczema	Contact eczema - allergic
Hand eczema	Photosensitive eczema
Seborrhoeic eczema	Lichen simplex/nodular prurigo
Venous ('gravitational') eczema	
Asteatotic eczema	

leakage of fluid in the epidermis between the keratinocytes ('spongiosis') and an upper dermal perivascular infiltrate of lymphohistiocytic cells. In more chronic disease there is marked thickening of the epidermis ('acanthosis').

Atopic eczema

This type of eczema (often called 'endogenous eczema') occurs in individuals who are 'atopic' (p. 912). It is common, occurring in up to 5% of the UK population. It is commoner in early life, occurring at some stage during childhood in up to 10-20% of all children.

Aetiology

The exact pathophysiology is not fully understood but there is a selective activation of Th2-type CD4 lymphocytes in the skin which drives the inflammatory process. In at least 90% of cases there is a raised serum total IgE level. Atopic eczema is a genetically complex, familial disease with a strong maternal influence. A positive family history of atopic disease is often present: there is a 90% concordance in monozygotic twins but only 20% in dizygotic twins. If one parent has atopic disease the risk for a child of developing eczema is about 20-30%, and 50% if both parents are affected. Genetic studies in atopy have so far shown linkage to several different loci where pathologically relevant candidate genes exist: e.g. the α -subunit of the high-affinity IgE receptor (11q13); Th2 cytokine genes (5q31-33); the α -subunit of IL-4 (16q12); and RANTES (17q11). Both eczema and psoriasis have been linked to chromosome 1q21 and 17q25, suggesting common candidate genes controlling skin inflammation. Genetic heterogeneity is likely and it may be that certain genes are more involved in developing eczema rather than asthma, and other genes may be significant in determining severity of the disorder or age of onset. The disease is also significantly influenced by environmental factors.

Exacerbating factors

Infection either in the skin or systemically can lead to an exacerbation, possibly by a superantigen effect. Paradoxically, lack of infection (in infancy) may cause the immune system to follow a Th-2 pathway and allow eczema to develop (the so-called 'hygiene hypothesis'). Strong detergents, chemicals and even woollen clothes can be irritant and exacerbate eczema. Teething is another factor in young children. Severe anxiety or stress appear to exacerbate eczema in some individuals. Cat and dog fur can certainly make eczema worse, possibly by both allergic and irritant mechanisms. The role of house dust mite and diet is less clear cut. There is some evidence that food allergens may play a role in triggering atopic eczema and that dairy products may exacerbate eczema in a few selected infants under 12 months of age.

Clinical features

Atopic eczema can present as a number of distinct morphological variants. The commonest presentation is of itchy erythematous scaly patches, especially in the



Fig. 23.10 Atopic eczema behind the knees.

flexures such as in front of the elbows and ankles, behind the knees (Fig. 23.10) and around the neck. In infants eczema often starts on the face before spreading to the body. Very acute lesions may weep or exude and can show small vesicles. Scratching can produce excoriations, and repeated rubbing produces skin thickening (lichenification) with exaggerated skin markings.

In patients with pigmented skin, eczema often shows a reverse pattern of extensor involvement. Also, the eczema may be papular or follicular in nature and lichenification is common. A final problem in pigmented skin is of post-inflammatory hyper- or hypopigmentation which is often very slow to fade after control of the eczema.

Associated features

Involvement of the nail bed may produce pitting and ridging of the nails. In some atopic individuals the skin of the upper arms and thighs may feel roughened because of follicular hyperkeratosis ('keratosis pilaris'). The palms may show very prominent skin creases ('hyperlinear palms'). There may be an associated dry 'fish-like' scaling of the skin which is non-inflammatory and often prominent on the lower legs ('ichthyosis vulgaris').

Complications

Broken skin commonly becomes secondarily infected by bacteria. This is usually due to *Staphylococcus aureus* although streptococci can colonize eczema, especially in macerated flexural areas such as the neck and groin. Clinically this infection may appear as crusted, weeping impetigo-like lesions. Occasionally *Pseudomonas* can be grown from skin swabs but this rarely causes a clinical problem. Cutaneous viral infections (e.g. viral warts and molluscum) are often widespread in atopic eczema and are probably spread by scratching. HSV can cause a widespread eruption called eczema herpeticum (Kaposi's varicelliform eruption). This can occasionally be a very severe infection and rarely can be fatal. This appears as multiple small blisters or punched-out crusted lesions associated with malaise and pyrexia, and needs rapid treatment with oral (or intravenous if severe) aciclovir. Ocular complications of atopic eczema include conjunctival

Skin disease

irritation and less commonly keratoconjunctivitis and cataract. Retarded growth may be seen in children with chronic severe eczema; it is due to the disease itself and not the use of topical steroids.

Investigations

The diagnosis of atopic eczema is normally clinical. Atopy is characterized by high serum IgE levels or high specific IgE levels to certain ingested or inhaled antigens. The latter can be tested by radio-immunoabsorbent assay (RAST tests) of blood, or indirectly by skin prick testing (p. 918). A peripheral blood eosinophilia may also be

Prognosis

The majority (90%) of children with early-onset atopic eczema will spontaneously improve and 'clear' before the teenage years, 50% being clear by the age of 6. A few will get a recurrence as adults, even if just as hand eczema. However, if the onset of eczema is late in childhood or in adulthood, the disorder follows a more chronic remitting/relapsing course.

Treatment (Box 23.2)

General measures

These include avoiding known irritants (especially soaps or furry animals), wearing cotton clothes, and not getting too hot. Manipulating the diet (e.g. dairy-free diet) is rarely beneficial except in children under 12 months with a hereditary risk of eczema. Any change in diet should be done under supervision, especially with growing children who may need supplements such as calcium.

Topical therapies

Topical therapies (p. 1364) are sufficient to control atopic eczema in most people. The 'triple' combination of topical steroid, frequent emollients (see Table 23.16) and bath oil and soap substitute (e.g. aqueous cream) helps.

Written information or a practical demonstration of how to apply these treatments improves compliance.

Use of topical Steroids. Unjustified fear about the dangers of topical steroids has often led to under-treatment of eczema. Providing appropriate-strength steroid preparations are used for the right body site, these

Box 23.2 Management of atopic eczema

- Education and explanation
- Avoidance of irritants/allergens
- Emollients
- Bath oils/soap substitutes
- Topical therapies:
 - steroids
 - immunomodulators
- Adjunct therapies:
 - oral antibiotics
 - sedating antihistamines
 - bandaging
- Phototherapy/systemic therapy (for severe cases)

Table 23.4 Classification of topical steroids by potency

Very potent	0.05% clobetasol propionate 0.3% diflucortolone valerate 0.1%
Potent	betamethasone valerate 0.025% fluocinolone acetonide 0.025%
Diluted potent	betamethasone valerate 0.00625% fluocinolone acetonide 0.05%
Moderately potent	clobetasone butyrate 0.05% alclometasone dipropionate 2.5%
Mild	hydrocortisone 1% hydrocortisone

compounds can be used quite safely on a long-term intermittent basis. Topical steroids can be divided into five groups depending on their potency (Table 23.4).

The following guidelines should be followed to allow their safe use in common chronic inflammatory skin conditions.

- The face should be treated with mild steroids.
- In adults the body should be treated with either mild, moderately potent or diluted potent steroids.
- In young children the body should be treated with mild and moderately potent steroids.
- Potent steroids may be used for short courses (7-10 days).
- Treatment of the palms and soles (but not the dorsal surfaces) may require potent or very potent steroids as the skin is much thicker.
- Regular use of emollients may lessen the need for steroid use.
- Only use steroids on inflamed skin. Do not use as an emollient.
- 'Apply sparingly' means use sufficient to leave a glistening surface to the skin after application.
- Use weaker steroid preparations in flexures (e.g. the groin, and under breasts) as apposition of the skin at these sites tends to occlude the treatment and increase absorption.

Topical immunomodulators

Tacrolimus ointment (0.1% and 0.03%) and the less potent pimecrolimus (a skin-selective inflammatory cytokine inhibitor) cream have recently been licensed for atopic eczema in patients over 2 years old. They have the advantage over potent steroids of not causing atrophy and are thus very useful for treating sensitive areas such as the face and eyelids. They can be very irritant when first used (although this settles with continued use) and 9% of patients develop flushing after alcohol. The long-term side-effects remain unknown. They do not work so well on lichenified eczema, probably because of poor absorption. Current advice is to avoid vaccinations and sun exposure when using these agents. The milder potency steroid creams should still be considered as first-line therapy but tacrolimus is a useful alternative to excessive use of potent steroids.

Antibiotics

These are needed for bacterial infection and are usually given orally for 7-10 days. Flucloxacillin (500 mg four times daily) is effective against *Staphylococcus*, and penicillin V (500 mg four times daily) acts against *Streptococcus*. Erythromycin (500 mg four times daily) is useful if there is allergy to penicillin. Topical antiseptics may be useful in cases of recurrent infection but they can be irritant. They are usually added to the bath water rather than directly onto the skin. Combination topical steroid/antibiotic creams are used for short periods but there is little evidence that they are better than topical steroids alone.

Sedating antihistamines

These (e.g. oral hydroxyzine 25 mg) are useful at night-time. They help by their sedative properties, not by their antihistamine activity.

Bandaging

Paste bandaging can be useful for resistant or lichenified eczema of the limbs. It helps absorption of treatment and acts as a barrier to prevent scratching. Wet tubular gauze bandages are useful for inpatient therapy but are difficult and time-consuming to use at home.

Second-line agents

These may be considered in severe non-responsive cases, especially if the eczema is significantly interfering with an individual's life (e.g. growth, sleeping, schoolwork or job). Ultraviolet phototherapy (see p. 1339), prednisolone (initial doses up to 30 mg daily), ciclosporin (3-5 mg/kg daily) and azathioprine (1-2 mg/kg daily) (p. 1347) can all be effective treatments. However, they all have side-effects and the risk/benefit ratio must be openly discussed with the patient before they are used.

Use of ciclosporin. Ciclosporin is a selective immunosuppressant that inhibits interleukin-2 production by T lymphocytes. A large number of other drugs interact with ciclosporin (e.g. erythromycin, NSAIDs) and should be avoided. Renal damage and hypertension are the two most serious side-effects so blood pressure and serum creatinine should be measured every 6-12 weeks. Creatinine clearance should be measured yearly in people on long-term therapy. Renal damage becomes increasingly common with time and tends to be dose-dependent but is mostly reversible. Hypertrichosis, paraesthesia and nausea are less serious side-effects. Pregnancy should be avoided.

Discoid eczema (nummular eczema)

Discoid eczema is a morphological variant of eczema, characterized by well-demarcated scaly patches especially on the limbs, and this can be confused sometimes with psoriasis. It is commoner in adults and can occur in both atopic and non-atopic individuals. It tends to follow an acute/subacute course rather than a chronic pattern. There is often an infective component (*Staphylococcus aureus*).



Fig. 23.11 Pompholyx eczema (courtesy of Dr A Bewley, London).

Hand eczema

Eczema may be confined to the hands (and feet). It can present with:

- itchy vesicles or blisters of the palm and along the sides of the fingers (also called 'pompholyx') (Fig. 23.11)
- a diffuse erythematous scaling and hyperkeratosis of the palms
- a scaling and peeling most marked at the finger tips.

Hand eczema is not unusual in atopies but more frequently occurs in non-atopic individuals, and a cause is not always found. A history of contact with irritants (e.g. detergents, chemicals) and an occupational history should be sought, especially in finger-tip eczema. Patch testing for specific allergic or contact eczema should always be considered, as up to 10% of individuals with hand eczema will show a positive test. Finally look for evidence of fungal infection, as this can occasionally induce a secondary pompholyx of the hands or feet (a so-called 'Id reaction').

Seborrhoeic eczema

Aetiology

Overgrowth of *Pityrosporum ovale* (also called *Malassezia furfur* in its hyphal form) together with a strong cutaneous immune response to this yeast produces the characteristic inflammation and scaling of seborrhoeic eczema. The condition is more common in parkinsonism as well as in HIV disease.

Clinical features

Seborrhoeic eczema affects body sites rich in sebaceous glands, although these do not appear to be involved in its cause. Three age groups are affected:

- *In childhood* it is common and presents in the first few months of life as 'cradle cap' in most babies. This may in part be due to the effect of maternal androgens on infant sebaceous glands. Yellowish, greasy, thick crusts are seen on the scalp. A more widespread erythematous, scaly rash can be seen over the trunk,

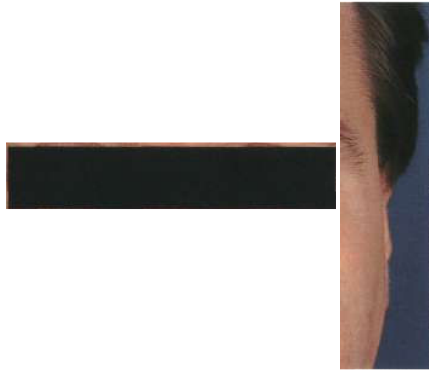


Fig. 23.12 Seborrhoeic eczema affecting the sides of the nose.

especially affecting the nappy area. Unlike with atopic eczema, the child is normally unbothered as there is little associated pruritus. The rash normally improves spontaneously after a few weeks.

- *In young adults* (especially males) it occurs in 1-3% of the population. The rash is more persistent and presents as an erythematous scaling along the sides of the nose (Fig. 23.12), in the eyebrows, around the eyes and extending into the scalp (which shows marked dandruff). It affects the skin over the sternum, axillae and groins, and the glans penis. A blepharitis may also be present.
- *In elderly people* seborrhoeic eczema can be more severe and progress to involve large areas of the body and even cause erythroderma.

Treatment

This is suppressive rather than curative. A combination of a mild steroid ointment (e.g. 1% hydrocortisone applied twice daily) and a topical antifungal cream (e.g. miconazole cream applied twice daily) will help to control the eruption. Two per cent sulphur or 2% salicylic acid can be added to help control resistant cases. Recent studies have shown 0.1% tacrolimus ointment to be very effective. Ketoconazole shampoo and arachis oil are useful for the scalp. Emollients and a soap substitute are useful adjuncts.

Venous eczema (varicose eczema, gravitational eczema)

This type of eczema occurs on the lower legs because of chronic venous hypertension (usually of more than 2 years' duration) (see p. 1353). The exact cause remains unknown but it has been suggested that venous hypertension causes endothelial hyperplasia and extravasation of red and white blood cells, which in turn causes inflammation, purpura and pigmentation.

Clinical features

Venous eczema tends to occur in older people, especially women. It usually appears on the lower legs around the

ankles. There may be a past history of venous thrombosis or previous surgery for varicose veins. Brownish pigmentation (haemosiderin) is seen in the skin and a venous leg ulcer or varicose veins may be present.

Superimposed contact eczema is common in venous eczema patients, especially when there have been chronic venous leg ulcers. This is usually due to an allergic reaction to topical therapies or skin dressings. Patch testing is useful in treatment-resistant cases.

Treatment

This should include emollients and a moderately potent topical steroid. Support stockings or compression bandages, together with leg elevation, help reverse the underlying venous hypertension (p. 1353).

Asteatotic eczema (winter eczema, eczema craquele, senile eczema)

This is a dry plate-like cracking of the skin with a red, eczematous component which occurs in elderly people. It occurs predominantly on the lower legs and the backs of the hands, especially in winter. The exact cause is unknown but the repeated use of soaps in the elderly may be causal. The loss of the stratum corneum lipids with age may also be of some relevance. Rarely, asteatotic eczema can be the presenting sign of myxoedema or can follow the commencement of diuretic therapy.

Treatment

Avoiding soaps, and the regular use of emollients and bath oils should be encouraged. Humidifying centrally heated rooms may help. If the skin is very inflamed, a mild topical steroid can be used.

Contact and irritant eczema

These types of eczema can be caused by many environmental agents (exogenous eczema); they are often in an unusual or localized distribution (Fig. 23.13). There is no personal or family history of atopic disease. A history of an exacerbation of eczema at the workplace is also



Contact eczema secondary to perfume allergy.

Fig. 23.13

suggestive. This can happen by two mechanisms: direct irritation or an allergic reaction (type IV delayed hypersensitivity, p. 226). A detailed history of occupation, hobbies, cosmetic products, clothing and contact with chemicals is necessary.

Allergic contact eczema occurs after repeated exposure to a chemical substance but only in those people who are susceptible to develop an allergic reaction. It is common, occurring in up to 4% of some populations. Many substances can cause this type of reaction but the commoner culprits are nickel (in costume jewellery and buckles), chromate (in cement), latex (in surgical gloves), perfume (in cosmetics and air fresheners), and plants (such as primula or compositae). A good history is necessary and if suspicious, patch testing should be arranged to prove any allergy.

Irritant contact eczema can occur in any individual. It often occurs on the hands after repeated exposures to irritants such as detergents, soaps or bleach. It is therefore common in housewives, cleaners, hairdressers, mechanics and nurses.

Treatment

Treatment is as for atopic eczema as well as strict avoidance of any causative agent. This may also involve the wearing of protective clothing such as gloves, or in extreme cases (such as with chromate sensitivity in builders) even changing occupation or hobbies.

Photosensitive eczema

This is discussed on page 1340.

Lichen simplex/nodular prurigo (neurodermatitis)

These two terms are applied to a pattern of cutaneous response to scratching or rubbing in the absence of an underlying dermatosis. They are more common in Asians and also in black African and Oriental patients.

Lichen simplex appears as thickened, scaly and hyperpigmented areas of lichenification (Fig. 23.14). It starts with intense itching that becomes tender with increased



Fig. 23.14 Lichen simplex from chronic rubbing.

rubbing or scratching. It is rare before adolescence and is commoner in females. Common sites are the nape of the neck, the lateral calves, the upper thighs, the upper back and the scrotum or vulva but any accessible site can be affected.

Nodular prurigo is a different pattern of cutaneous response to scratching, rubbing or picking. Individual, itchy papules and domed nodules appear especially on the upper trunk and the extensor surfaces of the limbs. They show significant surface damage from scratching. This is a chronic unremitting condition which is often resistant to treatment.

These two conditions overlap, with some patients showing mixed features. Atopic individuals seem predisposed to develop these conditions (in the absence of obviously active eczema). However, they can occur in non-atopics. Emotional stress appears to be a contributory factor in many of these patients.

The diagnosis is made by exclusion of other pathologies and may require a skin biopsy. General medical causes of pruritus should be excluded (p. 1344). In the elderly, nodular prurigo may be an early sign of bullous pemphigoid, before the more typical blistering phase has appeared.

Treatment

Treatment is often difficult as symptoms can be intractable. Very potent topical steroids (e.g. 0.05% clobetasol propionate) with occlusive tar bandaging sometimes help. Intralesional steroids can also be useful but there is a risk of atrophy. For resistant cases (especially of prurigo lesions), phototherapy (p. 1339) and even ciclosporin (3-5 mg/kg/day) can be used but the risk/benefit ratio must be discussed with the patient as these therapies are potentially toxic.

PSORIASIS

Psoriasis is a common papulo-squamous disorder affecting 2% of the population and is characterized by well-demarcated, red scaly plaques. The skin becomes inflamed and hyperproliferates to about 10 times the normal rate. It affects males and females equally and can affect all races. The age of onset occurs in two peaks. Early onset (age 16-22) is commoner and is often associated with a positive family history. Late-onset disease peaks at age 55-60 years.

Aetiology

The condition appears to be polygenic but is also dependent on certain environmental triggers. Twin studies show 73% concordance in monozygotic twins compared with 20% of dizygotic pairs. Five genetic regions (on chromosomes 6-21p, 17q, 4q, 1q and 3q) have been linked to psoriasis but as yet no genes have been identified. Infection (group A *Streptococcus*), drugs (e.g. lithium), *ultraviolet light*, *alcohol abuse* and possibly stress may trigger or exacerbate disease in certain individuals. The exact aetiology is unknown but it is likely that psoriasis is a T-lymphocyte driven disorder to

Skin disease
Keratinocyte

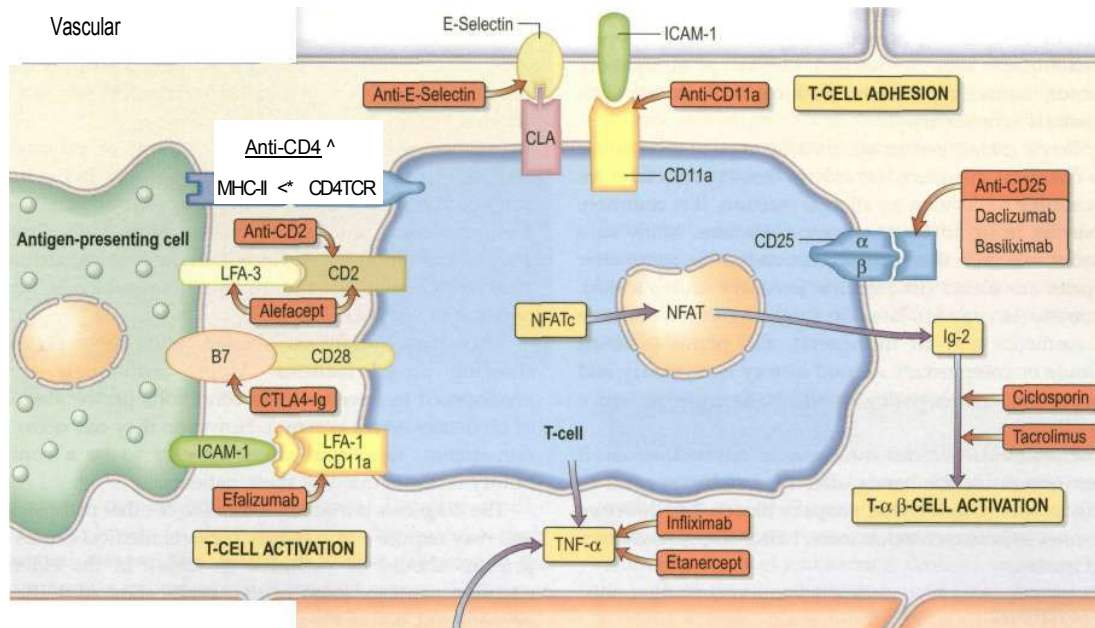


Fig. 23.15 Psoriasis - pathogenesis. The figure shows the interaction of T cells with antigen-presenting cells and keratinocytes. Novel T-cell-targeted therapies are shown (red). NFAT, nuclear factor of activated T cells; ICAM, intracellular adhesion molecule; LFA, lymphocyte function-associated antigen; MHC, major histocompatibility complex; TNF, tumour necrosis factor; IL, interleukin; CLA, cutaneous lymphocyte antigen; B7 = CD80.

an unidentified antigen(s) with a possible altered response from the keratinocyte (Fig. 23.15). The initial T cell activation requires a complex interaction between T lymphocyte and antigen-presenting cell and this has provided a number of potential 'targets' for the newly developed biological therapies. This activation results in upregulation of Th1-type T cell cytokines, e.g. gamma-interferon (INF- γ), interleukins (IL-1, -2, -8), growth factors (TGF- α and TNF- α) and adhesion molecules (ICAM-1) and these are all potential therapeutic targets. The cytokine TNF- α is also produced by keratinocytes and this may be involved in both initiation and maintenance of psoriatic lesions. TNF- α blockade seems to be the most promising of the new biological agents (see Fig. 23.15).

Pathology

Skin biopsy shows acanthosis and parakeratosis, reflecting the increase in skin turnover. The granular layer is often absent. Polymorphonuclear abscesses may be seen in the upper epidermis. The epidermal rete ridges appear elongated and clubbed as they fold down into the dermis. Dermal changes include capillary dilatation surrounded by a mixed neutrophilic and lymphohistiocytic peri vascular infiltrate.

Clinical features

Psoriasis can present in different clinical patterns but there is an overlap between the different forms. Certain drugs can make psoriasis worse - notably lithium, antimalarials and rarely beta-blockers.

Chronic plaque psoriasis

This is the 'common' type of psoriasis. It is characterized by pinkish red scaly plaques, especially on extensor surfaces such as knees (Fig. 23.16a) and elbows. The lower back, ears and scalp are also commonly involved. New plaques of psoriasis occur at sites of skin trauma - the so-called Koebner phenomenon. The lesions can become itchy or sore.

Flexural psoriasis

This tends to occur in later life. It is characterized by well-demarcated, red glazed plaques confined to flexures such as the groin, natal cleft and sub-mammary area. As these sites are apposed there is rarely any scaling. In the absence of psoriasis elsewhere the rash is often misdiagnosed as Candida intertrigo but the latter will normally show satellite lesions.

Guttate psoriasis

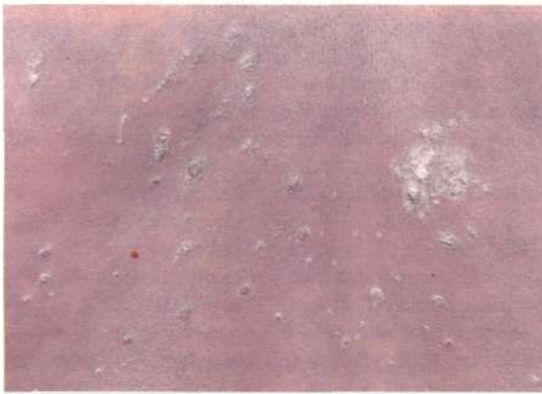
'Raindrop-like' psoriasis is a variant most commonly seen in children and young adults (Fig. 23.16b). An explosive eruption of very small circular or oval plaques appears over the trunk about 2 weeks after a streptococcal sore throat.

Erythrodermic and pustular psoriasis

These are the most severe types of psoriasis reflecting 3 widespread intense inflammation of the skin. They can occur together ('Von Zumbusch' psoriasis) and may be associated with malaise, pyrexia and circulatory disturb-



(a)



(b)

Fig. 23.16 (a) Psoriasis of the knees.
(b) Guttate psoriasis in an African (courtesy of Dr P Matondo, Lusaka, Zambia).

ance. This form can be life-threatening. The pustules are not infected but are sterile collections of inflammatory cells. There is also a more localized variant of pustular psoriasis that confines itself to the hands and feet (palmoplantar psoriasis) but is not associated with severe systemic symptoms. This latter type is more common in heavy cigarette smokers.

Associated features

Nails. Up to 50% of individuals with psoriasis develop nail changes (Fig. 23.17) and, rarely, these can precede the onset of skin disease. There are five types of nail change: (a) pitting of the nail plate; (b) distal separation of the nail plate (onycholysis); (c) yellow-brown discoloration; (d) subungual hyperkeratosis; (e) rarely, a damaged nail matrix and lost nail plate. Treatment of nail dystrophy is very difficult.

Arthritis. From 5-10% of individuals develop psoriatic arthritis and most of these will have nail changes.

Treatment

This is concerned with control rather than cure. It should



Fig. 23.17 Psoriasis of the nail - yellowish brown discoloration and distal nail plate separation (onycholysis).

be tailored to the patient's wishes and not just to the doctor's assessment of disease severity. Treatments include topical agents (dithranol, tar, calcipotriol, tazarotene and corticosteroids), UVB and PUVA therapy (p. 1340) and systemic immunosuppressive/immunomodulating agents. Severe cases may require inpatient treatment.

Chronic plaque psoriasis: emollients should always be used to hydrate the skin. Mild to moderate topical steroids, synthetic vitamin D₃ analogues (e.g. calcipotriol, calcitriol, tacalcitol), 0.05% tazarotene (a vitamin A antagonist, i.e. a retinoid) and purified coal tar are the most popular specific therapies. Salicylic acid can be a useful adjunct. All should be applied once to twice daily to palpable lesions. Once lesions have flattened, therapy can be discontinued. Dithranol can also be helpful but it causes staining of the skin and clothing and it may prove difficult to use at home on a regular basis. It is normally applied for 20-60 minutes and then washed off. It must be applied carefully to the lesions as it causes irritation to normal skin. Dithranol is more likely to induce remission than other topical therapies. Tazarotene and calcipotriol can be very irritant (calcitriol somewhat less so) so they are often used in combination with steroid creams. Vitamin D analogues should be used with caution in erythrodermic or pustular psoriasis because of hypercalcaemia.

Topical therapies are sometimes used in combination with UVB or PUVA. The 'Goeckerman regimen' consists of tar and UVB; the 'Ingram's regimen' consists of dithranol and UVB. The latter has similar results to oral PUVA in terms of clearance rates and lengths of remission - approximately 75% in 6 weeks.

Flexural psoriasis is usually treated with mild steroid and/or tar topical creams. Calcitriol and 0.1% tacrolimus ointment are also useful for treating flexural (facial and genital) psoriasis where irritation can be a problem.

Guttate psoriasis is usually treated with topical therapies and/or UVB phototherapy.

Palmoplantar psoriasis is treated with very potent topical steroids, coal tar paste or local hand and foot PUVA.

Skin disease

Systemic therapy (such as methotrexate, acitretin, mycophenolate, ciclosporin or hydroxycarbamide (hydroxyurea)) are used for resistant cases.

Erythrodermic psoriasis also requires systemic therapy (but not phototherapy) as well as general supportive measures (p. 1341).

All systemic treatments must be monitored for toxicity.

Use Of methotrexate. Methotrexate is normally given once weekly. Some patients experience severe nausea on the day they take it, which can be lessened by folic acid therapy. Both males and females should avoid conception during and for 3 months after therapy. Some patients are allergic to methotrexate and develop a pyrexia and mouth ulceration. Regular blood tests need to be done to monitor for bone marrow suppression and liver damage. Alcohol must be avoided as this increases the risk of hepatotoxicity. NSAIDs should also be avoided as these inhibit renal excretion. Lower doses should be used in the elderly. Long-term users will need either a liver biopsy every 2-3 years to monitor for hepatic damage or, if available, regular monitoring of their serum procollagen III peptide. Patients with concomitant psoriatic arthritis are more likely to develop pulmonary fibrosis.

Biological agents (see Fig. 23.15)

A large number of specific biological agents are being developed but only one is licensed in the UK for use in cutaneous psoriasis. They show variable efficacy and all need to be given by injection. All are prohibitively expensive.

The *TNF- α blockers* infliximab, adalimumab and etanercept (p. 563) seem to be the most effective with almost 60-80% of patients having at least a 75% improvement within 12 weeks. Many of the other agents show a disappointing lower efficacy with only 30-50% of patients showing such improvement, i.e. less than with phototherapy or methotrexate. Alefacept (a fusion protein of LFA-3 and IgG which binds to CD2) was the first biological agent to be licensed for cutaneous psoriasis, but so far only in the USA. Efalizumab is now licensed in Europe.

Long-term side-effects of these new biological agents are unknown. Infection (especially reactivation of tuberculosis) and increased malignant disease (such as skin cancer and lymphoma) remain real concerns. It seems sensible to restrict these new therapies to those patients who have failed to respond to (or cannot tolerate because of toxicity) all the conventional systemic treatments.

Prognosis

Most individuals who develop chronic plaque psoriasis will have the condition lifelong but 80% will get a remission at times. It fluctuates in severity and there are no available tests to predict outcome. Guttate psoriasis resolves spontaneously over 1–2 months and in up to a third of individuals does not recur. However, two-thirds will go on to get recurrent guttate attacks or will progress to chronic plaque psoriasis.



Fig. 23.18 Urticaria.

URTICARIA

Urticaria (hives, 'nettle rash') is a common skin condition characterized by the acute development of itchy weals or swellings in the skin because of leaky dermal vessels (Fig. 23.18). Urticaria is described as 'acute' if it lasts less than 6 weeks and 'chronic' if it persists beyond this.

Aetiology

The final event in pathogenesis involves degranulation of cutaneous mast cells, which releases a number of inflammatory mediators (including histamine) that in turn make the dermal capillaries leaky. In most cases the underlying cause is unknown. Occasionally urticaria is secondary to viral or parasitic infection, drug reactions (e.g. aspirin or penicillin allergy), food allergy (e.g. to strawberries, food colourings or seafood), or rarely systemic lupus erythematosus. There is evidence for an autoimmune aetiology in some of the 'idiopathic' cases as certain individuals develop autoantibodies against the high-affinity IgE receptor α -subunit of the mast cell. Urticaria is commoner in atopic individuals and usually presents in children and young adults.

Clinical features

The history is of cutaneous swellings or weals developing acutely over a few minutes. They can occur anywhere on the skin and last between minutes and hours before resolving spontaneously. Lesions are intensely itchy and show no surface change or scaling. Lesions are normally erythematous but if very acutely swollen, they may appear flesh-coloured or whitish and people often mistake them for blisters. Severe urticaria with subcutaneous involvement can present as soft tissue swelling (angio-oedema) especially around the eyes, the lips and the hands. This can be very alarming to the patient. It can also be dangerous if mucosal areas such as the mouth and larynx are involved but fortunately this is very rare.

Physical urticarias

Occasionally urticaria can be caused by physical stimuli such as cold (cold urticaria), deep pressure (delayed pressure urticaria), stress or heat (cholinergic urticaria),

sunlight (solar urticaria, p. 1340), water (aquagenic urticaria) or chemicals such as latex (contact urticaria).

Cholinergic urticaria is one of the commonest physical urticarias and has rather different clinical lesions from the other forms. Small itchy papules rather than weals appear on the upper trunk and arms after exercise or anxiety.

Pressure can cause two types of urticaria. More superficial pressure can cause *dermographism*, which is relatively common. This presents as urticated weals occurring a few minutes after application of light pressure. Even scratching or rubbing will bring up linear weals in dermatographic individuals. *Delayed pressure urticaria* is rare and occurs as deep swellings some hours after pressure is removed (e.g. on the soles of the feet or under a tight belt).

Investigations

The history is often the best guide to determining the cause of urticaria. Investigation is probably not justified unless the history suggests one of the underlying causes listed above. The physical urticarias should be reproducible by applying the relevant stimulus.

Treatment

Any identifiable underlying cause should be treated. Patients should avoid salicylates and opiates as they can degranulate mast cells. Oral antihistamines (H₁ blockers) are the most useful in treating idiopathic cases. Therapy should be started with regular use of a non-sedating antihistamine (e.g. cetirizine 10 mg daily or loratadine 10 mg daily). If control proves difficult, addition of a sedating antihistamine or an H₂ blocker may be helpful. Dietary manipulation (e.g. additive and colouring free diets) helps a small proportion of patients with chronic urticaria but it is generally unrewarding. Angio-oedema of the mouth and throat may require urgent treatment with intramuscular epinephrine (adrenaline) and intravenous steroids (see Emergency box 16.1).

Prognosis

Most cases of 'idiopathic' urticaria last a few weeks to months before disappearing spontaneously. A small percentage of people go on to develop chronic urticaria which can last for several months or years. The physical urticarias (especially cholinergic urticaria) are more persistent, often lasting for years, and they are often resistant to therapy.

Urticarial vasculitis

This is a variant of urticaria and should be suspected if individual urticarial lesions last longer than 24 hours and leave bruising behind after resolution. There is often an associated arthralgia or myalgia and a small proportion may go on to develop a connective tissue disease. The diagnosis is confirmed by skin biopsy. A full vasculitis screen should be carried out for an underlying cause (p. 581).

Treatment is with antihistamines, oral dapsone (50-100 mg daily) or immunosuppressants.

Hereditary angio-oedema. This is an extremely rare autosomal dominant condition due to an inherited deficiency of C1-esterase inhibitor, a component of the complement system. The defect may be due to either reduced function or reduced absolute levels. Serum C2 and C4 levels are normally low but C1 and C3 are normal. Rarely this condition is acquired and associated with lymphoma or SLE. These types show low C1 esterase inhibitor levels but also low C1 levels.

Clinical features

It presents with attacks of non-itchy cutaneous angio-oedema (but no urticaria) which may last up to 72 hours. It may also present with recurrent abdominal pain (due to intestinal oedema) and there may be a family history of sudden death (due to laryngeal involvement). A non-specific erythematous rash may precede an attack of angio-oedema but urticaria is not a feature.

Treatment

In the acute setting treatment is with C1 esterase inhibitor concentrates and fresh frozen plasma. Epinephrine (adrenaline) and steroids are often ineffective. Maintenance treatment with the anabolic steroid stanozolol (or danazol) stimulates an increase in hepatic synthesis of C1 esterase inhibitor but this should not be used in children. Family members should be screened.

PITYRIASIS ROSEA

Pityriasis rosea is a self-limiting rash seen in adolescents and young adults. The cause is unknown but it is thought to be viral or post-viral. There is an increased incidence in spring and autumn and outbreaks may occur in institutions.

Clinical features

The rash consists of circular or oval pink macules with a collarette of scale and is more prominent on the trunk than on the limbs. The long axis of the oval lesions tends to run along dermatomal lines giving a 'Christmas tree' pattern on the back. The rash may be preceded by a large solitary patch with peripheral scaling ('herald patch') and this is most commonly found on the trunk. The rash is usually asymptomatic and spontaneously resolves over 4-8 weeks.

Treatment

Treatment is not normally required but 1% menthol in aqueous cream helps relieve any itch. In persistent cases UVB may be helpful.

LICHEN PLANUS

Lichen planus is a pruritic inflammatory dermatosis that is commonly associated with mucosal involvement and rarely with nail dystrophy and scarring alopecia.

The cause is unknown but a T-cell driven immune mechanism is postulated, as an almost identical rash can be caused by certain drugs (e.g. gold, levamisole,



Fig. 23.19 Lichen planus.

penicillamine or antimalarials) or by graft-versus-host disease.

Pathology

A mixed lymphohistiocytic infiltrate is seen at the dermoepidermal junction, which becomes ragged and saw-toothed. The basal layer shows liquefactive degeneration with the production of colloid bodies in the upper dermis. There may be acanthosis and a hyperkeratosis of the epidermis.

Clinical features

The rash is characterized by small, purple flat-topped, polygonal papules that are intensely pruritic (Fig. 23.19). It is common on the flexors of the wrists and the lower legs but can occur anywhere. There may be a fine lacy white pattern on the surface of lesions (Wickham's striae). Lesions may fuse into plaques, especially on the lower legs and in black Africans. Hyperpigmentation is common after resolution of lesions, especially in patients with pigmented skin. Atrophic, hypertrophic and annular variants can occur. Lichen planus lesions often localize to scratch marks. If lesions occur in the scalp they may cause a scarring alopecia.

Mucosal involvement is common. The mouth is the most commonly affected but the oesophagus and the anogenital region can be involved. It can present as lacy white streaks, white plaques or as ulceration. The prominent mucosal symptom is of severe pain rather than itch. Nails may be dystrophic and can be lost altogether (with scarring and 'wing' formation) in severe disease.

Prognosis

The condition often clears by 18 months but can recur at intervals. The hypertrophic and atrophic variants and

mucosal disease are more persistent, lasting years. Ulcerative mucosal disease is premalignant.

Treatment

This requires the use of potent topical steroids (0.05% clobetasol propionate) and occasionally oral prednisolone (30 mg daily for 2-4 weeks). Occlusion of topical treatments can be helpful. Resistant cases may respond to PUVA, oral retinoids (0.5 mg/kg/day) or azathioprine (1-2 mg/kg daily). Topical 0.1% tacrolimus ointment has proved a very useful off-license therapy for painful mucosal disease.

GRANULOMA ANNULARE

Granuloma annulare is a dermatosis predominantly of children and young adults. It is characterized by clusters of small dermal papules (with no surface change) that often form into rings or part of a ring. They are common on the dorsal surface of the hands and feet. They are flesh coloured or slightly erythematous and are usually asymptomatic. As they heal the centre becomes dusky and altered in texture. A deep form, which is tender, exists in children. Diffuse granuloma annulare may be associated with diabetes mellitus. The pathology shows a granulomatous dermal infiltrate with foci of degeneration of collagen (necrobiosis). Spontaneous resolution often occurs but cryotherapy or triamcinolone injection may help localized disease.

LICHEN SCLEROSUS ET ATROPHICUS

Lichen sclerosus et atrophicus is a common inflammatory dermatosis that occurs in all age groups and particularly affects the anogenital region. It is more common in females. It presents with atrophic ivory-white macules with a well-defined edge, on the vulva, glans penis, foreskin or perianal skin. Telangiectasia is seen over the surface. Occasionally lesions involve the shaft of the penis and the urethral meatus. Lesions are often itchy but are sore at times. Long-standing vulval lesions are associated with fissuring and a marked loss of architecture, especially of the clitoral hood and the labium minora, which may become fused. Early lesions in young girls present as haemorrhagic blisters and these are occasionally mistaken as signs of sexual abuse. Involvement of the foreskin can cause phimosis, and urethral disease may interfere with micturition. Perianal lesions can fissure and cause constipation.

Rarely lichen sclerosus can affect non-genital skin. It is most common in females and shows rather more hyperkeratosis and follicular plugging than is seen in the anogenital region.

If the clinical picture is unclear, diagnosis may require biopsy to exclude genital lichen planus and extramammary Paget's disease. Vulval scarring can also occur with cicatricial pemphigoid (p. 1348), so occasionally immunofluorescence studies are needed.

The underlying cause is unknown but HLA associations and recent studies showing antibodies to extracellular matrix protein-1 suggest an autoimmune aetiology.

Treatment with very potent topical steroids helps control the symptoms. Hydroxychloroquine (200 mg twice daily) is used in resistant cases. The condition can burn itself out after many years, especially in children. There is a risk of developing squamous cell carcinoma in long-standing lesions. Male patients may require circumcision if phimosis does not respond to medical therapy.

FURTHER READING

Burden AD (2000) Identifying a gene for psoriasis on chromosome 6. *British Journal of Dermatology* 143: 237-243. Grattan C et al. (2001) Management and diagnostic guidelines for urticaria and angio-oedema. *British Journal of Dermatology* 144: 708-714. Heydendael VMR et al. (2003) Methotrexate versus ciclosporine in moderate-to-severe psoriasis. *New England Journal of Medicine* 349: 658-665. Kupper TS (2003) Immunological targets in psoriasis. *New England Journal of Medicine* 349:1987-1990. Leung DYM, Bieber T (2003) Atopic dermatitis, *lancet* 361:151-160. Oyama N et al. (2003) Autoantibodies to extracellular matrix protein 1 in lichen sclerosus. *Lancet* 362: 118-123. Powell JT et al. (1999) Lichen sclerosus - seminar. *Lancet* 353:1777-1783. Schon W, Boehncke WH (2005) Psoriasis. *New England Journal of Medicine* 352:1899-1912.

FACIAL RASHES

Facial rashes often cause diagnostic confusion but a close examination of the clinical signs should help differentiate the underlying cause (Table 23.5). All facial rashes, by virtue of their visibility, can cause significant distress to the patient and this should never be underestimated.

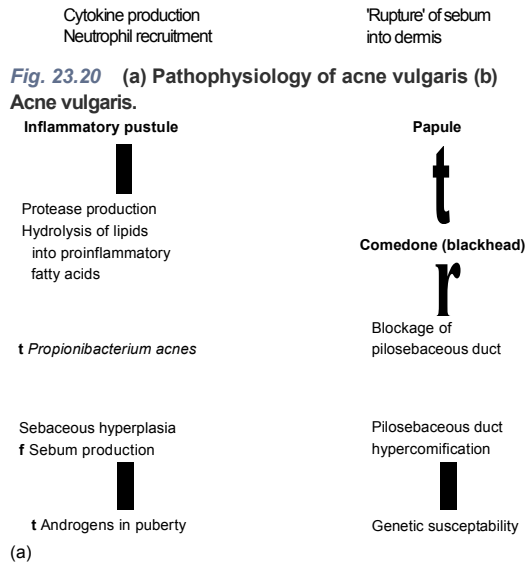
Acne vulgaris

Acne is a common facial rash occurring in adolescence and rarely in early and mid-adult life. The cause is multifactorial but the blockage of pilosebaceous units with surrounding inflammation is the main pathological process and this can be due to a number of different factors (Fig. 23.20a).

Clinical features

Acne presents in areas rich in sebaceous glands such as the face, back and sternal area. The three cardinal features are:

Acne vulgaris	Perioral dermatitis
Rosacea	Photosensitivity
Seborrhoeic eczema	Sarcoidosis
Atopic eczema	Chronic discoid lupus erythematosus
Contact eczema	Systemic lupus erythematosus
Dermatomyositis	Subacute lupus erythematosus



- open comedones (blackheads) or closed comedones (whiteheads)
- inflammatory papules
- pustules (Fig. 23.20b).

The skin may be very greasy (seborrhoea). Rupture of the inflamed lesions may lead to deep-seated dermal inflammation and nodulocystic lesions, which are more likely to cause facial scarring. A premenstrual exacerbation of acne is sometimes noticed. There is a tendency for spontaneous improvement over a number of years but acne can persist unabated into adult life.

A number of clinical variants exist:

- **Infantile acne.** Facial acne is occasionally seen in infants and is sometimes cystic. It is thought to be due to the influence of maternal androgens and resolves spontaneously.
- **Steroid acne.** Acne may occur secondary to corticosteroid therapy or Cushing's syndrome. Comedones and cysts are rare in this variant but involvement of the back and sriouftfers (rather than (he race/ is> common. Clinically the rash often appears as a pustular folliculitis.

Skin disease

- *Oil acne*. This is an industrial disease seen in workers who have prolonged contact with oils or other hydrocarbons and is common on the legs and other exposure sites.
- *Acne fulminans*. This is a rare variant seen most commonly in young male adolescents. Severe necrotic and crusted acne lesions appear, associated with malaise, pyrexia, arthralgia and bone pain (due to sterile bone cysts). It requires urgent treatment with oral prednisolone (30 mg daily) and analgesics followed by a course of oral isotretinoin (see below).
- '*Follicular occlusion triad*'. This is a rare disorder most commonly seen in black Africans. It is characterized by the presence of severe nodulocystic acne, dissecting cellulitis of the scalp (p. 1361) and hidradenitis suppurativa (p. 1320). It has been suggested that this is caused by a problem of follicular occlusion rather than having an infective aetiology.

Treatment

Treatment is aimed at decreasing sebum production, decreasing bacteria, normalizing duct keratinization or decreasing inflammation.

Regular washing with acne soaps to remove excess grease should be encouraged (normal soaps can be comedogenic). 'Picking' should be discouraged.

First-line therapy

Topical agents are used for mild acne such as antibiotics (tetracycline, clindamycin) and keratolytics (benzoyl peroxide); these are similar in efficacy and the latter have the advantage of not causing antibiotic resistance. Topical retinoids (tretinoin) or retinoid-like agents (adapalene) are also used. If these fail, second-line agents should be added.

Second-line therapy

m Low-dose oral antibiotic therapy often helps but must be given for at least 3-4 months. Oxytetracycline 500 mg twice daily is often used first. Minocycline 100 mg daily, erythromycin 500 mg twice daily or trimethoprim 100 mg twice daily is also used.

- An extra treatment 'cyproterone acetate 2 mg/ ethinylestradiol 35 µg' (co-cyprindolj) is of value in females if there is no contraindication to oral contraception. This acts as a normal combined contraceptive but has antiandrogen activity. It may take 6-8 months to have its maximum effect.
- *UVB phototherapy* can be helpful but is rarely used now owing to the development of retinoid drugs.

Third-line therapy

Third-line treatment with a retinoid drug (isotretinoin) should be given if:

- the above measures fail
- there is nodulocystic acne with scarring
- there is severe psychological disturbance.

Use of retinoids (isotretinoin or acitretin). Retinoids are synthetic vitamin A analogues that affect cell growth and differentiation. They are very teratogenic.

Isotretinoin is a 'hospital-only drug' in most countries because of its teratogenicity and is restricted to the use of dermatologists. A pregnancy test and contraceptive advice are mandatory prior to its use in fertile women, and new UK regulations demand that this is done monthly during treatment. It is given as a 4-month course at a dose of 0.5-1 mg/kg/day. Over 90% of individuals will respond to this therapy and 65% of people will obtain a long-term 'cure'.

Patients must avoid pregnancy during therapy and for 1 month after stopping isotretinoin (but for 2 years after stopping acitretin as it is very lipophilic). Both drugs cause drying of the skin, especially of the lips and nasal mucosa. Hair thinning and exercise-induced myalgia are not uncommon. Blood count, liver function and fasting lipids need to be monitored during therapy. In a few individuals retinoids may cause depression but it should also be remembered that acne itself has been a cause of suicide.

Potential new treatment

A single study has shown pulsed-dye laser therapy to have some benefit in mild to moderate acne but was not curative. Further work is needed to establish its effectiveness, the optimum 'dosing' schedule and long-term safety.

Rosacea

Rosacea (Fig. 23.21) is a common inflammatory rash predominantly affecting the face. The onset is usually in middle age and it is commoner in women. It often causes significant psychological distress.

The cause is unknown. Theories have suggested an underlying problem in vasomotor stability of blood vessels or a role of the skin mite *Demodex* but there is little evidence to confirm these speculations.



Fig. 23.21 Rosacea. Papules and pustules on a background erythema. There are no comedones.

Clinical features

The cardinal features are of facial flushing, inflammatory papules and pustules affecting the nose, forehead and cheeks. The flushing may precede the other signs by some years. There are no comedones. Additional features may include dilated blood vessels (telangiectasia), inflammation of the eyelid margins (blepharitis), keratitis and sebaceous gland hypertrophy especially of the nose. The latter is commoner in men and can cause a disfiguring enlargement of the nose called rhinophyma. The flushing may be exacerbated by alcohol, hot drinks, sunlight and changes in ambient temperature. Prolonged use of topical steroids can exacerbate or trigger the condition. As the disease progresses the flushing may be replaced by a permanent erythema.

Treatment

This is suppressive rather than curative. Long-term use of topical 0.075% metronidazole may help. Avoid topical steroids. A 3-month course of oral tetracycline (500 mg twice daily) is also helpful. Oral metronidazole (400 mg twice daily) or oral isotretinoin (0.5-1 mg/kg/day) is occasionally given in resistant cases (p. 1338). The papules and pustules tend to respond best to therapy but repeat courses may be necessary. The flushing and erythema are often resistant to treatment but cosmetic camouflage can be helpful for these features. Intense pulse light or pulsed-dye laser therapy can help the erythema and telangiectasia but often needs to be repeated as they tend to recur. Rhinophyma can be treated with plastic surgery or by carbon dioxide laser.

Perioral dermatitis

Perioral dermatitis is a common rash found around the mouth, especially in young females. The exact cause is unknown but it often has an iatrogenic component as topical steroids often exacerbate the condition in the long term.

Clinical features

It presents with erythema, scaling, papules and occasionally pustules around the mouth. It usually spares a halo of skin immediately adjacent to the lips.

Treatment

Treatment involves stopping topical steroids, although they may have to be withdrawn slowly to prevent too severe a rebound after withdrawal. The mainstay of treatment is with a 3- to 4-month course of low-dose oxytetracycline or erythromycin (both 500 mg twice daily) and topical metronidazole.

FURTHER READING

- [Anonymous] (2003) Acne isotretinoin and depression. (Review) *Drugs and Therapeutics Bulletin* 41: 76-78.
James WD (2005) Acne. *New England Journal of Medicine* 352:1463-1472
Seaton ED et al. (2003) *Pulsed-dye laser treatment for inflammatory acne vulgaris: randomised controlled trial.* *Lancet* 362:1347-1352 (and editorial, p. 1342).

PHOTODERMATOLOGY

Sunlight - light in the ultraviolet (UV) part of the spectrum - combines short, medium and long wavelengths (UVC, UVB, and UVA respectively). Both UVB and UVA can penetrate the atmosphere and reach the skin. This light energy is potentially mutagenic and carcinogenic but it can also suppress cutaneous inflammation. Thus UV irradiation can both *cause* skin disease and be used to *treat* it.

Photosensitive rashes usually appear on sites exposed to the sun's rays, such as the face, the anterior 'V' of the chest, the ears and the backs of the hands. Certain 'protected' areas are characteristically spared such as under the chin or the upper eyelid and between the finger webs. Porphyria, drug sensitivity and lupus erythematosus should be excluded in all photosensitive patients.

Photosensitive rashes may be divided into photoexacerbated/provoked rashes and the idiopathic photodermatoses (Table 23.6). The former are discussed on pages 574 (SLE), 245 (pellagra) and 1148 (porphyria).

Phototherapy and photoprotection

Phototherapy

UVB and UVA are both used in the treatment of inflammatory dermatoses. They have a suppressive effect on cutaneous inflammation and there is evidence that they can suppress systemic immunoreactivity to some degree. However, both types can cause skin ageing and predispose to skin malignancy if excessive doses are used. This is more of a problem in white-skinned

Table 23.6 Differential diagnosis of photosensitive rashes

Photoexacerbated/provoked rashes

Systemic disease	SLE, CDLE, SCLE (p. 574)
Metabolic disease	Porphyrias (pp. 1148 and 1346), pellagra (p. 245)
Drugs	Thiazides, phenothiazines, tetracyclines, amiodarone
Plant phototoxins	Phytophotodermatitis (photosensitivity induced by contact of the skin with certain plants, e.g. celery, hogweed, rue)
Skin disease	Rosacea Rarely atopic eczema, psoriasis, lichen planus (these normally improve in sunlight)

Idiopathic photodermatoses

Polymorphic light eruption
Chronic actinic dermatitis
Solar urticaria

CDLE, chronic discoid lupus erythematosus SCLE, subacute cutaneous lupus erythematosus

individuals. Unaffected regions of skin or high-risk areas like the scrotum can be screened during phototherapy.

UVB is less carcinogenic than *UVA*. *Narrow-band UVB* (311 nanometre) is used more than broad-band *UVB* because it is much more effective and less likely to burn. It is used in the treatment of eczema and psoriasis (especially in children) and is given three times per week for 6-10 weeks. Eye protection needs to be worn during therapy.

UVA is relatively ineffective on its own so is used in conjunction with a photosensitizer ('psoralen') hence the term 'PUVA'. The psoralen can be given by mouth or applied to the skin in bath water. PUVA is given twice per week and eye protection must be worn *for the whole of the treatment day* as the psoralen sensitizes the retina. It is more effective than narrow-band *UVB* but is limited by its carcinogenic potential, especially squamous cancer. A maximum dose is given over a lifetime depending on skin type (1000 joules or 200 sessions approximately). It is used for many conditions including psoriasis, eczema, cutaneous T cell lymphoma, some photosensitive dermatoses and vitiligo.

Sunbeds are used for tanning and consist of predominantly *UVA* light; they are therefore rarely effective in treating skin disease. If used frequently there is an increased risk of skin cancer and premature ageing.

Photoprotection

There are two broad classes of sunblock cream: they either absorb UV light (e.g. aminobenzoic acid or methoxycinnamate) or reflect it (e.g. titanium dioxide). Most modern creams protect against *UVA* and *UVB* to varying degrees. *UVB* protection is graded by the 'sun protection factor' (SPF): an SPF of 15 implies you can spend 15 times as long in the sun before burning providing it is applied correctly. SPFs above 15 confer little extra protection. There is no standardized way of assessing efficiency against *UVA*. Some sunscreens (especially aminobenzoates) may rarely cause photosensitization. This can be proven by photopatch testing.

IDIOPATHIC PHOTODERMATOSES

Polymorphic light eruption (PLE)

This is the most common photosensitive eruption in temperate regions, affecting up to 10-20% of the population. It is most common in young women. In many it is mild and often goes undiagnosed. An itchy rash appears some hours after sun exposure which is strictly confined to the exposed sites. Lesions may be papules, vesicles or plaques. They can last for several hours or several days. The condition starts in spring and often improves during the summer because of skin 'hardening'.

Treatment

Avoidance of sunlight and the use of sunblocks are helpful in mild cases. Topical steroids help treat an attack. In those individuals who only get PLE after very intense sun exposure (e.g. on sunny holidays) a short course

of oral prednisolone (30 mg daily for 7-10 days) will often prevent or treat an attack. For resistant cases 'desensitization' with low-dose PUVA (or narrow-band *UVB*) in the springtime may be required but patients will need to 'top up' their sun exposure from natural sunlight during the summer to keep their skin desensitized.

Chronic actinic dermatitis (photosensitive eczema, actinic reticuloid)

This is a relatively rare type of eczema occurring in a photosensitive distribution over the face, neck and hands. It typically affects middle-aged or elderly males. There may be a pre-existing eczema, so the subsequent development of photosensitivity is often missed. This is further confounded by the fact that the eczema usually will spread to affect skin not exposed to sunlight, and in fact the patient can become erythrodermic. The skin has typical features of eczema but there is often marked skin thickening. Histology is often atypical and can look almost lymphoma-like. The diagnosis can be confirmed by specialist monochromator light-testing. The most severe cases can be exacerbated by even artificial lighting, as these patients can become exquisitely photosensitive.

Treatment

This consists of strict avoidance of sunlight, including high-factor sunblocks and screening of house and car windows. Topical steroids and emollients are useful in milder cases. Oral prednisolone may be needed and azathioprine (1-2 mg/kg daily) should be considered for long-term suppression. Low-dose PUVA under steroid cover may help with 'desensitization'.

Solar urticaria

This is extremely rare. Itchy urticarial lesions occur within minutes of sun exposure and characteristically settle within 1-2 hours. Sun avoidance, sunblocks, H₁ antihistamines and low-dose PUVA are all used in treatment.

FURTHER READING

Hawk JLM (ed) (1999) *Photodermatology*, London:
Arnold. Stern RS (2004) Treatment of photoaging. *New England Journal of Medicine* 350:1526-1534.

ERYTHRODERMA

Erythroderma, meaning 'red skin', refers to the clinical state of inflammation or redness of all (or nearly all) of the skin. It is sometimes called *exfoliative dermatitis*, but dermatitis is not always present.

Aetiology

There are a number of underlying causes (Table 23.7); previous skin disease and drugs are the most common.

Table 23.7 Causes of erythroderma

Common
Atopic eczema
Psoriasis
Drugs (e.g. sulphonamides, gold, sulphonylureas, penicillin, allopurinol, captopril)
Seborrhoeic eczema
Idiopathic
Rare
Chronic actinic dermatitis
Cutaneous T-cell lymphoma (Sezary syndrome) (p. 1353)
Malignancy (especially leukaemias)
Pemphigus foliaceus
Pityriasis rubra pilaris (a hereditary disorder of keratinization) HIV infection
Toxic shock syndrome (p. 64)

Clinical features

It is commoner in males and later in life. Patients often complain of their skin feeling 'tight' as well as itchy. Long-standing erythroderma is often associated with hair loss, ectropion of the eyelids and even nail shedding. Systemic symptoms are common such as malaise, pyrexia, widespread lymphadenopathy and other complications (see below). Erythroderma can occasionally lead to death so it should be regarded as a medical 'emergency'.

Examination should specifically look for pustules and nail changes suggestive of psoriasis.

A skin biopsy may elucidate the cause, especially of cutaneous lymphoma. Techniques such as T-cell receptor gene rearrangement studies (looking for evidence of clonal T cell expansion in the skin and blood) are also useful in the diagnosis of lymphoma.

A number of cases defy an exact diagnosis and a lymph node biopsy is required. If there is no malignancy, lymph nodes normally show non-specific, reactive (dermatopathic) changes.

Complications

The skin is one of the largest organs of the body; perhaps it is no surprise that inflammation of the whole organ can cause metabolic and haemodynamic problems including:

- high-output cardiac failure from increased blood flow
- hypothermia from heat loss
- fluid loss by transpiration
- hypoalbuminaemia
- increased basal metabolic rate
- 'capillary leak syndrome'.

Capillary leak syndrome is the most severe complication and has been responsible for a fatal outcome in some cases of psoriasis, although this is extremely rare. It is thought that the inflamed skin releases large quantities of cytokines that cause a generalized vascular leakage. This can cause cutaneous oedema and leaky vessels in the lungs, resulting in acute lung injury (p. 986).

Treatment

Treatment of erythroderma is best initiated in hospital. Patients must be kept very warm (with space blankets and heaters), with fluid-balance charts. Their vital signs should be monitored regularly. Changes in electrolytes, albumin and circulatory status should be monitored regularly. Swabs should be taken to detect any secondary skin infection.

The skin condition is treated with bed rest and either a bland emollient or a mild topical steroid. All non-essential drugs should be stopped. Where known, the underlying cause should be treated. The blanket use of systemic steroid therapy for erythroderma remains controversial in view of possible side-effects.

Advanced capillary leak syndrome will require specialized haemodynamic management in an intensive care unit.

FURTHER READING

Rothe MJ et al. (2000) Erythroderma. *Dermatologic Clinics* 18: 405-415.

CUTANEOUS SIGNS OF SYSTEMIC DISEASE

Some dermatoses are associated with a variety of underlying systemic diseases. Furthermore some medical conditions may present with cutaneous features.

Erythema nodosum

Erythema nodosum has a number of underlying causes (Table 23.8). It presents as painful or tender dusky blue-red nodules, commonly over the shins or lower limbs, which fade over 2-3 weeks leaving a bruised appearance (see Fig. 23.39). It is most common in young adults, especially females. It may be associated with arthralgia, malaise and fever. The inflammation involves the dermis and the subcutaneous layer (panniculitis).

Treatment

Symptomatic therapy with non-steroidal anti-inflammatory drugs (avoid in pregnancy), light compression bandaging and bed rest are all that are necessary as the condition resolves spontaneously. The underlying cause

Table 23.8 Causes of erythema nodosum

Streptococcal infection*
Drugs* (e.g. sulphonamides, oral contraceptive)
Sarcoidosis*
Idiopathic*
<i>Yersinia</i> infection
Fungal infection (histoplasmosis, blastomycosis)
Tuberculosis
Leprosy
Inflammatory bowel disease
<i>Chlamydia</i> infection

*Common causes in the UK

Skin disease

should be treated. In very persistent cases dapsone (100 mg daily), colchicine (500 µg twice daily) or prednisolone (up to 30 mg daily) can be useful.

Erythema multiforme

Erythema multiforme (EM) is a hypersensitivity rash of acute onset frequently caused by infection or drugs. A cell-mediated T lymphocytic response is seen in the skin, which causes epidermal cell death.

In 50% of cases, the cause is not found but the following should be considered:

- herpes simplex virus (the most common identifiable cause)
- other viral infections (e.g. EBV, orf disease)
- drugs (e.g. sulphonamide, anticonvulsants)
- mycoplasma infection
- connective tissue disease (e.g. SLE, polyarteritis nodosa)
- HIV infection
- Wegener's granulomatosis
- carcinoma, lymphoma.

Clinically the lesions can be erythematous, polycyclic, annular or show concentric rings called 'target lesions' (Fig. 23.22). Frank blistering is not uncommon. The rash tends to be symmetrical and commonly affects the limbs, especially the hands and feet where palms and soles may be involved. Occasionally there is severe mucosal involvement leading to necrotic ulcers of the mouth and genitalia, and a conjunctivitis ('EM major' - previously called Stevens-Johnson syndrome - see Box 23.3). The term 'EM minor' may be used for cases without mucosal involvement.

Erythema multiforme usually resolves in 2-4 weeks. Rarely, recurrent erythema multiforme can occur and this is triggered by herpes simplex infection in 80% of

Box 23.3 Stevens-Johnson syndrome

This term is now used for a mild form of toxic epidermal necrolysis (p. 1359) which shares similar mucosal lesions to 'erythema multiforme major' but does not show typical target lesions. Both Stevens-Johnson syndrome and toxic epidermal necrolysis are more likely to be drug induced.

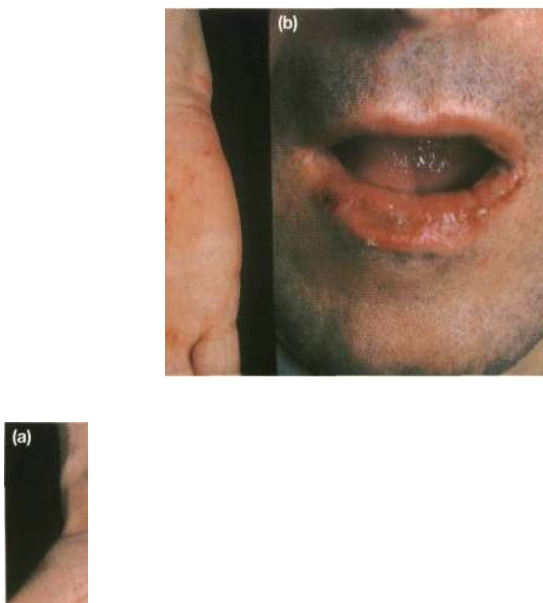


Fig. 23.22 Erythema multiforme major - target lesions of (a) the palm and (b) with mucosal involvement around the mouth.

Treatment

This is symptomatic and involves treating the underlying cause. Some advocate the use of oral steroids in severe disease but this remains controversial.

Recurrent erythema multiforme can be treated with prophylactic oral aciclovir (200 mg twice daily) even if no cause has been found, as 80% appear to be driven by herpes simplex virus. In resistant cases, azathioprine (1-2 mg/kg daily) is used.

Pyodermagangrenosum

Pyoderma gangrenosum is of unknown aetiology and presents with erythematous nodules or pustules which frequently ulcerate (Fig. 23.23). The ulcers can be large and grow at an alarming speed. The ulcer has a typical bluish black ('gangrenous') undermined edge and a purulent surface ('pyoderma'). There may be an associated pyrexia and malaise. Biopsy through the ulcer edge shows an intense neutrophilic infiltrate and occasionally a vasculitis but the diagnosis depends mostly on the clinical appearance. The main causes are:

- inflammatory bowel disease
- rheumatoid arthritis
- myeloma, leukaemia, lymphoma
- liver disease (primary biliary cirrhosis)
- idiopathic (> 20% in some series).

Treatment

This is with very potent topical steroids or 0.1% tacrolimus ointment. High-dose oral steroids may be needed to prevent rapidly progressive ulceration. Oral dapsone and minocycline may help. Other immunosuppressants, such as ciclosporin, are useful in resistant cases. The underlying cause should be treated.



Fig. 23.23 Pyoderma gangrenosum.



Fig. 23.24 Acanthosis nigricans.

Acanthosis nigricans

Acanthosis nigricans presents as thickened, hyperpigmented skin predominantly of the flexures (Fig. 23.24). It can appear warty or velvety when advanced. In early life it is seen in obese individuals who have very high levels of insulin owing to insulin resistance (and this is sometimes termed 'pseudo-acanthosis nigricans'). In older people it normally reflects an underlying malignancy (especially gastrointestinal tumours). Rarely it is associated with hyperandrogenism in females.

Treatment

Topical or oral retinoids (0.5 mg/kg/day) may help (p. 1338) and weight loss is advised in the obese. Any underlying malignancy should be treated.

permatomyositis (see also p. 579)

The rash is distinctive. Facial erythema and a magenta-coloured rash around the eyes with associated oedema are often present. Bluish red nodules or plaques may be present over the knuckles and extensor surfaces. The nail folds are frequently ragged with dilated capillaries. The diagnosis is made from the clinical appearance, muscle biopsy, EMG and a serum creatine phosphokinase. Skin biopsy is not diagnostic.

There is a childhood form which usually occurs before the age of 10 and which eventually resolves. This type is often associated with calcinosis in the skin and can cause significant long-term functional problems with weak muscles and contractures. Life-threatening bowel infarction can also occur in the childhood form. The adult form usually occurs after the age of 40. Some cases are associated with an underlying malignancy, whereas others appear to reflect a 'connective tissue disease'. This latter group may overlap with scleroderma and lupus erythematosus.

Treatment

Skin disease may respond to hydroxychloroquine (200 mg twice daily) as well as immunosuppressants, e.g. azathioprine or ciclosporin.

Scleroderma (see also p. 577)

The term scleroderma refers to a thickening or hardening of the skin owing to abnormal dermal collagen. It is not a diagnostic entity in itself. Systemic sclerosis and morphea both show sclerodermatous changes but are separate conditions.

Systemic sclerosis (often called scleroderma) has cutaneous and systemic features and is discussed fully on page 577.

Morphea is confined to the skin and usually presents in children or young adults. It is commoner in females and the cause is unknown. Lesions are usually on the trunk and appear as bluish red plaques which progress to induration and then central white atrophy. A linear variant exists in childhood which is more severe as it can cause atrophy of underlying deep tissues and thus can cause unequal limb growth or scarring alopecia.

Rarely, sclerodermatous skin changes may be seen in chronic Lyme disease (acrodermatitis chronica atrophicans), chronic graft-versus-host disease, polyvinyl chloride disease, eosinophilic myalgia syndrome (due to tryptophan therapy) and bleomycin therapy.

Lupus erythematosus (LE)

There are three clinical variants to this disease but some patients may show features of more than one type.

- chronic discoid lupus erythematosus (CDLE)
- subacute lupus erythematosus (SCLE)
- systemic lupus erythematosus (SLE).

The aetiology is unknown but is due to abnormality in immune function as variable autoantibodies may be found in all types. Very rarely it can be induced by certain drugs such as phenothiazines, hydralazine, methyl dopa, isoniazid, tetracycline, mesalazine and penicillin.

Chronic discoid lupus erythematosus (CDLE)

CDLE is the most common type of LE seen by dermatologists and more frequently affects females. Clinically it presents with fixed erythematous, scaly, atrophic plaques with telangiectasia, especially on the face or other sun-exposed sites (Fig. 23.25). Hypopigmentation is common and follicular plugging occurs. Scalp involvement leads to a scarring alopecia. Oral involvement (erythematous patches or ulceration) occurs in 25% of cases.

CDLE can be triggered and exacerbated by UV exposure. A few patients also suffer with Raynaud's phenomenon or unusual chilblain-like lesions (chilblain lupus). Only 5% of cases will go on to develop SLE but this is more common in children. Serum antinuclear antibody (ANA) is positive in 30% of cases.

Skin disease

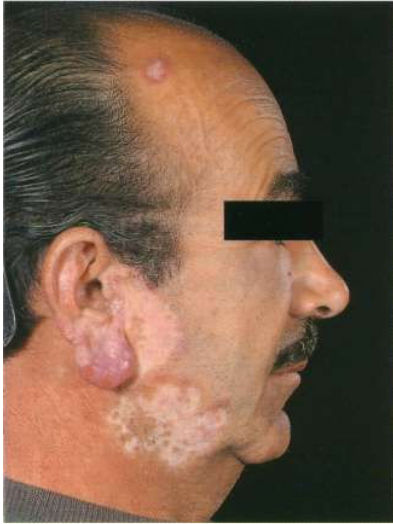


Fig. 23.25 Chronic discoid lupus erythematosus, showing scaling, atrophy and hypopigmentation.



Fig. 23.26 Systemic lupus erythematosus - showing the structural sites of damage in bullous disorders. LAD, linear IgA disease; EB, epidermolysis bullosa.

Skin biopsy shows a dense patchy, dermal lymphohistiocytic infiltrate which often is centred on appendages. Epidermal basal layer damage, follicular plugging and hyperkeratosis may be present. Direct immunofluorescence studies of lesional skin may show the presence of IgM and C3 at the dermoepidermal junction ('lupus band').

Treatment

First-line therapy is with sunscreens and potent topical steroids. Certain oral antimalarials (hydroxychloroquine 100-200 mg twice daily and mepacrine 100 mg daily) can prove very useful and are generally safe for long-term intermittent use. Oral prednisolone is beneficial but its use is limited by its side-effect profile. Azathioprine, retinoids, ciclosporin and thalidomide can be useful in resistant cases.

Prognosis

The disease is usually chronic, although it may fluctuate in severity. CDLE remains confined to the skin in most patients and it will eventually go into remission in up to 50% of cases (after many years).

Subacute lupus erythematosus (SCLE)

SCLE is a rare cutaneous variant of LE. It presents with widespread indurated, sometimes urticated, erythematous lesions, often on the upper trunk. The lesions can also be annular. Photosensitivity is often a prominent feature. Complications, such as arthralgia and mouth ulceration, are seen but significant organ involvement is rare. ANF and extractable nuclear antibodies (anti-Ro and anti-La) are usually positive (see p. 534).

Treatment is with oral dapsone, antimalarials or systemic immunosuppression (prednisolone and ciclosporin).

Systemic lupus erythematosus (SLE)

(see also p. 574)

The cutaneous involvement of SLE is one of the minor problems of the disease but it may be the presenting feature.

Features include macular erythema over the cheeks, nose and forehead ('butterfly rash', Fig. 23.26). Palmar erythema, dilated nail fold capillaries, splinter haemorrhages and digital infarcts of the finger tips may also be seen but are not always noticed by the patient. Joint swellings, livedo reticularis and purpura are occasionally seen. Rarely SLE can be complicated by an atypical erythema multiforme-like rash ('Rowell's syndrome'). Treatment (p. 576) is usually managed by a rheumatologist.

Pruritus

The pathophysiology of pruritus is poorly understood but is due to peripheral mechanisms (e.g. skin disease), central or neuropathic mechanisms (e.g. multiple sclerosis), neurogenic (e.g. cholestasis/u.-opioid receptor stimulation, p. 386) or psychogenic mechanisms (e.g. parasitophobia). Evidence suggests that low stimulation of unmyelinated C-fibres in the skin is associated with the sensation of itch (high stimulation produces pain). Histamine, tachykinins (e.g. substance P) and cytokines (e.g. interleukin-2) may also play a role peripherally in the skin. The major nerve pathways for itch and the influence of the central nervous system are not well characterized but opioid μ -receptor-dependent processes can regulate the perception and intensity of itch.

Pruritus (see lichen simplex, nodular prurigo/neurodermatitis) in the absence of a demonstrable rash can be caused by a number of different medical problems (Table 23.9).

Table 23.9 Medical conditions associated with pruritus

Iron deficiency anaemia
Internal malignancy (especially lymphoma)
Diabetes mellitus
Chronic renal failure
Chronic liver disease (especially primary biliary cirrhosis)
Thyroid disease
HIV infection
Polycythaemia vera

Asteatotic eczema and cholinergic urticaria are common causes of pruritus where the rash is often missed. The term idiopathic pruritus or 'senile' pruritus probably overlaps with asteatotic eczema and this is common in the elderly.

Treatment involves avoiding soaps and using symptomatic measures (as for asteatotic eczema). Phototherapy may help intractable cases. Oral opiate antagonists, which act centrally, are under assessment. Underlying medical problems should be treated.

SarCOidOSJS (see also p. 934)

Sarcoidosis is a multisystem granulomatous disorder of unknown aetiology. It can present as reddish brown dermal papules and nodules, especially around the eyelid margins and the rim of the nostrils. More polymorphic lesions (papules nodules and plaques) may appear on the body. It is most common in black Africans where it is often accompanied by hypo- or hyperpigmentation. Rarely it can present with a bluish red infiltrate or swelling, especially of the nose or ears, called lupus pernio. Both these types of lesion can be seen anywhere on the body but are common on the face. Erythema nodosum (p. 1341) of the shins is sometimes seen in acute-onset sarcoidosis. Erythema nodosum is an immunological reaction and not due to sarcoid tissue infiltration. Swollen fingers from a dactylitis occur. Whilst sarcoidosis may be confined to the skin, all patients should be investigated for evidence of systemic disease (p. 934).

Treatment of cutaneous lesions includes very potent topical steroids (0.05% clobetasol propionate), intra-lesional steroids, oral steroids and occasionally methotrexate or antimalarials.

Neurofibromatosis type 1 (von Recklinghausen's disease) (see also p. 1257 and Table 3.4)

Type 1 neurofibromatosis is an autosomal dominant condition with complete penetrance. It often presents in childhood with a variety of cutaneous features. Many cases are new mutations in the *NF1* gene. Early signs include *cafe-au-lait* spots (brown macules, greater than 2.5 cm in diameter and more than five lesions) and axillary freckling. Lisch nodules (hyperpigmented iris hamartomas) may be seen in the eyes by slit lamp examination. Later on, fleshy

skin tags and deeper soft tumours (neurofibromas) appear and they may progress to completely cover the skin causing significant cosmetic disability. Learning difficulties and skeletal dysplasias occur. A number of endocrine disorders may be rarely associated including pheochromocytoma, acromegaly and Addison's disease.

Tuberous sclerosis (epiloia)

Tuberous sclerosis is also an autosomal dominant condition of variable severity which may not present until later childhood. It is characterized by a variety of hamartomatous growths. The three cardinal features are (a) mental retardation, (b) epilepsy, and (c) cutaneous abnormalities - but not all have to be present. The skin signs include:

- adenoma sebaceum (reddish papules/fibromas around the nose)
- periungual fibroma (nodules arising from the nail bed)
- shagreen patches (firm, flesh-coloured plaques on the trunk)
- ash-leaf hypopigmentation (pale macules best seen with UV light)
- forehead plaque (indurated flesh-coloured patch)
- *cafe-au-lait* patches
- pitting of dental enamel.

Internal hamartomas can arise in the heart, kidney, retina and CNS. Parents of a suspected case should be carefully examined (under UV light) as they may have a forme fruste of the condition which can manifest just as hypopigmented patches. This would have genetic implications for future offspring.

Diabetes mellitus (see also p. U3i)

Diabetes mellitus can have a number of cutaneous features. Complications of diabetes itself include:

- fungal infection (e.g. candidiasis)
- bacterial infections (e.g. recurrent boils)
- xanthomas
- arterial disease (ulcers, gangrene)
- neuropathic ulcers.

Specific dermatoses of diabetes include:

- necrobiosis lipoidica (a patch of spreading erythema over the shin which becomes yellowish and atrophic in the centre and may ulcerate)
- diffuse granuloma annulare (p. 1336)
- diabetic dermopathy (red-brown flat-topped papules)
- blisters (usually on the feet or hands)
- diabetic stiff skin (tight waxy skin over the fingers with limitation of joint movement owing to thickened collagen - also called cheiroarthropathy).

Chronic liver disease (see also p. 357)

Chronic liver disease may present with jaundice, palmar erythema, spider naevi, white nails, hyperpigmentation and pruritus.

Skin disease

Porphyria cutanea tarda (PCT, p. 1149) is a rare genetic disorder associated with liver disease usually due to hepatic damage from excessive alcohol consumption or hepatitis C infection: 75% of cases are sporadic, 25% familial. Overall, 20% of cases have underlying hereditary haemochromatosis (p. 386). It presents clinically on exposed skin with sun-induced blisters, skin fragility, scarring, milia and hypertrichosis. Treatment of the cutaneous features is with repeated venesection and/ or very low-dose chloroquine plus an avoidance of alcohol. There is anecdotal evidence that specific treatment of hepatitis C (p. 373) will also help the skin, presumably through improving liver function. All forms of PCT are at risk of hepatic carcinoma.

Chronic renal failure (see also p. 668)

Chronic renal failure is commonly associated with intractable pruritus. Pallor, hyperpigmentation and ecchymoses are commonly seen. Rarely it is associated with non-inflammatory blisters, pseudo-porphyrria cutanea tarda and cutaneous calcification. Long-standing renal transplant patients often suffer with recurrent viral warts and squamous cell carcinomas due to the immunosuppression.

Thyroid disease (see also p. 1069)

Hypothyroidism may cause dry firm gelatinous (myxoedematous) skin with diffuse hair thinning and a loss of the outer third of the eyebrows. Hyperthyroidism may be associated with warm sweaty skin and a diffuse alopecia. Graves' disease is rarely associated with thyroid acropachy ('clubbing' with underlying bone changes) and pretibial myxoedema (a red-brown mucinous infiltration of the shins which can become lumpy and tender).

Cushing's syndrome (see also p. 1085)

Cushing's syndrome may cause hirsutism, a moon face, a buffalo hump, stretch marks (striae) and a pustular folliculitis (often called steroid acne) of the skin.

Hyperlipidaemias (see also p. 1138)

Hyperlipidaemias can present with xanthomas, which are abnormal collections of lipid in the skin. All patients with xanthomas should be investigated for hyperlipidaemia although the most common type called xanthelasma (yellow plaques around the eyes) are usually associated with normal lipids. There are a number of other clinical variants of xanthomas such as (i) tuberous xanthoma (firm orange-yellow nodules and plaques on extensor surfaces), (ii) tendon xanthoma (firm subcutaneous swellings attached to tendons), (iii) plane xanthoma (orange-yellow macules often affecting palmar creases), (iv) eruptive xanthoma (numerous small yellowish papules commonly on the buttocks).

Table 23.10 Non-metastatic cutaneous manifestations of underlying malignancy

Dermatosis	Tumour
Dermatomyositis	Lung, GI tract, GU tract
Acanthosis nigricans	GI tract, lung, liver
Paget's disease (localized patch of eczema around the nipple)	Ductal breast carcinoma
Erythroderma	
Tylosis (thickened palms/soles)	Lymphoma/leukaemia
Ichthyosis (dry flaking of skin)	Oesophageal carcinoma
Erythema gyratum repens (concentric rings of erythema which change rapidly)	Lymphoma Lung, breast
Necrolytic migratory erythema (burning, geographic and spreading annular areas of erythema)	Glucagonoma

Cutaneous amyloid

Cutaneous amyloid can be confined to the skin or be part of systemic disease (p. 1148). Macular amyloid is a common, purely cutaneous variant seen in Asians. It is characterized by itchy brown rippled macules on the upper back.

Systemic amyloid may be associated with reddish brown papules, nodules or plaques, especially around the eyes, the flexural areas and mucosal surfaces. Distinctive periorbital bruising and macroglossia may also be present.

Systemic malignant disease

Certain rashes may be a non-metastatic manifestation of an underlying malignancy (Table 23.10). Rarely tumours can metastasize to the skin where they normally present as papules or nodules which may proceed to ulceration.

FURTHER READING

- Crawford GH et al. (2002) Skin signs of systemic disease: an update. *Advances in Dermatology* 18:1—27.
- English JC et al. (2001) Sarcoidosis. *Journal of the American Academy of Dermatology* 44: 725-743.
- Robinson-Boston L (2000) Cutaneous manifestations of end-stage renal disease. *Journal of the American Academy of Dermatology* 43: 975-986.
- Sommer S et al. (2002) Connective tissue disease and the skin. *Clinical Medicine* 2: 9-14.
- Twycross R et al. (2003) Itch: scratching more than the surface. *Quarterly Journal of Medicine* 96: 7-26.
- Yosipovitch G et al. (2003) Itch. *Lancet* 361: 690-694.

BULLOUS DISEASE

Primary blistering diseases of the skin are rare. A variety of skin proteins hold the skin together. Inherited abnormalities or immune damage of these proteins causes abnormal cell separation, inflammation, fluid accumulation

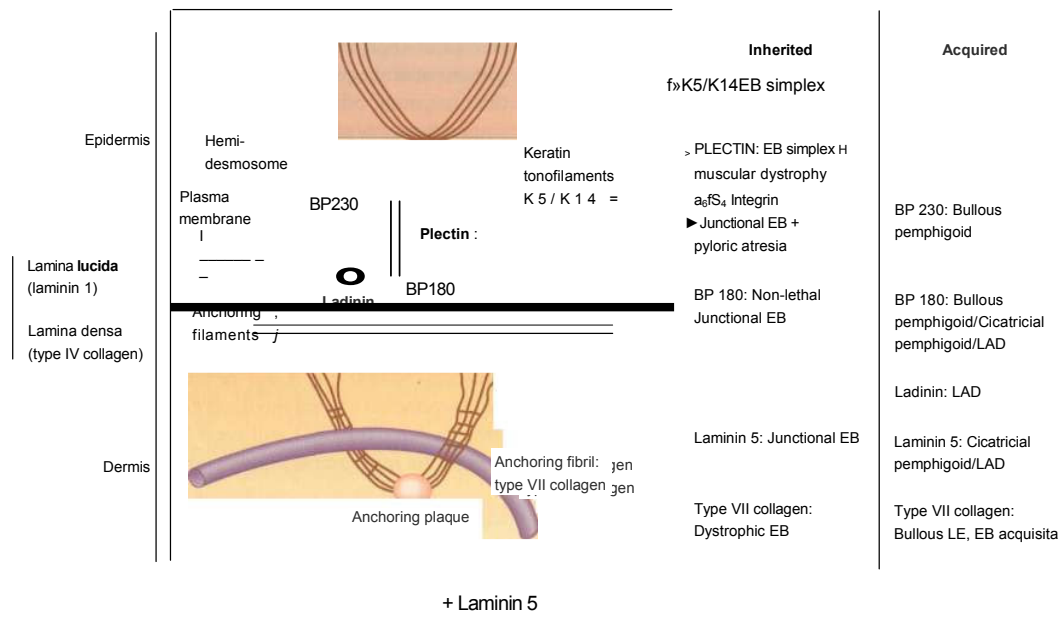


Fig. 23.27 Section of the basement membrane zone, showing the structural sites of damage in bullous disorders. LAD, linear IgA disease; EB, epidermolysis bullosa.

and blistering (Fig. 23.27). The level of blistering determines the clinical picture as well as the prognosis. Therefore skin biopsy for light and electron microscopy together with immunofluorescence (IMF) studies is paramount in diagnosis. However, remember that the commonest causes of skin blistering are chickenpox, herpes, impetigo, pompholyx eczema and insect bite reactions, although these are often localized.

IMMUNOBULLOUS DISEASE

Pemphigus vulgaris

Pemphigus vulgaris is a potentially fatal blistering disease occurring in all races but commoner in Ashkenazi Jews and possibly in people from the Indian sub-continent. Onset is usually in middle age and both sexes are affected equally. Prior to the development of oral steroids this condition was frequently fatal. The development of autoantibodies against the desmosomal protein, desmoglein 3, is pathogenic in this disease and they can be measured experimentally as markers of disease activity. Rarely the disease can be drug induced (e.g. penicillamine or captopril).

Skin biopsy shows a superficial intraepidermal split just above the basal layer with acantholysis (separation of individual cells). In the rarer variant, pemphigus foliaceus (characterized by anti-desmoglein 1 autoantibodies), the split is higher in the upper epidermis. Both direct IMF of skin (perilesional) and indirect IMF using patients' serum show intercellular staining of IgG within the epidermis.

Clinical features

Mucosal involvement (especially oral ulceration) is common and is the presenting sign in up to 50% of cases.

This is followed by the appearance of flaccid blisters, particularly involving the trunk. They tend to be sore rather than itchy. Blistering usually becomes widespread but they rapidly denude; thus pemphigus often presents with erythematous, weeping erosions. Blisters can be extended with gentle sliding pressure (Nikolsky's sign). Flexural lesions often have a vegetative appearance. In *pemphigus foliaceus* the blisters and erosions often start in a seborrhoeic distribution (scalp, face and upper chest) before becoming more widespread.

Treatment

This is with very high-dose oral prednisolone (60-100 mg daily) or pulsed methylprednisolone, and this may need to be lifelong. Other immunosuppressants such as azathioprine, or mycophenolate mofetil (or occasionally cyclophosphamide or ciclosporin) are used as steroid-sparing agents but they often take many weeks to be effective. Intravenous immunoglobulin infusions may help gain quick control whilst waiting for these other drugs to work. Anti-CD20 monoclonal antibody (rituximab) has recently been reported to help multidrug-resistant cases.

Whilst treatment is normally effective, perhaps up to 10% of patients may die, either because of complications of the disease or more commonly from side-effects of the treatment.

Use of azathioprine. Azathioprine can cause bone marrow suppression and an allergic hepatitis. Therefore blood count and liver function tests should be regularly monitored during therapy (every 6 weeks). Long-term use with other immunosuppressants causes a slightly increased risk of malignancy, especially of the skin.



Fig. 23.28 Bullous pemphigoid.

Bullous pemphigoid

Bullous pemphigoid is more common than pemphigus. It presents in later life (usually over 60 years old) and mucosal involvement is rarer. Autoantibodies against a 230 kDa or 180 kDa hemidesmosomal protein ('bullous pemphigoid antigens 1 and 2') play an aetiological role.

Skin biopsy shows a deeper blister (than in pemphigus) owing to a subepidermal split through the basement membrane. Direct and indirect IMF studies show linear staining of IgG along the basement membrane.

Clinical features

Large tense bullae appear anywhere on the skin (Fig. 23.28) but often involve limbs, hands and feet. They may be centred on an erythematous or urticated background and they can be haemorrhagic. Pemphigoid can be very itchy. Mucosal ulceration is uncommon but a variant of pemphigoid exists which predominantly affects mucosal surfaces with scarring (cicatricial pemphigoid).

Treatment

This is with high-dose oral prednisolone (30-60 mg daily) and steroid-sparing agents such as azathioprine or mycophenolate mofetil. Weekly methotrexate is also occasionally used. In general disease control is easier than with pemphigus. Treatment can often be withdrawn after 2-3 years. Pemphigoid treatment frequently causes side-effects, especially as most patients are elderly. Occasionally localized or mild disease can be controlled with superpotent topical steroids, oral dapsone or high-dose oral minocycline.

Dermatitis herpetiformis (see also p. 303)

Dermatitis herpetiformis (DH) is a rare blistering disorder associated with gluten-sensitive enteropathy (coeliac disease). DH and celiac disease are associated with other organ-specific autoimmune disorders.

Skin biopsy shows a subepidermal blister with neutrophil microabscesses in the dermal papillae. Direct IMF studies of uninvolved skin show IgA in the dermal papillae and patchy granular IgA along the basement membrane. The jejunal mucosa usually shows a partial villous atrophy.

Clinical features

Dermatitis herpetiformis is commoner in males and can present at any age but is most likely to appear for the first time in young adult life. It presents with intensely itchy, small blisters of the skin. The lesions have a predilection for the elbows, extensor forearms, scalp and buttocks. The tops of the blisters are usually scratched off; thus crusted erosions are often seen at presentation. Remissions and exacerbations are common.

Treatment

This should always be with a gluten-free diet (GFD). Control of the skin disease can be obtained with oral dapsone (50-200 mg daily) or sulphonamides. If a strict GFD is adhered to, oral medication can often be withdrawn after 2 years. The GFD will need to be lifelong. It protects against the rare complication of small bowel lymphoma.

Use of dapsone. Dapsone frequently causes a mild, dose-related haemolytic anaemia but the haemolysis can be devastating if there is G6PD deficiency. Liver damage, peripheral neuropathy and aplastic anaemia can also rarely occur, so regular monitoring of a blood count and liver function is needed.

Linear IgA disease (chronic bullous dermatosis of childhood)

Linear IgA disease is a subepidermal blistering disorder of adults and children. Pathogenic IgA autoantibodies can bind to a variety of basement membrane proteins including laminin, BP 180 antigen and laminin 5 (see Fig. 23.27). It is the most common immunobullous disease seen in children. Rarely it is drug induced by vancomycin.

Clinical features

Linear IgA disease can present with circular clusters of large blisters, a pemphigoid type of blistering or a dermatitis herpetiformis picture. Mucosal involvement of the mouth, vulva and eyes is not uncommon and can cause scarring. Direct IMF studies of skin show linear IgA deposition along the basement membrane.

Treatment

This is with oral dapsone (50-200 mg daily) or sulphonamides. Occasionally immunosuppression is needed. Many patients show spontaneous resolution after 3-6 years.

MECHANOBULLOUS DISEASE (EPIDERMOLYSIS BULLOSA, 'EB')

These are due to inherited abnormalities in structural skin proteins which lead to 'skin fragility'. The resultant blistering tends to arise secondary to trauma and often appears at or shortly after birth. These conditions can be a mild inconvenience, severely disabling or fatal but fortunately are very rare. There are three groups of disorders in which the fundamental gene/protein abnor-

malities have been characterized. This enables prenatal amniocentesis diagnosis.

Epidermolysis bullosa simplex

This is a group of autosomal dominant genodermatoses characterized by 'superficial' blistering owing to mutations of cytoskeleton proteins within the basal layer of the epidermis, e.g. keratin 5 (chromosome 12q) or keratin 14 (chromosome 17q). Most forms of EB simplex show mild disease with intermittent blistering of the hands and feet, especially in hot weather. The teeth and nails are normal and scarring is absent.

Epidermolysis bullosa dystrophica

This group of genodermatoses is characterized by 'deeper' blistering associated with scarring and milia formation. The level of split is deep within the basement membrane and is due to a mutation in the *COL-7A1* gene (locus at chromosome 3p21.1) which causes a loss of collagen VII in the anchoring fibrils. Nails, mucosae and even the larynx are often involved. The autosomal dominant variety is milder but the autosomal recessive type produces severe disease with disabling scarring, fusion of digits, joint contractures and dysphagia. Life expectancy is significantly reduced. Repeated scarring results in the development of multiple squamous cell carcinomas and most die from this complication in early adult life. The average life expectancy after the appearance of the first squamous cell carcinoma is 5 years.

Junctional epidermolysis bullosa

This, the most severe form, is characterized by a split in the lamina lucida of the basement membrane and is due to mutations in various proteins, mainly laminin 5 but also $\alpha_6\beta_4$ integrin or the 180 kDa bullous pemphigoid-2 antigen. It presents at birth with widespread blistering and areas of absent skin. Erosions of the central face and hoarseness from laryngeal involvement are common. Nail and teeth abnormalities are also common. Both a lethal and a rarer non-lethal form of junctional EB exist and they show an autosomal recessive inheritance. The lethal form causes death in infancy or early childhood.

Investigation and treatment

Investigation and treatment of EB should be carried out in a specialist centre. Diagnosis at birth on clinical grounds is difficult and should be avoided. Exact diagnosis depends on ultrastructural analysis of induced blisters in the skin and immunohistochemistry. Only then can prognosis and genetic counselling be given accurately to parents. Prenatal diagnosis is available for the more severe forms of EB.

FURTHER READING

Allen J et al. (2003) Linear IgA disease. *British Journal of Dermatology* 149: 977-985,1055-1058. Cooper et al. (2003) Treatment of resistant pemphigus vulgaris with an anti-CD20 monoclonal antibody (rituximab). *Clinical and Experimental Dermatology* 28: 366-368.

Diaz LA, Giudice GJ (2000) End of the century overview of skin blisters. *Archives of Dermatology* 136:106-112. Fine J-D et al. (2000) Inherited epidermolysis bullosa comes into the new millennium. *Journal of the American Academy of Dermatology* 43:135-137. Harman KE et al. (2003) Guidelines for the management of pemphigus. *British Journal of Dermatology* 149: 926-937. Trent JT et al. (2003) Epidermolysis bullosa: identification and treatment. *Advances in Skin & Wound Care* 16: 284-290. Wojnarowska F et al. (2002) Guidelines for the management of bullous pemphigoid. *British Journal of Dermatology* 147: 214-221.

SKIN TUMOU

BENIGN CUTANEOUS TUMOURS

Melanocytic naevi (moles)

Moles are a benign overgrowth of melanocytes that are common in white-skinned people. They appear in childhood and increase in number and size during adolescence and early adult life. They often start as flat brown macules with proliferation of melanocytes at the dermoepidermal junction (junctional naevi). The melanocytes continue to proliferate and grow down into the dermis (compound naevi), which causes an elevation of the mole above the skin surface. The pigmentation is usually even and the border regular. They eventually mature into a dermal naevus (cellular naevus) often with a loss of pigment.

Blue naevus is an acquired asymptomatic blue-looking mole. It is due to a proliferation of melanocytes deep in the mid-dermis.

Basal cell papilloma (seborrhoeic wart)

This is a common benign overgrowth of the basal cell layer of the epidermis. The lesion can be flesh coloured, brown or even black and often has a greasy appearance. The surface is irregular and warty and the lesions appear very superficial as though stuck on to the skin (Fig. 23.29).

##

t

Fig. 23.29 Seborrhoeic warts (basal cell papillomas).

Tiny keratin cysts may be seen on the surface. They can be treated with cryotherapy or curettage.

Dermatofibroma (histiocytoma)

Dermatofibromas appear as firm, elevated pigmented nodules which may feel like a button in the skin. A peripheral ring of pigmentation is sometimes seen. They are often found on the leg and are commoner in females. There may be a preceding history of trauma or insect bite. The lesion consists of histiocytes, blood vessels and varying degrees of fibrosis. If symptomatic, excision is required.

Epidermoid cyst (previously 'sebaceous cyst')

Epidermoid cysts present as cystic swellings of the skin with a central punctum. They contain 'cheesy' keratin rather than sebum; thus the old term 'sebaceous cyst' should be avoided. These cysts occasionally rupture causing significant dermal inflammation which is not infected.

Pilar cyst (trichilemmal cyst)

Pilar cysts are smooth cysts without a punctum, usually found on the scalp. They may be multiple and familial.

Keratoacanthoma

Keratoacanthomas are rapidly growing epidermal tumours which develop central necrosis and ulceration (Fig. 23.30). They occur on sun-exposed skin in later life and can grow up to 2-3 cm across. Whilst they may resolve spontaneously over a few months, they are best excised, both to exclude a squamous cell carcinoma (which they can mimic) and to improve the cosmetic outcome.

Pyogenic granuloma (granuloma telangiectaticum)

Pyogenic granulomas are a benign overgrowth of blood vessels. They present as rapidly growing pinkish red nodules which are friable and readily bleed. They may follow trauma and are often found on the fingers and lips. They are best excised to exclude an amelanotic malignant melanoma.



Fig. 23.30 Keratoacanthoma.

Cherry angioma (Campbell de Morgan spots)

They are benign angiokeratomas that appear as tiny pinpoint red papules, especially on the trunk, and increase with age. No treatment is required.

POTENTIALLY PRE-MALIGNANT

CUTANEOUS TUMOURS

Solar keratoses (actinic keratoses)

These frequently develop later in life in white-skinned people who have had significant sun exposure. They appear on exposed skin as erythematous silver-scaly papules or patches with a conical surface and a red base (Fig. 23.31). The background skin is often inelastic, wrinkled and may show flat brown macules (Tiver spots' or solar lentigos) reflecting diffuse solar damage. A small proportion of these keratoses can transform into squamous cell carcinoma but only after many years.

Treatment of lesions is with cryotherapy, topical 5-fluorouracil cream or 5% imiquimod cream.

Bowen's disease

This is a form of intraepidermal carcinoma-in-situ which rarely can become invasive. It presents on exposed skin as an isolated scaly red patch or plaque, looking rather like psoriasis, although it has a rather irregular edge. The lesions do not clear but slowly increase in size with time. A variant which can show partial or full-thickness dysplasia can involve the epidermis of the mucosa or neighbouring skin - this can affect the vulva, the glans penis and perianal skin. It is termed vulval- (penile-, or anal-) intraepithelial dysplasia. Clinically it can present as non-specific erythema or as a warty thickening. These diseases have a stronger link with HPV and probably have a higher premalignant potential than Bowen's disease. They are commoner in immunosuppressed individuals. The anal form is increasingly reported in HIV-positive patients and extension into the rectum has been reported.



Fig. 23.31 Solar keratoses with background actinic damage.

Treatment is with topical 5-fluorouracil, 5% imiquimod cream, cryotherapy, curettage, photodynamic therapy or a tissue-destructive laser.

Atypical mole syndrome (dysplastic naevus syndrome)

This is often familial. A large number of melanocytic naevi begin to appear in childhood, even on unexposed sites. Individual lesions may be large with irregular pigmentation and border, and histologically they may show cytological and architectural atypia but no frank malignant change. Individuals with this condition have an increased risk of developing malignant melanoma. They should have their moles photographed and be regularly reviewed. Suspicious lesions should be excised.

Giant congenital melanocytic naevi

These are very large moles present at birth. They show an increased risk of developing malignant melanoma. Approximately 10% of lesions larger than 20 cm across will develop a malignant melanoma in childhood. Excision should be undertaken if possible.

Lentigo maligna

This is a slow-growing macular area of pigmentation seen in elderly people, commonly on the face. The border and pigmentation are often irregular. Some people regard this lesion as a melanoma-in-situ. There is an increased risk of developing invasive malignant melanoma. Treatment is by excision if possible but 5% imiquimod cream is currently under assessment in the very large lesions where surgery would be so disfiguring.

MALIGNANT CUTANEOUS TUMOURS

Basal cell carcinoma (rodent ulcer)

Basal cell carcinomas are the most common malignant skin tumour and most relate to excessive sun exposure. They are common later in life on exposed sites although rare on the ear. They present as a slow-growing papule or nodule (or rarely be cystic) which may go on to ulcerate (Fig. 23.32). Telangiectasia over the tumour or a skin-coloured jelly-like 'pearly edge' may be seen. A flat, diffuse superficial form exists and an ill-defined 'morphoeic' variant. Basal cell carcinomas will slowly grow and erode structures if untreated but these tumours almost never metastasize.

Treatment

Treatment is usually with surgical excision with a 3-5 mm border. Radiotherapy, photodynamic therapy, cryotherapy or 5% imiquimod cream can be useful for large superficial forms but follow-up for recurrence is required. Curettage is occasionally used in older patients, although not for central facial lesions as they often recur. Recurrent tumour or morphoeic basal cell carcinoma is best treated with Mohs' micrographic surgery to ensure adequate clearance.



Fig. 23.32 Ulcerating basal cell carcinoma.

Squamous cell carcinoma

Squamous cell carcinoma is a more aggressive tumour than basal cell carcinoma as it can metastasize if left untreated. Most relate to sun exposure and daily application of sun cream has been shown to reduce the incidence in Australia. They can arise in pre-existing solar keratoses or Bowen's disease or be due to chronic inflammation such as in lupus vulgaris. Rarely multiple tumours arise because of arsenic ingestion in early life. Multiple tumours occur in people who have had prolonged periods of immunosuppression, such as renal transplant patients where certain human papilloma virus subtypes may be involved in malignant transformation.

Clinically the lesions are often keratotic, rather ill-defined nodules which may ulcerate (Fig. 23.33). They can grow very rapidly. Examination of regional lymph



Fig. 23.33 Squamous cell carcinoma.

nodes is essential. They are most common on sun-exposed sites in later life. One should have a high index of suspicion for ulcerated lesions on the lower lip or ear.

Treatment is with excision or occasionally radiotherapy. Curettage should be avoided.

Malignant melanoma

Malignant melanoma is the most serious form of skin cancer as metastases can occur early and it causes a number of deaths even in young people. As with other types of skin cancer the incidence is continuing to increase, probably because of excessive exposure to sunlight. The history of childhood sun exposure and intermittent sun exposure appears to play a role in the development of malignant melanoma. Other risk factors include atypical mole syndrome, giant congenital melanocytic naevi, lentigo maligna and a positive family history of malignant melanoma. Malignant melanoma is commoner in later life; young adults are also affected. The tumour suppressor gene *p16* (on chromosome 9p) is frequently mutated or deleted in melanoma cell lines and its role in atypical mole syndrome/familial melanoma is currently under investigation.

Diagnosis of melanoma is not always easy but the clinical signs listed in Table 23.11 help distinguish malignant from benign moles. Examination with a dermatoscope can further help in detecting malignant lesions.

Four clinical types exist:

- *Lentigo maligna melanoma* is where a patch of lentigo maligna develops a papule or nodule signalling invasive tumour.
- *Superficial spreading malignant melanoma* is a large flat irregularly pigmented lesion which grows laterally before vertical invasion develops.
- *Nodular malignant melanoma* (Fig. 23.34) is the most aggressive type. It presents as a rapidly growing pigmented nodule which bleeds or ulcerates. Rarely they are amelanotic (non-pigmented) and can mimic pyogenic granuloma.

Table 23.11 Clinical criteria for the diagnosis of malignant melanoma

ABCDE criteria (USA)

Asymmetry of mole
Border irregularity
Colour variegation
Diameter > 6 mm
Elevation

The Glasgow 7-point checklist

Major criteria

- Change in size
- Change in shape
- Change in colour

Minor criteria

- Diameter more than 6 mm
- Inflammation
- Oozing or bleeding
- Mild itch or altered sensation



Fig. 23.34 Nodular malignant melanoma.

- *Acral lentiginous malignant melanoma* arises as pigmented lesions on the palm, sole or under the nail and it usually presents late.

Treatment

This consists of urgent wide excision (2 cm margin) of the lesion. Histological analysis will determine the depth of invasion ('Clark's level') and the thickness of the tumour ('Breslow thickness'). These two factors are significant in predicting prognosis and 5-year survival rates: 96% for local lesions, 60% for regional spread and 14% for distant metastases. For localized melanomas the thickness and presence or absence of ulceration are the strongest independent predictors of outcome. Excision and histology interpretation should only be done by experts to ensure optimum treatment and assessment of prognosis. Sentinel node biopsy for patients with thicker lesions is required for predicting prognosis: 15% will be positive without clinical lymphadenopathy. Metastatic disease is best managed by an oncologist with a multidisciplinary team and can involve surgery to lymph nodes, radiotherapy, immunotherapy and chemotherapy. Initial optimism for high-dose alpha-interferon therapy in advanced disease has recently been challenged with a systematic review suggesting no clear benefit.

The role of governments and medical personnel in public health education to discourage sunbathing and to use sunscreens is of the utmost importance in skin cancer prevention.

Cutaneous T-cell lymphoma (mycosis fungoides)

This is a rare type of skin tumour which often follows a relatively benign course. It presents insidiously with scaly patches and plaques which can look eczematous or psoriasiform. Lesions often appear initially on the buttocks. These lesions may come and go or remain persistent over many years. Patients may well die of unrelated causes. Skin biopsy confirms the diagnosis, showing invasion by atypical lymphocytes. T-cell receptor gene rearrangement studies show that there is often a monoclonal expansion of lymphocytes in the skin.

Occasionally the disease can progress to a cutaneous nodular or tumour stage which may be accompanied by systemic organ involvement. In elderly males the disease may progress rarely to an erythrodermic variant accompanied by lymphadenopathy and peripheral blood involvement ('Sezary syndrome').

All patients should be staged at the time of diagnosis to assess for any systemic involvement.

Treatment

Early cutaneous disease can be left untreated or treated with topical steroids or PUVA. More advanced disease of the skin, or systemic involvement, may require radiotherapy, chemotherapy, immunotherapy or electron beam therapy. Bexarotene, an agonist at the retinoid X receptor, can cause regression.

Kaposi's sarcoma

This is a tumour of vascular and lymphatic endothelium that presents as purplish nodules and plaques. There are three types:

- The 'classic' or 'sporadic' form (as described by Kaposi) occurs in elderly males, especially Jews from Eastern Europe. It presents as slow-growing purple tumours in the foot and lower leg **which** rarely cause any significant problem.
- The 'endemic' form occurs in males from central Africa and shows more widespread cutaneous involvement as well as lymph node (or occasionally systemic) involvement. Oedema is a prominent feature.
- The immunosuppression-related form is more severe and is most common in homosexual patients with HIV (p. 142). Lesions are widespread and often affect the skin, bowel, oral cavity and lungs.

All three types have a strong association with herpes virus type 8 but other factors must be involved as herpes type 8 seroprevalence in the general population is up to 10% in the USA and 50% in some African countries. HAART (p. 143) has significantly reduced the incidence of Kaposi's sarcoma in HIV.

Treatment

Treatment of advanced Kaposi's sarcoma is with radiotherapy, immunotherapy or chemotherapy.

FURTHER READING

- Antman K, Chang Y (2000) Kaposi's sarcoma. *New England Journal of Medicine* **342**:1027-1038.
- Girardi M, Heald PW, Wilson LD (2004) The pathogenesis of mycosis fungoides. *New England Journal of Medicine* **350**:1978-1988.
- Hill D (1999) Efficacy of sunscreens in protection against skin cancer. *Lancet* **354**: 699-700 (see also pp. 723-729).
- Perrott RE et al. (2003) Reassessing the role of lymphatic mapping and sentinel lymphadenectomy in the management of cutaneous malignant melanoma. *Journal of the American Academy of Dermatology* **49**: 567-588.

Ready N et al. (2003) Adjuvant high-dose interferon therapy for high-risk melanoma. *Archives of Dermatology* **139**:1635-1637.

Thomas JM et al. (2004). Excision margins in high risk malignant melanoma. *New England Journal of Medicine* **350**: 757-766 (and editorial, p. 823).

Thompson JF et al. (2005) Cutaneous melanoma. *Lancet* **365**: 687-701.

DISORDERS OF BLOOD VESSELS/LYMPHATIC

LEG ULCERS

Venous ulcers

Leg ulcers are common in western societies and can have many causes (Table 23.12). Venous ulcers are the most common type in developed countries.

Venous ulcers are the result of sustained venous hypertension in the superficial veins, owing to incompetent valves in the deep or perforating veins or to previous deep vein thrombosis. The increased pressure causes extravasation of fibrinogen through the capillary walls, giving rise to perivascular fibrin deposition, which leads to poor oxygenation of the surrounding skin.

Venous ulcers are common in later life and cause a significant drain on healthcare budgets as they are often chronic and recurrent; they affect 1% of the population over the age of 70 years. They are most commonly found on the lower leg in a triangle above the ankles (Fig. 23.35), and are associated with:

- venous eczema (p. 1330)
- brown pigmentation from haemosiderin
- varicose veins
- lipodermatosclerosis (the combination of induration, reddish brown pigmentation and inflammation)
- scarring white atrophy with telangiectasia (atrophic blanche).

Treatment

High-compression bandaging (e.g. Unna boot or four-layer bandaging) and leg elevation are used to try to

Table 23.12 Causes of leg ulceration

Venous hypertension
Arterial disease (e.g. atherosclerosis)
Neuropathic (e.g. diabetes, leprosy)
Neoplastic (e.g. squamous or basal cell carcinoma)
Vasculitis (e.g. rheumatoid arthritis, SLE, pyoderma gangrenosum)
Infection (e.g. ecthyma, tuberculosis, deep mycoses, tropical ulcer, syphilis, yaws)
Haematological (e.g. sickle cell disease, sprerucyfosij)
Drug (e.g. hydroxycarbamide (hydroxyurea))
Other (e.g. necrobiosis lipoidica, trauma, artefact)



Fig. 23.35 Venous leg ulcer.

decrease the venous hypertension. Doppler studies should always be done before bandaging to exclude arterial disease. This treatment is best delivered in the community by appropriately trained nurses. 'Four-layer bandaging' is increasingly popular as this provides high levels of graduated compression (with pressures decreasing up the leg). The choice of ulcer dressing is less critical but one should be chosen to keep the ulcer moist and free of slough and exudate. Up to 80% of ulcers can be healed within 26 weeks. Slower healing rates occur in patients with decreased mobility and if the ulcers are very large, present for longer than 6 months or are bilateral. Diuretics are sometimes helpful to reduce the oedema. Antibiotics are necessary only for overt bacterial infection. Unusual fungal infection ('tinea incognito') is increasingly reported under compression bandaging.

Venous leg ulcers can be very painful so adequate analgesia should be given, including opiates if required. Underlying venous disease is best investigated with duplex ultrasound or plethysmography. Split-thickness skin grafting is used in resistant cases. Life-long support stockings (individually fitted) should be worn after healing as this lessens recurrence.

Surgery for purely superficial venous disease can occasionally be useful for ulcer healing but, in general, venous surgery is unhelpful.

Arterial ulcers

Arterial ulcers may present as punched-out, painful ulcers higher up the leg or on the feet. There may be a history of claudication, hypertension, angina or smoking. Clinically the leg may be cold and show pallor. Absent peripheral pulses, arterial bruits and loss of hair may be present. Doppler ultrasound studies will confirm arterial disease (p. 866) and digital subtraction angiography will further delineate the extent and site of the disease.

Treatment depends on keeping the ulcer clean and covered, adequate analgesia and vascular reconstruction if appropriate.

Neuropathic ulcers

Neuropathic ulcers tend to be seen over pressure areas of the feet, such as the metatarsal heads, owing to repeated trauma. These are most commonly seen in diabetics because of peripheral neuropathy. In developing countries leprosy is a common cause.

Treatment depends on keeping the ulcer clean and removing pressure or trauma from the affected area. Diabetics should pay particular attention to foot care and correctly fitting shoes with the help of a specialist podiatrist (p. 1130).

PRESSURE SORES (DECUBITUS ULCERS, BEDSORES)

These occur in the elderly, immobile, unconscious or paralysed patients. They are due to skin ischaemia from sustained pressure over a bony prominence, most commonly the heel and sacrum. Normal individuals feel the pain of continued pressure, and even during sleep, movement takes place to change position continually. Pressure sores may be graded:

- Stage I: non-blanchable erythema of intact skin
- Stage II: partial-thickness skin loss of epidermis/dermis (blister or shallow ulcer)
- Stage III: full-thickness skin loss involving subcutaneous tissue but not fascia
- Stage IV: full-thickness skin loss with involvement of muscle/bone/ tendon/joint capsule.

There are numerous risk factors for development of pressure sores (Table 23.13).

The majority of pressure sores occur in hospital. Seventy per cent appear in the first 2 weeks of hospitalization, and 70% are in orthopaedic patients, especially those on traction. Between 20% and 30% of pressure sores occur in the community.

Table 23.13 Risk factors for the development of pressure sores

Prolonged immobility:
paraplegia
arthritis
severe physical disease
apathy
operation and postoperative states
plaster casts
intensive care
Decreased sensation:
coma, neurological disease, diabetes mellitus
drug-induced sleep
Vascular disease:
atherosclerosis, diabetes mellitus, scleroderma,
vasculitis
Poor nutrition:
anaemia
hypoalbuminaemia
vitamin C or zinc deficiency

Eighty per cent of patients with deep ulcers involving the subcutaneous tissue die in the first 4 months.

The early sign of red/blue discoloration of the skin can lead rapidly to ulcers in 1-2 hours. Leaving patients on hard emergency room trolleys, or sitting them in chairs for prolonged periods, must be avoided.

Management

Prevention

Prevention is better than cure. Specialist 'tissue-viability nurses' help identify at-risk patients and train other medical staff. Several risk-assessment tools have been devised for the immobile patient based on the known risk factors. The 'Norton scale' and Waterlow Pressure Sore Risk Assessment (Box 23.4) are two such validated systems which produce a numerical score, enabling staff to identify those at most risk.

Treatment

- m Bed rest with pillows and fleeces to keep pressure off bony areas (e.g. sacrum and heels) and prevent friction.
- Air-filled cushions for patients in wheelchairs.
- Special pressure-relieving mattresses and beds.
- Regular turning but avoid pressure on hips.
- Ensure adequate nutrition.
- Non-irritant occlusive moist dressings (e.g. hydro-colloid).
- Adequate analgesia (may need opiates).

- Plastic surgery (debridement and grafting in selected cases).
- Treatment of underlying condition.

VASCULITIS (see also p. 581)

Vasculitis is the term applied to an inflammatory disorder of blood vessels which causes endothelial damage. Cutaneous vasculitis (confirmed by skin biopsy) may be an isolated problem but occasionally is associated with vasculitis in other organs. The most commonly used classification is based on the size of blood vessel involved (see Tables 10.18 and 10.19).

The cutaneous features are of haemorrhagic papules, pustules, nodules or plaques which may erode and ulcerate. These purpuric lesions do not blanch with pressure. Occasionally a fixed livedo reticularis pattern may appear which does not disappear on warming. Pyrexia and arthralgia are common associations even in the absence of significant systemic involvement. Other clinical features depend on the underlying cause.

The most common cutaneous vasculitis affects small vessels and is called leucocytoclastic vasculitis (LCV) or angitis. This usually appears on the lower legs as a symmetrical palpable purpura. It is rarely associated with systemic involvement. This can be caused by drugs (15%), infection (15%), inflammatory disease (10%), malignant disease (< 5%) but often no cause is found (55-60%). Extensive investigations are probably best reserved for



Box 23.4 Pressure sore risk-assessment

tools Norton Scale for Pressure Sores

Physical	Neurology	Activity	Mobility	Incontinence
4 Good	4 Alert	4 Ambulant	4 Full	3 None
3 Fair	3 Apathetic	3 Walks with help	Slightly 2	3 Occasionally
2 Poor	2 Confused	2 Not bound	Limited* 1	2 Usually
1 Very poor	1 Stupor	1 Bedfast	Very limited	1 Double
			Immobile	

*Norton Scale for Pressure Sores. Low scores carry a high risk

Waterlow Pressure Sore Risk Assessment

Build/weight for height	Visual skin type	Continen	Mobility	Sex Age	Appetite
Average	0 Healthy	0 Complete	0 Fully mobile	Male	Average 0
Above average	2 Tissue paper	1 Occasionally	1 Restricted/difficult	Female 14-18	Poor 1
Below average	3	1 Dry incontinent	1 Restless/fidgety	50-64	Anorectic 2
	1 Oedematous Clammy	1 Catheter/incontinent of faeces	1 Apathetic Inert/traction	65-75	
		2 Doubly incontinent		75-80	
				81+	
				3	

Special risk factors

1. Poor nutrition; e.g. terminal cachexia
2. Sensory deprivation, e.g. diabetes, paraplegia, cerebrovascular accident
3. High-dose anti-inflammatory or steroids in use
4. Smoking 10+ per day
5. Orthopaedic surgery/fracture below waist

Assessment value

- At risk 10
- High risk 15
- Very high risk 20

those with persistent lesions or associated signs and symptoms. Whilst LCV often settles spontaneously, treatment with analgesia, support stockings, dapsone or prednisolone may be needed to control the pain and to heal up any ulceration. Urticarial vasculitis is discussed on page 1335.

LYMPHATICS

Lymphoedema

Lymphoedema refers to a chronic non-pitting oedema due to lymphatic insufficiency. It is most commonly seen affecting the legs and tends to progress with age. The legs can become enormous and prevent wearing of normal shoes. Chronic disease may cause a secondary 'cobblestone' thickening of the skin. Lymphoedema can be primary (and present early in life) owing to an inherited deficiency of lymphatic vessels (e.g. Milroy's disease) or can be secondary because of obstruction of lymphatic vessels (e.g. filarial infection or malignant disease).

Treatment is with compression stockings and physical massage. If there is recurrent cellulitis, long-term antibiotics are advisable as each episode of cellulitis will further damage the lymph vessels. Surgery should be avoided.

Lymphangioma circumscriptum

Lymphangioma circumscriptum is a rare hamartoma of lymphatic tissue. It usually presents in childhood with multiple small vesicles in the skin which weep lymphatic fluid and sometimes blood. They reflect deeper vessel involvement so surgery should be avoided. Cryotherapy or CO₂ laser treatment may help the superficial lesions.

FURTHER READING

- Cullum N et al. (2003) Pressure sores. *Clinical Evidence* 9: 2167-2176.
- Fiorentino DF (2003) Cutaneous vasculitis. *Journal of the American Academy of Dermatology* 48: 311-340.
- Health Technology Assessment Programme - Systematic Reviews of Wound Care Management (1999) Vol. 3, No. 17 (parts I and II); (2000) Vol. 4, No. 21; (2001) Vol. 5 No. 9. London: Department of Health. Online. Available: <http://www.ncchta.org>.
- Topham EJ et al. (2002) Chronic lower limb oedema. *Clinical Medicine* 2: 28-31.
- Valencia IC et al. Chronic venous insufficiency and venous leg ulceration (2001) *Journal of the American Academy of Dermatology* 44: 401-421.

DISORDERS OF COLLAGEN AND ELASTIC TISSUE

Ehlers-Danlos syndrome (see also p. 602)

Ehlers-Danlos syndrome can be subdivided into at least 10 variants. They are all inherited disorders causing

abnormalities in collagen of the skin, joints and blood vessels. Clinically this causes increased elasticity of the skin, hypermobile joints and fragile blood vessels causing easy bruising or in some cases internal haemorrhage. The skin is hyperextensible but recoils normally after stretching. It is easily injured and heals slowly with scarring like tissue paper. Pseudotumours may occur at the sites of scarring (such as elbows and knees) consisting mainly of fat, but calcification can occur.

Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is a rare group of disorders characterized by abnormalities in collagen and elastic tissue affecting the skin, eye and blood vessels. The skin may be loose, lax and wrinkled. It can look yellowish and papular ('plucked chicken skin') and tends to lose its elastic recoil when stretched. Skin changes are best seen in the flexures especially the sides of the neck. Non-cutaneous features are not always present but they include recurrent gastrointestinal bleeding, early myocardial infarction, claudication and angioid streaks on the retina reflecting disruption of vascular elastic tissue.

Marfan's syndrome (see also p. 839)

Marfan's syndrome, an autosomal dominant disorder of connective tissue, is described on page 839. The syndrome is characterized by tall stature and long thin digits (arachnodactyly) (Fig. 13.98). The arm span can exceed the height of the patient and a high arched palate may be present. Lax ligaments result in frequent dislocation of joints. Inguinal and femoral hernias are common. Scoliosis and flat feet may be present. Pulmonary changes include emphysema, diaphragmatic hernia and spontaneous pneumothorax. Dislocation of the ocular lens is common. Skin changes are usually absent but striae may develop. Patients with homocystinuria (see p. 602), type III and VI Ehlers-Danlos syndrome (EDS) and 'marfanoid phenotype' have some similar features but often do not develop the life-threatening complications of Marfan's syndrome, so accurate diagnosis by an expert is essential.

Treatment

Patients should be reviewed by an ophthalmologist, an orthopaedic surgeon and a cardiologist to screen for and deal with the above complications. Genetic counselling should be offered to families.

Striae

Striae are visible linear scars due to dermal collagen damage and stretching. Histologically a thinned epidermis overlies parallel bundles of fine collagen. They occur commonly over the abdomen and breasts in pregnancy but also occur on the thighs and trunk in rapidly growing adolescents as well as in some obese individuals. They are also seen in Cushing's syndrome and corticosteroid therapy. Striae are initially reddish blue but fade

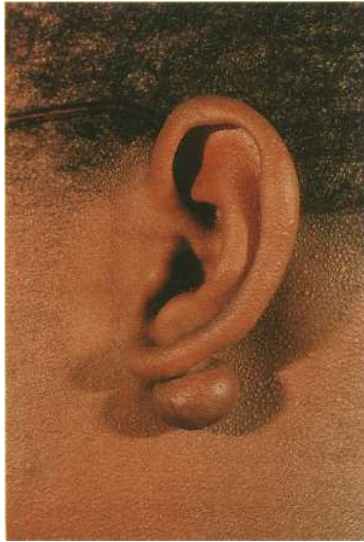


Fig. 23.36 Keloid scar of the lobe of the ear.

to white atrophic marks. Puberty-related striae normally disappear completely.

Keloid scars

Keloid scars are characterized by smooth hard nodules (Fig. 23.36) due to excessive collagen production. They may occur spontaneously or follow skin trauma/surgery, and they are often itchy. They tend to affect young adults and are much commoner in black Africans. Sites of predilection include the shoulders, upper back and chest, ear lobes and the chin. Unlike hypertrophic scars (which fade within 12 months) keloids are persistent and may fade with time.

Treatment is with triamcinolone injection, compression with silica gels or surgery but the latter must be followed by steroid injection or superficial radiotherapy or it may make the problem worse.

FURTHER READING

- Hu X et al. (2003) ABCC6/MRP6 mutations: further insight into the molecular pathology of pseudoxanthoma elasticum. *European Journal of Human Genetics* 11: 215-224. Ohtani T et al. (2002) Pseudoxanthoma elasticum. *Journal of Dermatology* 29: 615-620. Wordsworth P et al. (2001) The real connective tissue diseases. *Clinical Medicine* 1: 21—24.

DISORDERS OF PIGMENTATION

HYPOPIGMENTATION ^

Vitiligo

Vitiligo is a common disorder of depigmentation which probably has an autoimmune aetiology. Sufferers often



Fig. 23.37 Vitiligo of the hands showing areas of depigmentation.

have relatives with other organ-specific autoimmune disorders. It presents in childhood or early adult life with well-demarcated macules of complete pigment loss. There is no history of preceding inflammation. Patients are very susceptible to sunburn. Lesions are often symmetrical and frequently involve the face, hands (Fig. 23.37) and genitalia. The hair can also depigment. Trauma may induce new lesions. Spontaneous repigmentation can occur and often starts around hair follicles, giving a speckled appearance. However, repigmentation is rare if a lesion has persisted for more than 1 year or if the hair is depigmented. The psychological consequences of vitiligo can be devastating especially in Asian or black African people.

Treatment is very unsatisfactory and has no impact on the long-term outcome. Sunblocks should be used to prevent burning. Potent topical steroids or phototherapy help some individuals. Treatment with 0.1% tacrolimus ointment is currently under assessment, with conflicting early results. If vitiligo is almost universal and fixed, depigmentation with monobenzone may be considered. Finally, referral to a specialist camouflage clinic is often the most helpful 'treatment'.

Post-inflammatory hypopigmentation

This is one of the most common causes of pale skin. It is much more common in people with pigmented skin. It is seen as a consequence of eczema, acne or psoriasis and may even be the reason for individuals presenting to a doctor. Providing the skin disease is controlled, the pigmentation will recover slowly after many months. Post-inflammatory hyperpigmentation can also occur.

Oculocutaneous albinism

This is a group of rare autosomal recessive disorders affecting the pigmentation of skin, hair and eyes. It can affect all races. Melanocytes are in normal number but have abnormal function. Clinically it presents with universal pale skin, white or yellow hair and a pinkish iris. Photophobia, nystagmus and a squint are also present in most cases.

Treatment involves obsessive protection against sunlight to avoid sunburning and development of skin cancer.

Idiopathic guttate hypomelanosis

This occurs most commonly in black African people and is of unknown aetiology. It presents with small (2-4 mm) asymptomatic porcelain-white macules, often on skin exposed to sunlight. The borders are often sharply defined and angular. There is no effective treatment.

Leprosy (see also p. 80)

Both tuberculoid leprosy and indeterminate leprosy can present with anaesthetic patches of depigmentation and should always be considered in people from endemic regions. Loss of hair and decreased sweating may also be present in the lesions.

HYPERPIGMENTATION

Freckles (ephelides)

These appear in childhood as small brown macules after sun exposure. They fade in the winter months.

Lentigos

These are a more permanent macule of pigmentation similar to freckles but they tend to persist in the winter. Solar lentigos (also called 'liver spots') occur in older people on exposed skin because of actinic damage.

Chloasma

These are brown macules often seen symmetrically over the cheeks and forehead and are most common in women. They can occur spontaneously but are also associated with pregnancy and the oral contraceptive pill.

Metabolic/endocrine effects

A generalized skin darkening can occur with chronic liver disease, especially haemochromatosis. It also is seen sometimes in Cushing's syndrome, Addison's disease (more marked in palmar creases and buccal mucosa) and Nelson's syndrome.

Peutz-Jeghers syndrome (p. 309) This is an autosomal dominant genetic condition. It presents with brown macules of the lips and perioral region. It is associated with gastrointestinal polyposis which occasionally become malignant.

Urticaria pigmentosa (cutaneous mastocytosis)

This presents most commonly with multiple pigmented macules in children. These lesions tend to become red, itchy and urticated if they are rubbed (Darier's sign). Occasionally lesions may blister and in the rare congenital, diffuse form of the disease the skin can become thickened and leathery.

Occasionally, systemic symptoms are present, such as wheeze, flushing, syncope or diarrhoea, reflecting extensive mast cell degranulation from the skin. Anaphylaxis occurs very rarely and may be precipitated by mast cell degranulators such as aspirin or opiates. The condition

spontaneously resolves after some years in children but is persistent in adults.

Skin biopsy shows an excess of mast cells in the skin. Recently a mutation in the proto-oncogene *c-kit* has been demonstrated, resulting in mast cell proliferation and mast cell apoptosis. Monoclonal antibodies against mast cell markers (tryptase and CD117) on immunohistochemistry confirm the diagnosis.

Treatment of the skin, if required, is with anti-histamines or PUVA.

Rarely there may be infiltration of internal organs with mast cells (*systemic mastocytosis*), especially in adult disease or neonatal disease. This can involve any organ but especially the bone (where it can cause severe pain), gastrointestinal tract, liver and spleen. There is a small risk of developing leukaemia if the bone marrow is heavily infiltrated.

Other conditions with pigmentation

Café-au-lait macules are seen in neurofibromatosis types 1 and 2. They also occur in a wide variety of disorders including tuberous sclerosis, ataxia, telangiectasia, Fanconi's anaemia, multiple endocrine neoplasia type 1, McCune—Albright syndrome.

Multiple lentigines: apart from in Peutz-Jeghers syndrome these are also seen in xeroderma pigmentosum.

Acquired melanocytic naevi are seen in Turner's syndrome (p. 1064) and familial atypical mole-melanoma syndrome (dysplastic naevi, p. 1351).

FURTHER READING

Tharp MD et al. (2003) Mastocytosis. *Advances in Dermatology* 19: 207-236.

DRUG-INDUCED RASHES

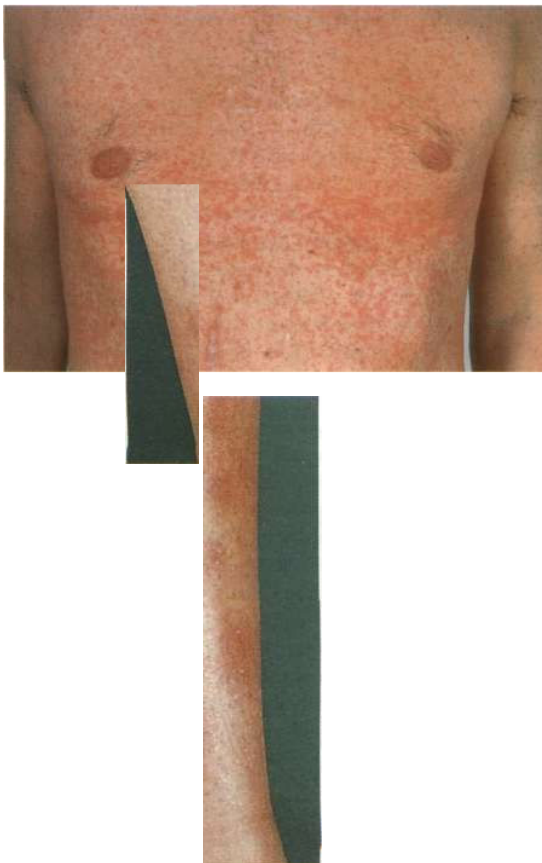
Drugs can be toxic and teratogenic but they can also cause problems through allergic reactions. This frequently presents in the skin where just about any type of skin rash can arise (Table 23.14) although a widespread symmetrical maculopapular rash is the most common type (Fig. 23.38). 'Fixed drug eruptions' may occur where a rash evolves and resolves at a specific site. The rash is reproduced at exactly the same site after a repeated exposure.

A thorough history is of great value and always think of a drug cause for any skin condition. The use of prick-testing and patch-testing is rarely helpful and not without risk. Drug allergy can only be proven by rechallenging but this is rarely justified as it carries some risks. Rechallenging is occasionally justified for anti-tuberculosis drugs or antiretroviral drugs but this should be carried out as an inpatient as there is a risk of anaphylaxis. Certain individuals (e.g. those with HIV infections) are more susceptible to drug rashes (Fig. 23.39).

Most rashes will settle spontaneously once the offending agent is removed. The commonest culprits in a hospital setting are antibiotics and chemotherapy agents.

Table 23.14 Morphological types of drug rashes and some common causes

Maculopapular	Penicillin/amoxicillin Penicillin, aspirin
Urticaria	Gold, hydralazine Phenolphthalein in laxatives,
Vasculitis Fixed drug rash	tetracyclines, paracetamol Minocycline (black), amiodarone (slate grey)
Pigmentation	Penicillamine, isoniazid
Lupus erythematosus	Thiazides, chlorpromazine,
Photosensitivity	sulphonamide, amiodarone Carbamazepine Sulphonamide, oral contraceptive Barbiturates
Pustular Erythema nodosum	Corticosteroids Chloroquine, thiazides, gold,
Erythema multiforme	allopurinol Methyldopa, gold,
Acneiform	lithium, beta-
Lichenoid	blockers Penicillin, co-trimoxazole,
Psoriasiform	carbamazepine, NSAIDs Penicillamine, ACE inhibitors Gold, sulphonylureas, allopurinol
Toxic epidermal necrolysi	Morbilliform drug rash due to penicillin
Pemphigus	<i>Fig. 23.38</i>
Erythroderma	allergy.

**Fig. 23.39** Erythema nodosum in a patient with HIV on co-trimoxazole.

The three most serious types of drug rashes are:

- erythroderma (p. 1340)
- toxic epidermal necrolysis
- anticonvulsant hypersensitivity syndrome.

Toxic epidermal necrolysis is characterized by a widespread subepidermal blistering and sloughing of most of the skin. The skin may be itchy but typically takes on a burning quality. Fever and mucosal involvement are common. The internal epithelial surfaces (lung, bladder, gastrointestinal tract) are also involved. Multiorgan failure and sepsis often occur. Toxic epidermal necrolysis can be fatal even after drug withdrawal and intensive care support. Patients should be managed in intensive care or a specialized burns unit. Occlusive cutaneous dressings significantly reduce the pain. Ophthalmological assessment and oral hygiene are necessary. Specific medical treatment with steroids or ciclosporin is controversial. Intravenous immunoglobulin may be beneficial if given early in the disease.

A variant exists called *Stevens-Johnson syndrome* where the damage is restricted to the mucosal surfaces with milder bullous involvement of the skin.

Anticonvulsant hypersensitivity syndrome is characterized by a generalized mucocutaneous rash, fever and lymphadenopathy with variable arthralgia, pharyngitis, periorbital oedema and hepatosplenomegaly. Rarely pustulation of the skin and conjunctivitis are present. The blood may show a peripheral eosinophilia, lymphocytosis with atypical lymphocytes, and a hepatic picture. It can progress to multiorgan failure. This reaction occurs typically 3-4 weeks into therapy. It can occur with any of the aromatic anticonvulsants (carbamazepine, phenytoin, phenobarbital, primidone and clonazepam). As they often cross-react, all these drugs must be avoided in the future. Sodium valproate is a suitable alternative. There is also potential for cross-reaction with the newer anticonvulsants vigabatrin and lamotrigine.

FURTHER READING

- Baba M et al. (2003) The anticonvulsant hypersensitivity syndrome. *Journal of the European Academy of Dermatology and Venereology* 17: 399-401.
- Breathnach SM (2002) Adverse cutaneous reactions to drugs. *Clinical Medicine* 2:15-19.
- Campione E et al. (2003) High-dose intravenous immunoglobulin for severe drug reactions: efficacy in toxic epidermal necrolysis. *Acta Dermato-venereologica* 83: 430-432.
- Fiszenson-Albala F et al. (2003) A 6-month prospective survey of cutaneous drug reactions in a hospital setting. *British Journal of Dermatology* 149:1018-1022.
- Sullivan et al. (2001) The drug hypersensitivity syndrome. *Archives of Dermatology* 137: 357-364.

DISORDERS OF NAILS

Psoriasis and *iunga nati* infection are the causes of nail dystrophy and are discussed on pages 1333 and 1323.

- *Nail pitting* can be caused by psoriasis, alopecia areata and atopic eczema. A few pits can be present because of trauma.
- i *Onycholysis* (distal nail plate separation) is caused by psoriasis, thyrotoxicosis, following trauma and rarely due to a photosensitive reaction to drugs such as tetracyclines.
- *Koilonychia* (thin spoon-shaped nails) can be caused by iron deficiency anaemia or rarely is congenital.
- *Leuconychia* (white nails) is seen in hypoalbuminaemia. A striate congenital leuconychia exists.
- *Beau's lines* (transverse lines) appear as solitary depressions which grow out slowly over many months. They arise due to a severe illness or shock which causes a temporary arrest in nail growth.
- *Yellow-nail syndrome* is a rare disorder of lymphatic drainage. It presents with thickened, slow-growing, yellow nails with associated pleural effusions, bronchiectasis and lymphoedema of the legs.
- *Onychogryphosis* is a gross thickening of the nail which is seen in later life especially in the big toe-nail. There is often a history of preceding trauma. Both psoriasis and fungal infection can also cause nail thickening.
- *Nail—patella syndrome* is an autosomal dominant condition which presents with triangular rather than half-moon-shaped lunulae, especially of the thumb and forefingers. The nail plates may be small or dystrophic. The patellae are hypoplastic or absent. Other skeletal anomalies can be present and renal impairment (glomerulonephritis) occurs in up to 30% of individuals.
- *Melanonychia* (longitudinal brown streaks) are seen as a normal variant in black-skinned patients. In a white patient it may reflect an underlying subungual melanoma, especially if the pigmentation progresses proximally onto the nail fold ('Hutchinson's sign').
- *Clubbing* is discussed on page 884.

FURTHER READING

Baran R, Dawber RPR (eds.) (2001) *Diseases of the Nails and their Management*, 3rd edn. Oxford: Blackwell Scientific Publications.

DISORDERS OF HAIR

HAIR LOSS

Hair loss can be due to a disorder of the hair follicle in which the scalp skin looks normal (non-scarring alopecia) or due to a disorder within the scalp skin that causes permanent loss of the follicle (scarring or cicatricial alopecia). This latter form causes shiny atrophic bald areas in the scalp which are devoid of follicular openings. There are many causes of alopecia (Table 23.15).

Androgenic alopecia

Androgenic alopecia (male pattern baldness) is the most common type of non-scarring hair loss and depends on

Table 23.15 Causes of alopecia

Scarring alopecia	Non-scarring alopecia
Discoid lupus erythematosus	Androgenic alopecia
(tinea capitis)	effluvium Alopecia areata
planus	Trichotillomania
X-irradiation	(self-induced hair-pulling)
Idiopathic	capitis Tinea capitis
'pseudopelade')	Traction alopecia
	Metabolic (iron deficiency, hypothyroidism)
	Drug (e.g. heparin, isotretinoin, chemotherapy)

genetic factors and an abnormal sensitivity to androgens. It presents in young men with frontal receding followed by thinning of the crown and there is often a positive family history. It also occurs in females but tends to occur at a later age, be milder and show little in the way of frontal recession. If acne and menstrual disturbance are also present, polycystic ovary syndrome and other endocrine disorders of androgens can be present.

Treatment. This may not be required. Topical 5% minoxidil lotion or oral finasteride (1 mg daily) can help arrest progression and may cause a small amount of regrowth, providing it is used early in disease but the treatment needs to be continued possibly lifelong. Approximately one-third of patients will not respond to either therapy. Finasteride is a selective inhibitor of 5 α -reductase type II and it can cause side-effects in 1% of patients such as loss of libido. It should not be used in females as it can affect the sexual development of a male fetus. However, antiandrogen therapy (e.g. cyproterone acetate or spironolactone) helps some women.

Alopecia areata

Alopecia areata is an immune-mediated type of hair loss. It is associated with other organ-specific autoimmune diseases. It presents in childhood or young adults with patches of baldness. These may regrow to be followed by new patches of hair loss. The presence of broken exclamation mark hairs (narrow at the scalp/wider and more pigmented at the tip) at the edge of a bald area is diagnostic. Regrowth may initially be with white hairs and often occurs slowly over months. Occasionally all of the scalp hair is lost (alopecia totalis) and rarely all body hair is lost (alopecia universalis). The nails may be pitted or roughened.

Treatment has no effect on the long-term progression. Potent topical or injected steroids are of limited use. Topical immunotherapy with diphencyprone, PUVA or topical 5% minoxidil are occasionally tried but often do

not help. Wigs can be provided for severe cases and patient support groups are often beneficial.

Traction alopecia

This refers to the 'mechanical damage' type of hair loss that arises from pulling the hair back into a bun or tight plaiting. It is more common in black Africans.

Telogen effluvium

Telogen effluvium refers to the pattern of diffuse hair loss that occurs some 3 months after pregnancy or a severe illness. It occurs because 'stress' puts all the hairs into the telogen phase of hair shedding at the same time. The hair fully recovers and the normal staggered hair growth/hair shedding cycle resumes within a few months.

Dissecting cellulitis

This is a chronic folliculitis affecting predominantly young black males. It presents with papules and pustules over the occipital region of the scalp with hair loss. If severe, the back of the scalp becomes a boggy swelling (discharging pus) with areas of scarring alopecia. It can be complicated by keloid scar formation ('acne keloidalis nuchae').

Treatment is difficult but prolonged courses of low-dose antibiotics are worth trying in early disease. Prolonged courses of isotretinoin can help a few individuals and deep surgical excision can be used in recalcitrant cases.

INCREASED HAIR_GROWTH

Hirsutism (p. 1058)

Hirsutism refers to the male pattern of hair growth seen in females. The racial variation in hair growth must be considered. Certain races (e.g. Mediterranean and Asian) have more male pattern hair growth than northern European females. This is not due to excess androgens but may reflect a genetically determined altered sensitivity to them. If virilizing features (deep voice, clitoromegaly, dysmenorrhoea, acne) are present, one should carry out a full endocrine assessment. Hirsutism can cause severe psychological distress to some individuals.

Treatment involves physical methods such as bleaching, waxing, electrolysis and laser therapy. Antiandrogen therapy is occasionally helpful.

Hypertrichosis

Hypertrichosis refers to the state of excessive hair growth at any site and occurs in both sexes. It can be seen in anorexia nervosa, porphyria cutanea tarda, and underlying malignancy and is caused by certain drugs (e.g. ciclosporin, minoxidil).

FURTHER READING

Barth JH (2000) Should men still go bald gracefully? *Lancet* 355: 161-162. MacDonald Hull SP et al. (2003) Guidelines for the management of alopecia areata. *British Journal of Dermatology* 149: 692-699. Price VH (1999) Treatment of hair loss. *New England Journal of Medicine* 341: 964-973. Wendelin DS et al. (2003) Hypertrichosis. *Journal of the American Academy of Dermatology* 48:161-179.

BIRTH MARKS/NEONATAL RASHES

Strawberry naevus (cavernous haemangioma)

Strawberry naevus affects up to 1% of infants. It presents at, or shortly after, birth as a single red lumpy nodule (Fig. 23.40) that grows rapidly for the first few months. Multiple lesions can be present. They will spontaneously resolve with good cosmesis but this may take up to 7 years for complete resolution. Occasionally plastic surgery is needed after resolution to remove residual slack skin. Reassurance of parents is usually all that is required.

Treatment is indicated if:

- the lesion interferes with feeding or vision * !
- the lesion ulcerates or bleeds frequently
- the lesion is associated with high-output cardiac failure from shunting of large volumes of blood
- the lesion consumes platelets and/or clotting factors causing potentially life-threatening haemorrhage ('Kasabach-Merritt syndrome').

The latter two complications are very rare and only tend to occur in large lesions with significant deep vessel involvement.

Treatment modalities include intralesional or oral corticosteroids, surgery (for selected lesions), and tunable



Fig. 23.40 Strawberry naevus (cavernous haemangioma).

dye laser (for treating ulceration). Alpha-interferon injections, vincristine or embolization is only used for life-threatening events.

Port-wine stain (naevus flammeus)

Port-wine stain is also called a capillary haemangioma but strictly speaking it is not a haemangioma but is just an abnormal dilatation of dermal capillaries. It presents at birth as a flat red macular area and is commonly found on the face. It does not improve spontaneously and it may become thickened with time. If the lesion is found in the distribution of the first division of the trigeminal nerve it may be associated with ipsilateral meningeal vascular anomalies which can cause epilepsy and even hemiplegia (Sturge-Weber syndrome, p. 1257). If a port-wine stain involves the skin near the eye, glaucoma is a risk and ophthalmic assessment is mandatory.

Treatment of port-wine stains is ideally carried out with the tunable dye laser.

Milia

'Milk spots' are small follicular epidermal cysts. They are small pinhead white papules commonly found on the face of infants. They resolve spontaneously.

Mongolian blue spot

This appears in infants as a deep blue-grey bruise-like area, usually over the sacrum or back, and is occasionally mistaken as a sign of child abuse. It is due to deep dermal melanocytes. It is very common in Oriental children, less common in black Africans and rare in Caucasians. It has usually disappeared by the age of 7 years.

Toxic erythema of the newborn (erythema neonatorum)

Toxic erythema of the newborn is a term used to describe a common transient blotchy maculopapular rash in newborns. The rash is occasionally pustular but the child is not toxic or unwell. It disappears within a few days, spontaneously.

Nappy rash ('diaper dermatitis')

This is an irritant eczema caused by occlusion of faeces and urine against the skin. It is almost universal in babies. The flexures are usually spared, which is a useful differentiating feature from seborrhoeic and atopic eczema. If satellite lesions are present around the edge, it may indicate a superimposed *Candida* infection. This rash can also occur in the elderly incontinent.

Treatment involves frequent changing of the nappy and regular application of a barrier cream.

Acrodermatitis enteropathica (p. 249)

This is due to a rare inherited deficiency of zinc absorption. It presents 4-6 weeks after weaning, or earlier in bottle-fed babies. There is an erythematous, sometimes blistering, rash around the perineum, mouth, hands and feet. It may be associated with photophobia, diarrhoea and alopecia.

Treatment is with lifelong oral zinc, which seems to override the poor absorption. The response is rapid.

FURTHER READING

Bruckner AL et al. (2003) Hemangiomas of infancy. *Journal of the American Academy of Dermatology* 48: 477-493. Harper J, Oranje A, Prose N (eds) (2000) *Textbook of Pediatric Dermatology*. Oxford: Blackwell Scientific.

HUMAN IMMUNODEFICIENCY VIRUS AND THE SKIN (p 34)

HIV infection commonly causes significant dermatological problems. A rash may even be the presenting feature of underlying HIV infection. It is estimated that 90% of HIV-positive patients will suffer with a mucocutaneous disorder during the illness. It is also estimated that up to 30% of people with AIDS will suffer from three different dermatoses. These rashes can often be clinically atypical and difficult to diagnose. One must have a low threshold for skin biopsy and skin culture. On top of this many of the skin problems are resistant to standard treatments. Most of these dermatoses have become less prevalent since the advent of HAART (p. 144).

Cutaneous infection and opportunistic infection

Not surprisingly, infections are increased because of the HIV-induced immune deficiency. Molluscum contagiosum are particularly common especially on the face. They are often multiple and of a 'giant' size measuring over 1 cm across. Molluscum are rarely seen in adults and they can be the presenting feature of HIV. Other viral infections such as extensive ulcerative herpes or widespread viral warts may be seen. Bacterial infections (e.g. staphylococcal boils) and fungal infections (e.g. ringworm and *Candida*) are also common. Recalcitrant and recurrent oropharyngeal candidiasis is a particular problem.

Opportunistic infections such as cutaneous cytomegalovirus (pustules or necrotic ulcers), sporotrichosis (linear nodules) or cryptococcus (red papules, psoriasiform or molluscum-like lesions) can pose diagnostic difficulties, stressing the need for skin biopsy and culture.

Inflammatory dermatoses

Inflammatory dermatoses show an increased incidence with HIV infection, probably due to an immune dys-

function or imbalance rather than as a consequence of immune suppression. Severe, extensive seborrhoeic eczema is very common and may be a presenting sign of HIV. Other types of eczema, psoriasis, ichthyosis (dry scaly skin), nodular prurigo and pruritus are all common in HIV infection and can be very severe. Granuloma annulare and lichen planus are probably increased in incidence. The treatment of these conditions is difficult as oral immunosuppressive therapies (e.g. prednisolone, ciclosporin) are best avoided in patients with low CD4 counts. Topical therapies and phototherapy seem relatively safe. Oral retinoids are useful in the management of psoriasis.

'Autoimmune dermatoses'

Bullous pemphigoid, thrombocytopenic purpura, and vitiligo seem to be increased in incidence. The polyclonal stimulation of B lymphocytes by HIV and the resulting abnormal antibody production may be involved in their aetiology. Erythroderma is sometimes seen in HIV disease where skin biopsy suggests a 'graft-versus-host disease' mechanism. This presumably reflects a severe underlying immune dysfunction of T lymphocyte control.

Drug rashes

Adverse drug rashes are much commoner in HIV patients. Reactions to co-trimoxazole, dapsone and antiretroviral drugs appear particularly common. Drug rashes may be severe (especially with nevirapine) resulting in erythroderma or toxic epidermal necrolysis. Other unusual rashes include a striking nail/mucosal pigmentation from zidovudine, paronychia from indinavir and facial lipodystrophy mostly from protease inhibitors.

Cutaneous tumours

Kaposi's sarcoma (p. 142) is much commoner in homosexuals with HIV than in other groups. Basal and squamous cell carcinomas and benign melanocytic naevi are also a little increased in incidence, presumably reflecting a loss of immune surveillance.

'Specific' HIV dermatoses

'Itchy folliculitis' of HIV (also called papular pruritic eruption)

Itchy follicular eruptions are common in HIV as CD4 counts decline. The previously described staphylococcal folliculitis, eosinophilic folliculitis, pityrosporum folliculitis, and demodex mite folliculitis are probably all part of a spectrum and the term itchy folliculitis is useful to encompass these. It presents with intensely itchy papules centred on hair follicles and occurring most commonly over the upper trunk and upper arms. The face is more commonly involved in black patients. Individual lesions frequently have the top scratched off, leaving a crateriform appearance. The aetiology is unknown but

may reflect a hypersensitivity reaction as high IgE and eosinophil counts may be present.

Treatment with oral minocycline, potent topical steroids and emollients may help. Phototherapy or oral isotretinoin is useful in resistant cases.

Oral hairy leucoplakia

This is characterized by white plaques with vertical ridging on the sides of the tongue. Unlike with oral *Candida*, the lesions cannot be peeled off to leave raw areas underneath. It was first recognized in HIV disease but can rarely occur in other forms of immunosuppression. It is thought to be due to co-infection with Epstein-Barr virus.

Treatment with aciclovir, ganciclovir or foscarnet may help.

FURTHER READING

Osborne GE et al. (2003) The management of HIV-related skin disease. Part I: infections. *International Journal of STD & AIDS* 14: 78-86.

Osborne GE et al (2003) The management of HIV-related skin disease. Part II: neoplasms and inflammatory disorders. *International Journal of STD & AIDS* 14: 235-240.

DERMATOSES OF PREGNANCY

There are a number of minor skin changes during pregnancy. There is an increase in spider naevi, melanocytic naevi, skin tags and chloasma. The abdomen shows mid-line pigmentation (linea nigra) and striae (stretch marks). There are four less common skin problems associated with pregnancy.

Polymorphic eruption of pregnancy (PEP)

This rash tends to appear in the last trimester of a first pregnancy in 1 in 160 cases. It is of unknown aetiology and recurs only rarely in subsequent pregnancies. It presents with very itchy urticated papules and plaques and occasionally small vesicles. Lesions usually start on the abdomen and striae but may spread to the upper arms and thighs. The umbilicus may be spared. PEP is commoner in twin pregnancies. The rash is not associated with any maternal or fetal risk. PEP has been shown to be associated with low maternal serum cortisol levels.

Treatment is with reassurance, bland emollients and mild topical steroids. The rash disappears after childbirth.

Prurigo of pregnancy

This affects 1 in 300 pregnancies. It usually starts on the abdomen in the third trimester but may persist for some months after delivery. Clustered excoriated papules

Skin disease

(prurigo-like lesions) occur on the abdomen and extensor surfaces of the limbs. The cause is unknown but pregnancy-related itch (pruritus gravidarum) may be due to cholestasis (p. 393). Rarely liver function tests are abnormal and urinary HCG levels may be elevated. It can recur in subsequent pregnancies. Some authors believe the condition is associated with an increase in fetal mortality but this remains controversial.

Treatment is with topical steroids and oral antihistamines.

Pruritic folliculitis of pregnancy

This occurs in the second or third trimester of pregnancy and is characterized by an itchy folliculitis which looks similar to steroid-induced 'acne'. It is not associated with any increased maternal or fetal risk.

Treatment with topical benzoyl peroxide and hydrocortisone cream help relieve symptoms.

Pemphigoid gestationis (herpes gestationis)

This is the rarest of the pregnancy-related rashes (1 in 60 000). The immune changes of pregnancy appear to set off bullous pemphigoid. It is characterized by an itchy blistering urticated eruption starting on the abdomen but may become widespread. Large bullae may be present. Unlike PEP it can occur early, starting in the second or even first trimester of pregnancy, and the umbilicus is often involved. It tends to recur in subsequent pregnancies and at an earlier stage. Diagnosis is confirmed by immunofluorescence studies.

A transient bullous eruption occurs in 5% of infants, presumably owing to transplacental passage of the offending antibody. There is no increase in fetal mortality but there is an increased incidence of prematurity and low birth weight, which is probably due to the autoantibody causing placental insufficiency. Therefore, it seems sensible to keep such pregnancies closely monitored and to advise on hospital rather than home delivery.

Treatment of mild cases may be with potent topical steroids but most cases will require oral corticosteroids. The steroid dose may need to be increased after delivery as there is often a postpartum flare-up of the disease. The rash can be set off again by the oral contraceptive pill and this should be avoided.

FURTHER READING

Kroumpouzou G et al. (2001) Dermatoses of pregnancy. *Journal of the American Academy of Dermatology* 45: 1-19.

PRINCIPLES OF TOPICAL THERAPY

Dermatology is unique in having such direct accessibility

to the affected organ. This allows the use of topical treatments, which can avoid certain systemic side-effects. A topical therapy consists of an *active ingredient*, an appropriate *vehicle* or *base* to deliver this, and often a *preservative* or *stabilizer* to maintain the product's shelf-life. Cosmetically acceptable products need to be found and patients should be instructed about their correct usage. Without this, compliance tends to be poor. Perfumed or scented products should be avoided.

Bases and their uses

Creams

These are a semisolid mixture of oil and water held together by an emulsifying agent. They need to have added preservatives such as parabens. They are 'lighter' and rub in more easily than ointments. They have a high cosmetic acceptability and are useful for topical treatments of the face and hands. Aqueous cream is particularly useful as a soap substitute.

Ointments

These are semisolid and contain no water, being based usually on oils or greases such as polyethylene glycol (water soluble) or paraffin (fatty). They feel greasy or sticky to the touch. They are the best treatment for dry, flaky skin disorders as they are good at hydrating the stratum corneum and they deliver an active ingredient (e.g. a steroid) more effectively.

If patients dislike the greasy nature of ointments, a cream is better than no treatment at all, but creams are less effective and do have to be used more frequently. A compromise may be to use a cream on the face and an ointment elsewhere (Table 23.16).

Lotions

These are based on a liquid vehicle such as water or alcohol. They are usually volatile and rapid evaporation promotes a cooling effect on the skin. They are useful for weeping skin conditions and are ideal for use on hairy skin (e.g. the scalp). The cooling effect can be a useful antipruritic. Alcohol-based lotions should be avoided on broken skin as they cause stinging.

Gels

These are semisolid preparations of high molecular weight polymers. They are non-greasy and liquefy on contact with the skin. They are useful for treating hairy skin (e.g. the scalp).

Table 23.16 Emollients commonly used in the UK

Greasy emollients	Lighter creams
Diprobase ointment*	E45 cream*
Oily cream	Diprobase cream*
Unguentum Merck* 50 : 50 white soft paraffin/liquid paraffin	Aveeno cream*
	Aqueous cream

*Trade names

Pastes

Pastes contain a high percentage (> 40%) of powder in an ointment base. They are thick and stiff and difficult to remove from the skin. They are useful when a treatment needs to be applied precisely to a skin lesion without it smearing on to surrounding normal skin. An example would be dithranol in Lassar's paste (used on plaques of psoriasis) as dithranol will burn the surrounding normal skin.

Safety of topical steroids

Providing that preparations of appropriate strength are used for the body site being treated, these compounds can be used safely on a long-term intermittent basis (p. 1328). If potent steroids are misused they will cause skin atrophy manifest as striae, wrinkling, fragility and telangiectasia.

Problems with topical therapies

- *Systemic absorption* may occur but only if very large areas of inflamed skin are treated topically and

especially if the treatment is occluded with bandages or polyurethane films. Neonates are particularly susceptible to this owing to the relative increase in body surface area to volume.

Contact allergy to topical preparations is not uncommon and may be suspected by unusually resistant disease or by apparent worsening of a condition after application of a substance. It is more common with creams as it often the result of allergy to the preservative or emulsifying agent. Allergy can also be due to the active ingredient itself (e.g. neomycin or hydrocortisone).

Folliculitis can occur because of blockage of hair follicles. Creams and ointments should be applied to the skin in the same direction as hair growth to try to prevent this blockage. It is a particular problem with the use of ointments in hot weather (especially if under occlusive bandages) and a lighter cream may be more appropriate at this time.

CHAPTER BIBLIOGRAPHY

- Champion RH, Burton JL, Ebling FJG (eds) (1998) *Textbook of Dermatology*, 6th edn. Oxford: Blackwell Scientific.
- Harper J, Oranje A, Prose N (eds) (2000) *Textbook of Pediatric Dermatology*. Oxford: Blackwell Scientific.

- Omary MB, Coulombe PA, Mclean I (2004) Mechanisms of disease: intermediate filament proteins and their associated diseases. *New England Journal of Medicine* **351**: 2087-100.
- Weedon D (ed) (2002) *Skin Pathology*, 2nd edn. Edinburgh: Churchill Livingstone.

UK PATIENT SUPPORT GROUPS (for full list see

- <http://www.bad.org.uk/patientsindex.htm>
British Association of Skin Camouflage: c/o Resources for Business, South Park Road, Macclesfield SKU 6SH DEBRA (Dystrophic Epidermolysis Bullosa Research Association): DEBRA House, 13 Wellington Business Park, Duke's Ride, Crowthorne, Berkshire RG11 6LS

- Hairline International: 1668 High Street, Knowle, West Midlands B93 0LY National Eczema Society: Hill House, Highgate Hill, London N19 5NA Psoriasis Association: Milton House, 7 Milton Street, Northampton NN2 7JG Vitiligo Society: 125 Kennington Road, London SE11 6SF

SIGNIFICANT WEBSITES

- <http://www.bad.org.uk>
British Association of Dermatologists
- <http://www.aad.org/MedWebGuide.html>
American Academy of Dermatology web guide
- <http://tray.dermatology.uiowa.edu/Dermlmag.htm>
Dermatologic image database (adult)
- <http://www.usc.edu/hsc/nml/e-resources/info/dermis.html> *Dermatologic image database (paediatric)*
- <http://www.eczema.org>
UK National Eczema Society (atopic eczema)
- <http://www.paalliance.org>
Psoriatic Athroathy Alliance (psoriasis)

- <http://www.skin-camouflage.net>
British Association of Skin Camouflage
- <http://www.debra.org.uk>
Dystrophic Epidermolysis Bullosa Association
- <http://www.hairlineinternational.co.uk>
Hairline International
- <http://tray.dermatology.uiowa.edu/Dermimag.htm>
Dermatology images (atlas)
- <http://www.usc.edu/hsc/nml/index.html>
Dermatology images (atlas)
- <http://www.psoriasis-association.org.uk>
Psoriasis Association
- <http://www.vitiligosociety.org.uk>
Vitiligo Society