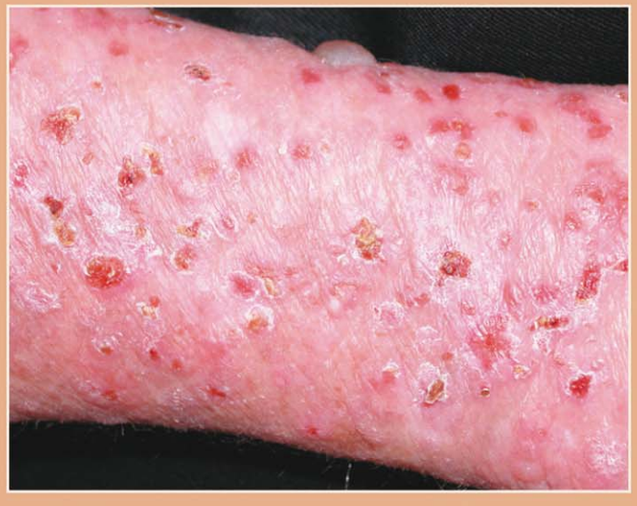
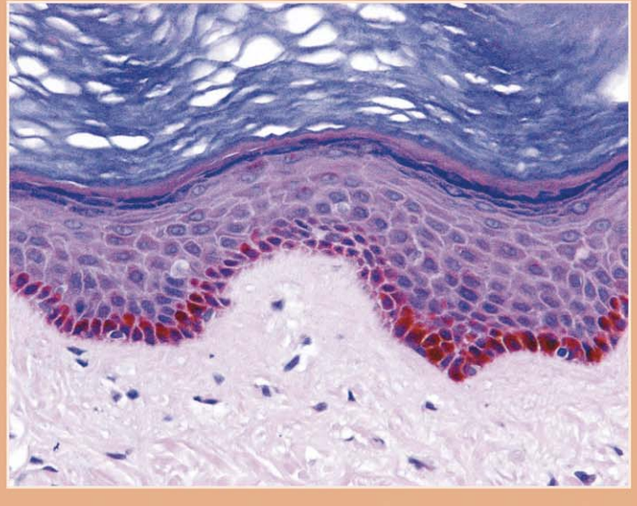
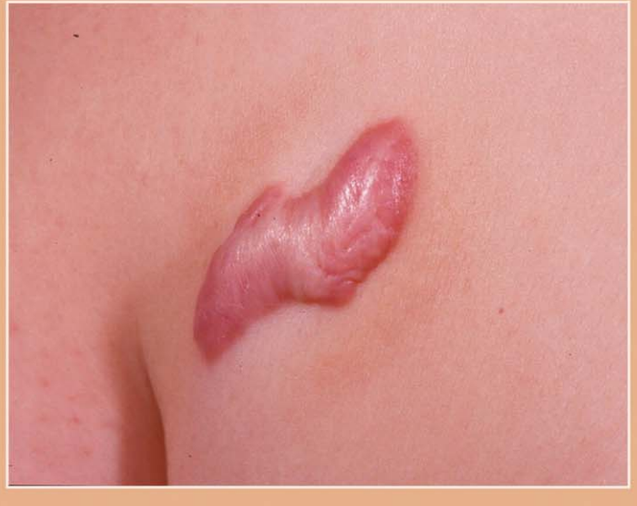
An Atlas of Diagnosis and Management

GENERAL DERMATOLOGY

John SC English







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Preface

Dermatology is about diagnosis, as without the correct diagnosis the patient cannot be managed well. In medicine, treatments are often administered empirically, especially where there is uncertainty over the diagnosis. If one knows what the condition is then one can give the best treatment and an accurate prognosis. In this book we have tried to facilitate the process of making a diagnosis and formulating a differential diagnosis in dermatology patients. It is aimed primarily at dermatology naive practitioners and students, whether they be GPs, medical students, hospital doctors, specialist nurses or community pharmacists. Nevertheless, experienced practitioners will find much here to refresh their memory; for all health professionals, we hope this book will help them make the correct diagnosis and so be able to offer the best possible course of management.

John SC English

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I thank Drs Andrew Affleck, Ruth Murphy, Kate Dalziel, and Roger Allen for providing illustrations where needed. My thanks also to all the chapter authors for their individual contributions.

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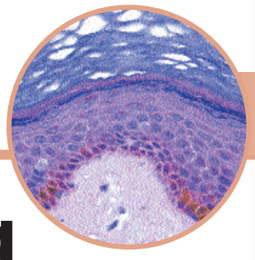
Abbreviations

ABPI ankle brachial pressure index
ACD allergic contact dermatitis
ACE angiotensin-converting enzyme
ALA-based PDT 5-aminolaevulinic acid-based photodynamic therapy
BCC basal cell carcinoma
CIN cervical intraepithelial neoplasia
CMN congenital melanocytic naevus
CT computed tomography
CYP cytochrome P
DLE discoid lupus erythematosus
DLSO distal and lateral subungual onychomycosis
DSAP disseminated superficial actinic porokeratosis
DVT deep vein thrombosis
EM erythema multiforme
GST glutathione S-transferase
HPV human papilloma virus
HSP Henoch–Schönlein purpura
HSV herpes simplex virus
ICD irritant contact dermatitis
IEC intraepithelial carcinoma
JPD Juvenile plantar dermatosis
KID keratosis, ichthyosis, deafness
LE lupus erythematosus
LP lichen planus
LS lichen sclerosis
MRI magnetic resonance imaging
NMSC nonmelanoma skin cancers
PCR polymerase chain reaction
PIN penile intraepithelial neoplasia
PUVA ultraviolet A light with psoralen
PV pityriasis versicolor
SCC squamous cell carcinoma
SCLE subacute cutaneous lupus erythematosus
SLE systemic lupus erythematosus
SSSS staphylococcal scalded skin syndrome
UVB ultraviolet B
VIN vulval intraepithelial neoplasia



Introduction to diagnosing dermatological conditions (basic principles)

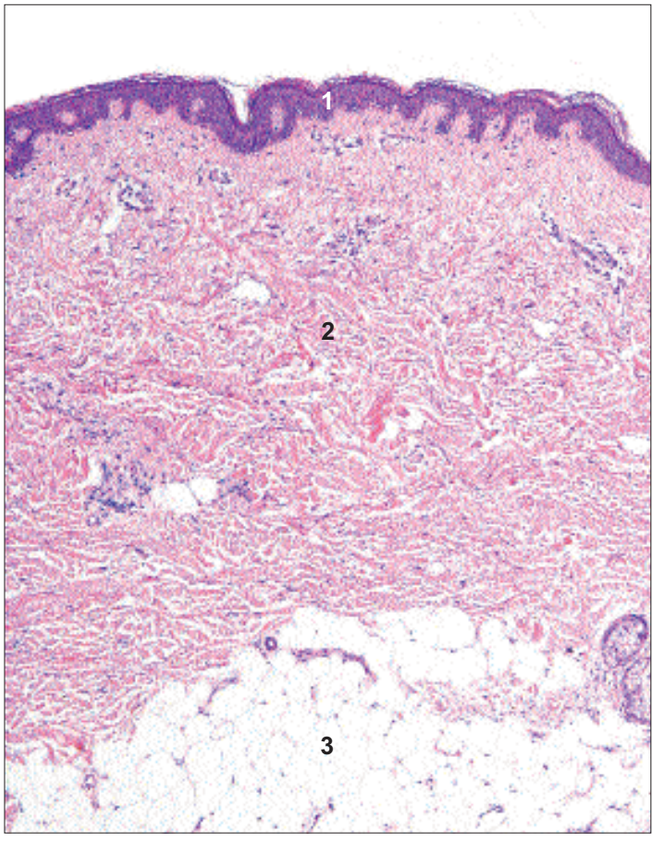
G Whitlock PhD, MRCP, John SC English FRCP, and Iain H Leach MD, FRCPath

Essentials of cutaneous anatomy and physiology

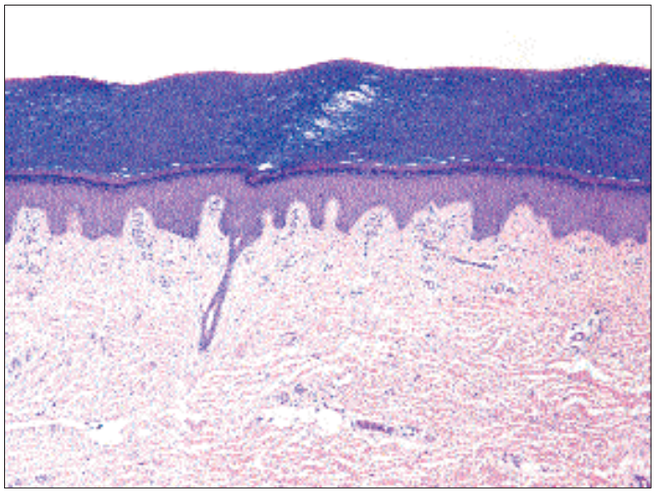
The skin is a large and specialized organ, which covers the entire external surface of the body. It plays an important role in protecting the body against external traumas and injurious agents such as infection, trauma, UV radiation, and extremes of temperature as well as providing waterproofing. Additional functions include detection of sensory stimuli and thermoregulation.

The skin has two main layers, the superficial epidermis and the dermis, which lies between the epidermis and subcutaneous fat (**1.1**). The microanatomy of the skin is essentially similar throughout, but there is considerable regional variation. For example, the surface keratin layer is much thicker on the palms and soles (**1.2**) than elsewhere, whilst the dermis is much thicker on the back than on the eyelids. There is also considerable regional variation in the numbers and size of skin appendages such as hair follicles, sebaceous glands, and sweat glands.

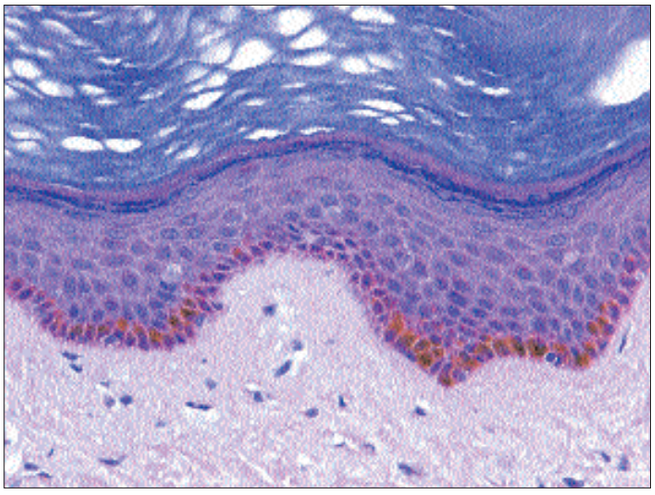
The epidermis is the surface layer of the skin and is a keratinizing stratified squamous epithelium, the principle cell type being the keratinocyte. The basal layer of the epidermis contains small cuboidal cells that continually divide to replenish the cells lost from the skin surface. The bulk of the epidermis is composed of the stratum spinosum or 'prickle cell' layer, so called because the intercellular connections or desmosomes are visible on histological sections as prickles surrounding each cell. The cells in this layer are large with abundant cytoplasm containing keratin tonofilaments. With maturation towards the surface the cells become flatter and accumulate dark keratohyalin granules to form the granular layer. These cells then lose their nuclei and the keratohyalin granules, and keratin filaments



1.1 Normal skin: epidermis (1), dermis (2). and subcutis (fat) (3) (H&E x4).



1.2 Acral skin (H&E x4).



1.3 Racially pigmented skin (H&E x20).

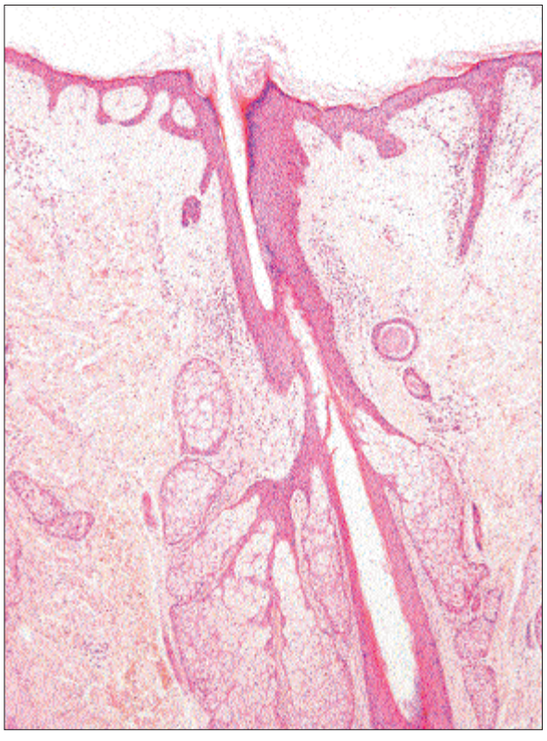
combine to form the surface keratin layer. Epidermal turnover is continuous throughout life, with the turnover time from basal cell to desquamation estimated at 30–50 days depending on site.

The epidermis also contains small numbers of melanocytes, Langerhans cells, and Merkel cells. Melanocytes are present scattered along the basal epidermis. They have long dendritic cytoplasmic processes, which ramify between basal keratinocytes. Melanocytes synthesize melanin pigment that is passed to basal keratinocytes via the dendritic processes in the form of granules or melanosomes. Melanin pigment varies in colour from red/yellow to brown/black. It is responsible for skin pigmentation and has an important role in protecting the skin from the effects of UV radiation. There is some regional variation in the number of melanocytes, with more being present on sun-exposed sites though the number is fairly constant between individuals. Racial skin pigmentation is related to increased activity and increased amounts of pigment rather than increased numbers of melanocytes (**1.3**).

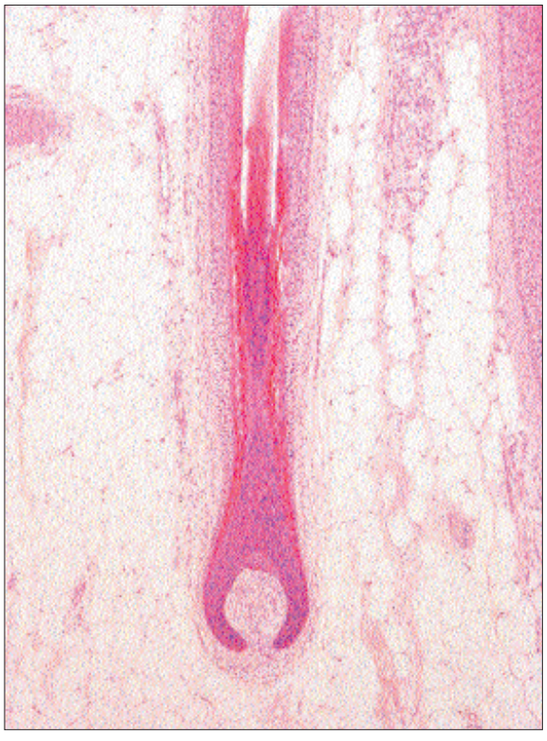
Langerhans cells are also dendritic cells and are located in the basal epidermis and stratum spinosum. They act as antigen presenting cells and are an important part of the immune system. Small numbers are present in normal skin, but numbers are increased in some inflammatory skin diseases, such as contact dermatitis. There are two types of allergic reaction in the skin: immediate reactions causing contact urticaria (hay fever is an immediate allergic reaction of the nasal mucosa), and delayed allergic reactions. This manifests as allergic contact dermatitis such as reactions from prolonged contact of nickel-containing metals with the skin. Merkel cells are difficult to visualize in routine histological sections but can be identified with special stains. Their precise function is not clear but they are thought to play a role in touch sensation. They can give rise to Merkel cell carcinoma, a rare aggressive malignant tumour most often seen in the elderly.

The dermis lies beneath the epidermis and is essentially fibrous connective tissue. The papillary dermis is a thin superficial layer containing fine collagen and elastic fibres, capillaries, and anchoring fibrils which help attach the epidermis to the dermis. The bulk of the dermis is formed by the reticular dermis which is mainly composed of thick collagen fibres and thinner elastic fibres. The collagen fibres provide much of the substance and tensile strength of the dermis, whilst elastic fibres provide the skin with elasticity. Small numbers of lymphocytes, macrophages, mast cells, and fibroblasts are present in the dermis together with blood vessels, lymphatic vessels, nerves, pressure receptors, and the skin appendages. The junction between the epidermis and dermis is not flat but has a complex three dimensional arrangement of downgrowths from the epidermis (rete ridges) and upgrowths from the papillary dermis (dermal papillae). This arrangement increases the surface area of the dermo-epidermal junction and enhances adhesion between the two layers.

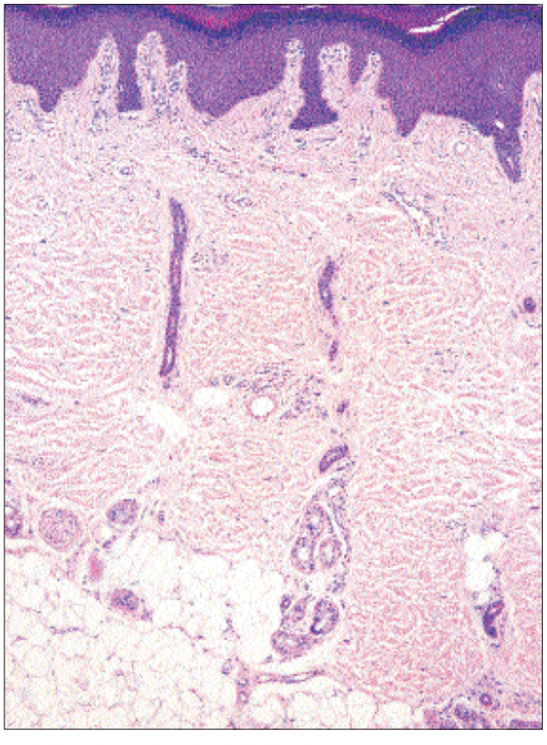
The skin appendages comprise the hair follicles with their attached sebaceous glands, the eccrine sweat glands and the apocrine glands (**1.4**–**1.7**). Hair follicles are widely distributed but are not present on the palms and soles. They



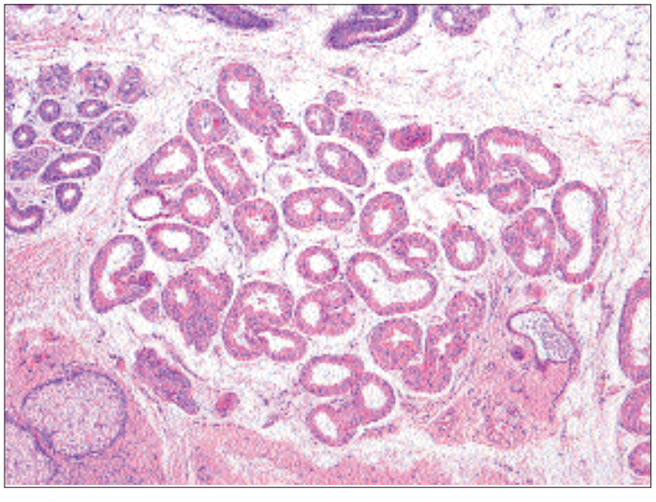
1.4 Pilo-sebaceous unit (H&E x4).



1.5 Hair bulb (H&E x4).



1.6 Eccrine glands (H&E x4).



1.7 Apocrine glands (H&E x4).

vary considerably in size from the large follicles of the scalp and male beard area to the more widespread small vellus follicles, present on the female face for example. The hair follicle is a tubular epithelial structure, which opens onto the skin surface and is responsible for producing hairs. The deepest part of the follicle, the hair bulb, is situated in the dermis or subcutaneous fat. The germinal matrix of the bulb consists of actively dividing cells that give rise to the hair shaft and inner root sheath. Keratinization of the epithelial cells occurs without keratohyalin and with no granular layer; this produces 'hard' keratin as opposed to the 'soft' keratin of the epidermis, which is produced with keratohyalin. The outer root sheath of the follicle is derived from a downgrowth of the epidermis. Melanocytes in the hair bulb produce melanin pigment, which is incorporated into the hair shaft and is responsible for hair colouration.

Hair follicle growth is cyclical with an active growth phase (anagen phase), which is followed by an involutional phase (catagen), and a resting phase (telogen) during which time hairs are shed. The anagen phase (during which time hairs are growing) lasts for at least 3 years, catagen lasts for approximately 3 weeks, and telogen 3 months. At any one time the majority of hair follicles (>80%) are in anagen phase, 1–2% are in catagen, and the remainder are in telogen phase.

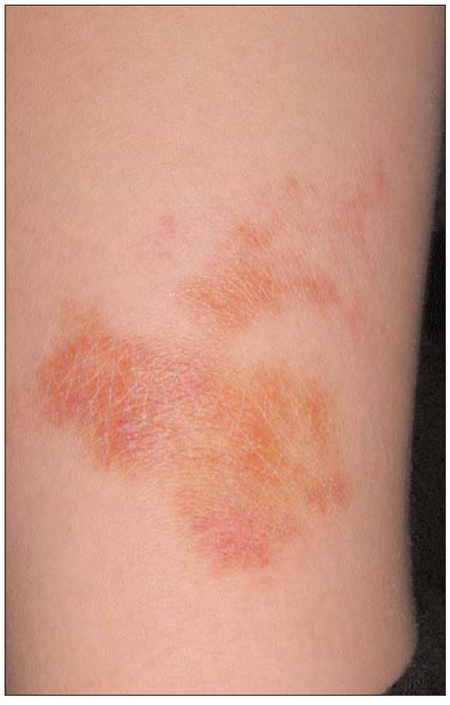
Sebaceous glands are normally associated with and attached to a hair follicle (**1.4**). They are widespread but are particularly large and numerous on the central face and are absent from the palms and soles. Sebaceous glands are largely inactive before puberty but subsequently enlarge and become secretory. The glands are composed of lobules of epithelial cells, the majority of which contain abundant lipid within the cytoplasm and appear clear on histological sections. The lipid-rich secretion, sebum, is formed through necrosis of the epithelial cells and is secreted into the upper portion of the hair follicle. The function of sebum may include waterproofing and protection of the hair shaft and epidermis as well as inhibition of infection. The other main component of the hair follicle is the arrector pili muscle. This is a small bundle of smooth muscle situated in the dermis but attached to the follicle. Contraction of the muscle makes the hair more perpendicular.

Eccrine sweat glands are responsible for the production of sweat and play an important role in temperature control. They are widely distributed and are particularly numerous on the palms and soles, the axillae, and the forehead. The secretory glandular component is situated in deep reticular dermis (**1.6**). The gland is composed of a tubular coil of secretory epithelial cells with an outer layer of contractile myoepithelial cells. Sweat is transported via a duct, which spirals upwards through the dermis to open onto the skin surface. Glandular secretion and sweating are controlled by the autonomic nervous system.

Apocrine glands are histologically similar to eccrine sweat glands but are slightly larger (**1.7**). They are much less widespread and are principally located in the axillae and ano-genital region. Their precise function in man is unclear, though in some other mammals they have an important role in scent production.

History taking

History taking is the first part of a skin consultation. This is no different to any other medical specialty: one seeks to know when the condition started, which part of the body is affected, and how the condition has progressed since presentation. Clues to the diagnosis may come from asking the patient's profession, if other family members or personal contacts are affected, and whether there has been exposure to allergens or irritants. Particular attention should be afforded to any treatments, both topical or systemic, that have been tried previously and if these have changed the character of the condition. In the past medical history, one considers whether the skin condition is a dermatological manifestation of a systemic disease, if there is a history of atopy (asthma, eczema, or hayfever), and also if the patient has suffered from previous skin complaints. Related to this, it is important to ask about family history of skin disease. Medications themselves can provoke skin eruptions and so a thorough drug history will include current and recent medications as well as any over-the-counter medicines or supplements. Often overlooked is the psychological impact of the skin condition. Changes in the patient's quality of life may be a major factor in the patient consulting the physician in the first place. Through questioning a patient about how the condition affects the patient's life, the physician will be able to assess what in particular is worrying the patient and explore the expectations for the consultation.



1.8 Macules and patches forming an area of lichen aureus on a child's leg. This is a harmless superficial capillaritis of the skin which leaks red cells leaving golden haemosiderin staining of the skin.

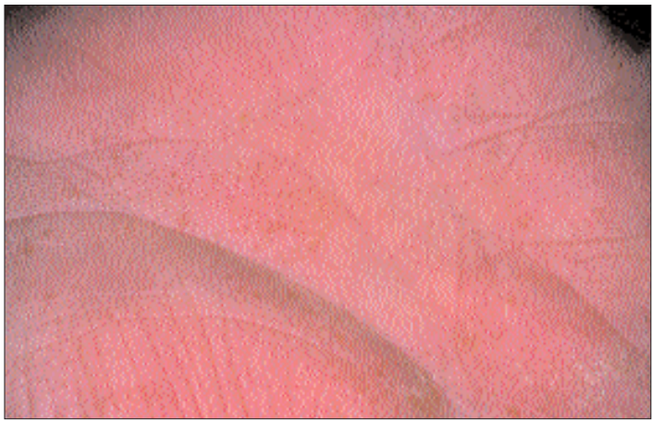
Examination of the skin

Dermatology has its own vocabulary to describe skin lesions. Some of these terms (for example, nodule and plaque) are also used in nonmedical contexts, and special care must be given to their particular meaning in dermatology.

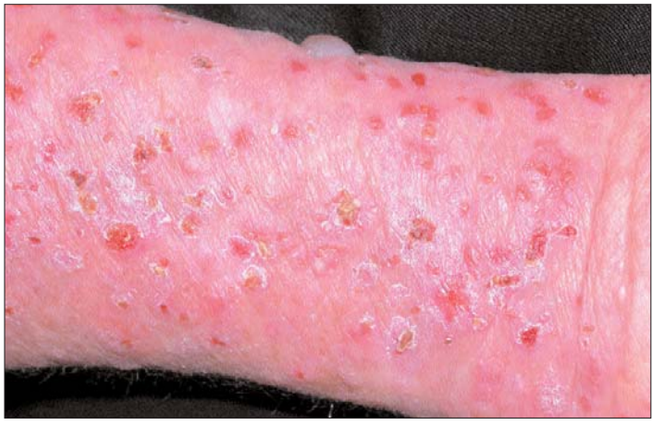
Flat lesions are discolourations of the skin and no change in texture is felt when passing a finger over the affected area. If the diameter of a flat lesion is smaller than 1–2 cm then it is called a macule. A larger flat lesion is known as a patch (**1.8**).

If the lesion is raised above the skin it may be a blister, a collection of free fluid beneath the skin. Again the terms used to refer to blisters depend on their diameter. A small blister is called a vesicle and large one, >0.5 cm in diameter, is a bulla (**1.9**, **1.10**). If a lesion is raised above the skin and contains pus, then it is known as a pustule (**1.11**).

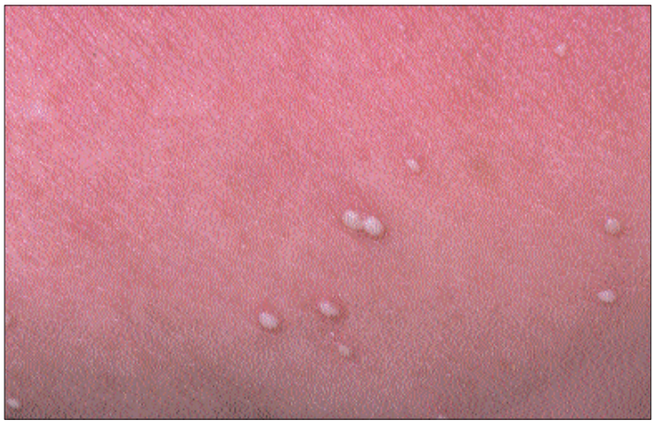
The description of a solid raised lesion, or what would commonly be called a 'lump', also depends on its diameter. A small lesion is referred to as a papule and a large lesion, >0.5 cm in diameter, as a nodule (**1.12**–**1.14**). However, some dermatologists distinguish between the two terms, with a nodule meaning a lesion that has a firmer consistency than a papule. Plaque is used for a raised lesion of large diameter (>2–3 cm) that is characteristically flat topped and often oval or disc shaped (**1.15**).



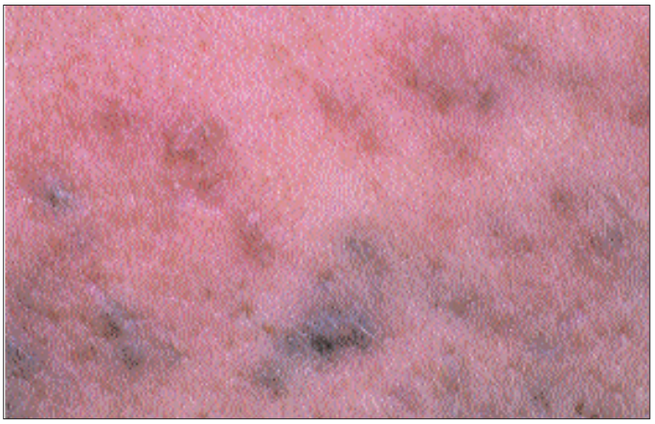
1.9 Vesicular hand eczema of the palms in a patient allergic to Compositae plants (see Chapter 5).



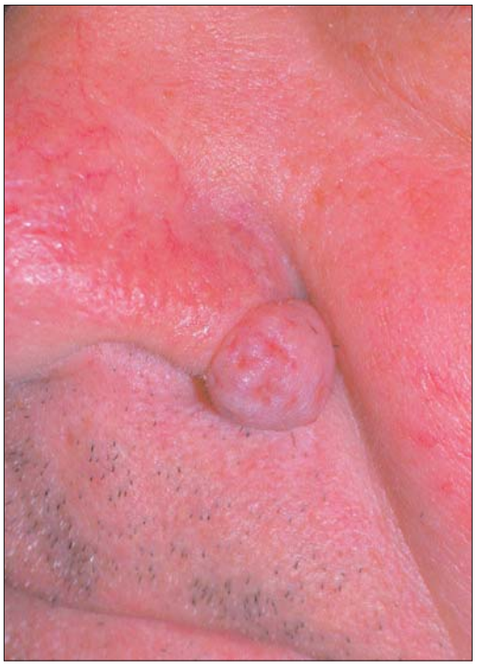
1.10 Vesicles and a bulla in a patient with bullous pemphigoid.



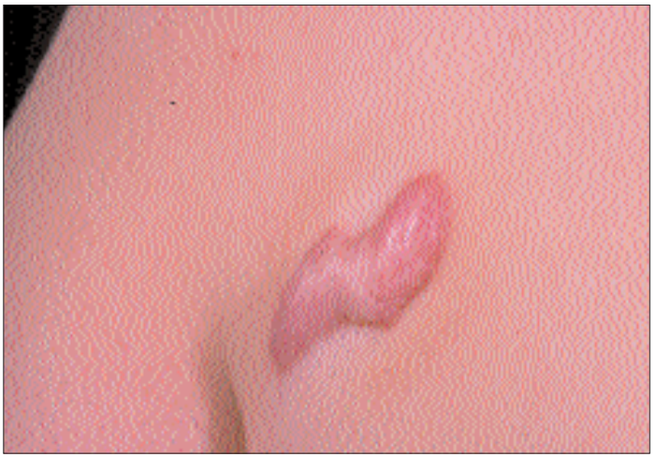
1.11 Pustular drug eruption.



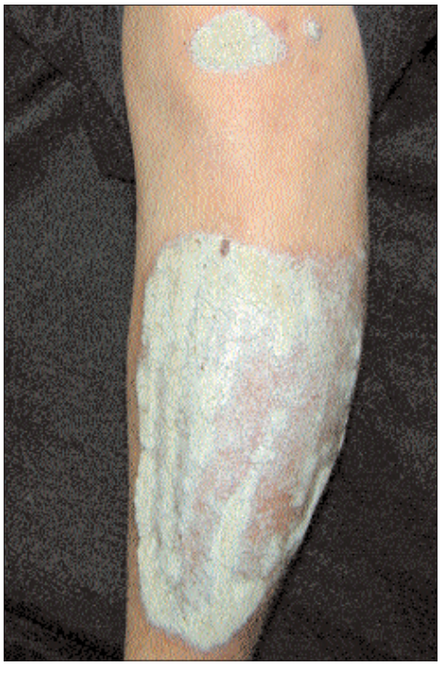
1.12 Papular acne lesions with inflammation and hyperpigmentation due to minocycline.



1.13 Nodular intradermal naevus on the side of the nose.



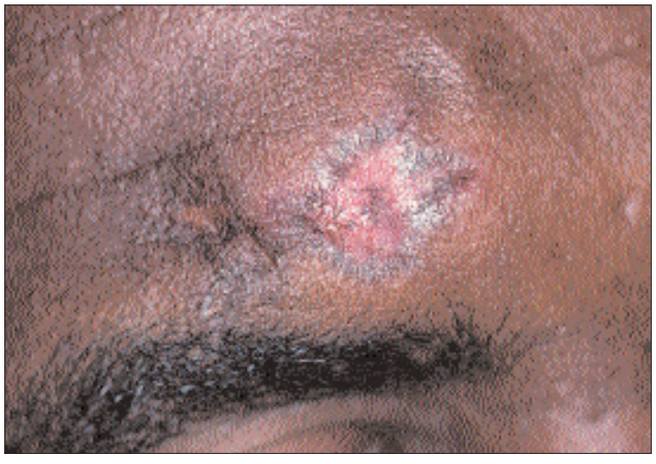
1.14 Keloid nodule on the back.



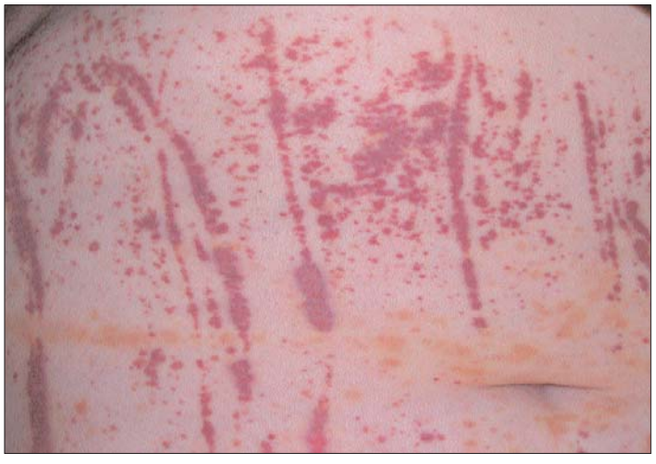
1.15 Hyperkeratotic plaques of psoriasis with obvious silvery scale.

Colour is also an important feature of a skin lesion. An area may be brown with pigment; it may be less pigmented than the surrounding skin or hypopigmented (**1.16**). In fact, it may have any colour. The physician should note if the area is uniformly coloured or not. Where a lesion is red, it is useful to compress the overlying skin to see if it blanches on pressure. Red macules that do not blanch on pressure are known as purpura (**1.17**). The redness is due to blood lying outside the blood vessels, which cannot be pushed away with compression. A small purpuric lesion is referred to as a petechia (plural: petechiae) and a large purpuric lesion as an ecchymosis (plural: ecchymoses), which is known to most people as a bruise (**1.18**). By contrast, erythema refers to skin reddening that does blanch on pressure.

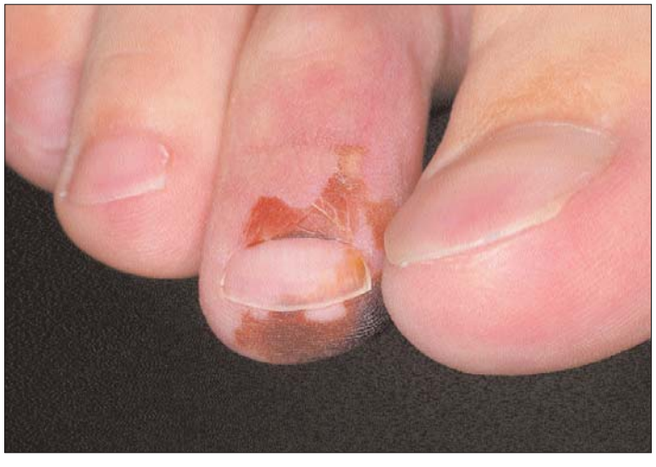
There may be changes in the skin overlying the area of interest. The area may be scratched or excoriated, and with this there may be fresh or dried blood (**1.19**).Crust is dried serum that is typically golden in colour that can overlie a lesion; it suggests inflammation due to eczema or impetigo (**1.20**, **1.21**). This must be differentiated from scale, which is the detached keratin of the top layer of skin. Depending on the skin condition, scale will be of differing adherence to



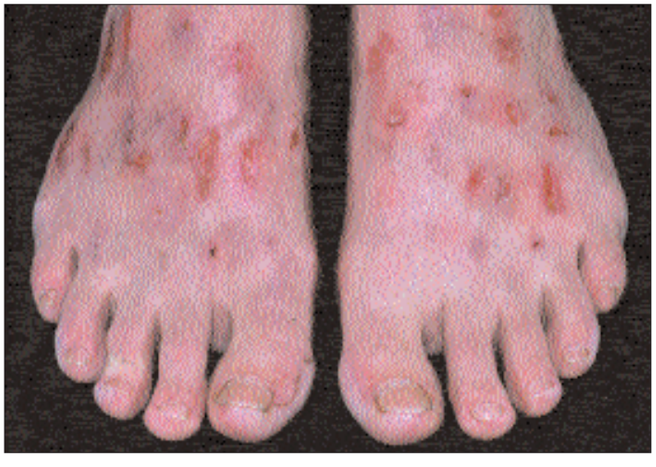
1.16 Hyper- and hypopigmentation in a small plaque of discoid lupus erythematosus on the forehead (see Chapter 6).



1.17 Purpuric rash on the abdomen of a patient with vasculitis. Not the Koebner phenomenon where she has scratched the skin and the yellow-brown pigmentation where the lesions have faded.



1.18 Haematoma in the stratum corneum of the second toe mimicking an acral lentiginous melanoma.

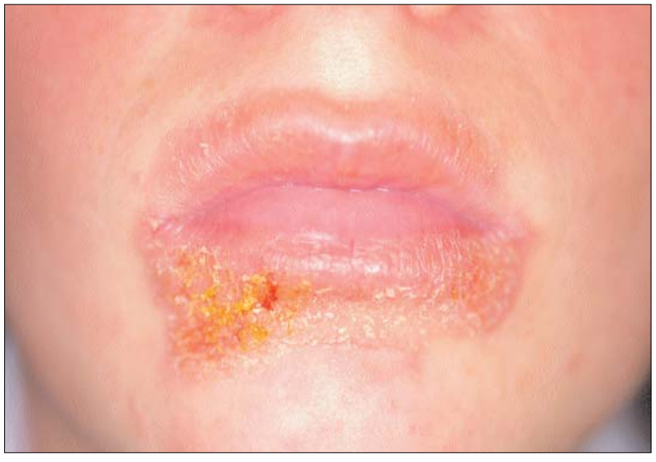


1.19 Excoriated lesions on the feet.

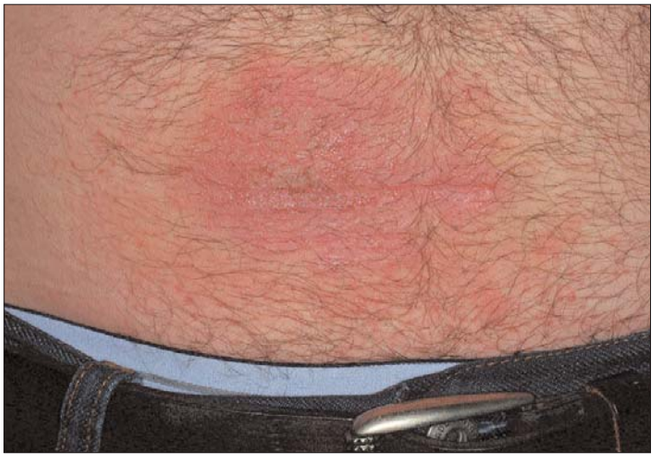
the lesion's surface. Often it is useful to remove overlying scale and crust in order to look at the underlying skin.

When examining in dermatology, good lighting must be used. The skin should be observed and then palpated. Rashes and isolated lesions should be approached in the same logical manner. The mnemonic DCM can be used to describe dermatological conditions: Distribution, Configuration, and Morphology.

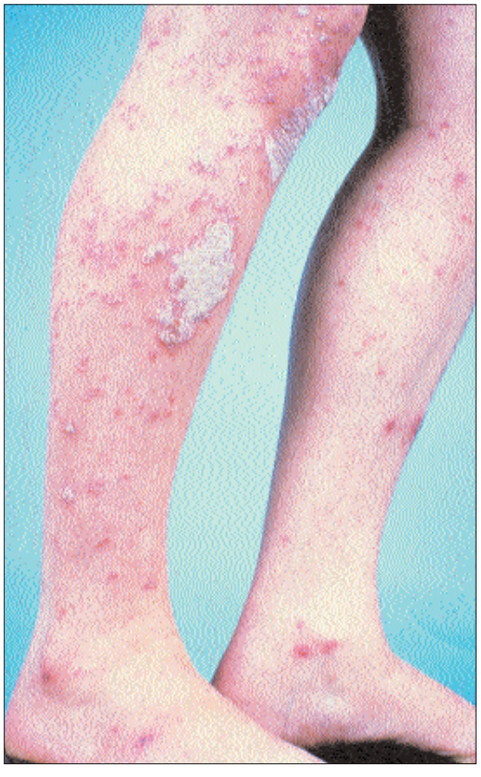
- Distribution: which area or areas of the skin are affected; for instance does the rash tend to affect the flexor or extensor surfaces of the skin (**1.22**, **1.23**)?



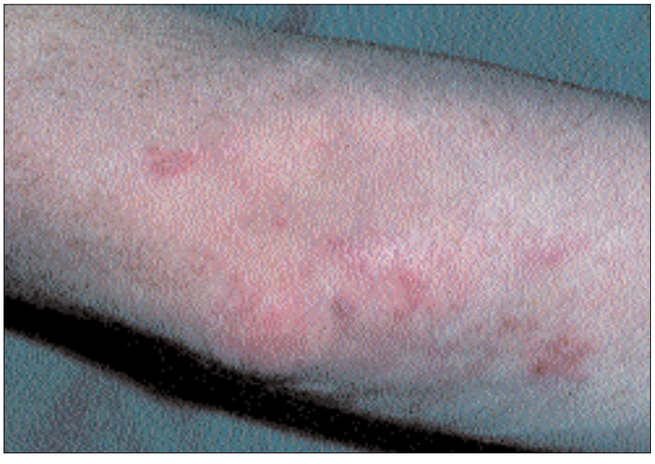
1.20 Impetiginized eczema of the lips and surrounding skin.



1.21 Weeping allergic dermatitis due to contact with nickel in the belt buckle.



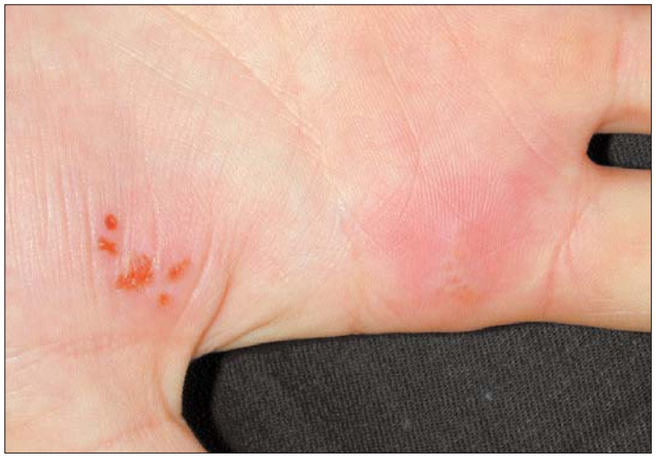
1.22 Plaques of psoriasis affecting the extensor surface of the lower leg.



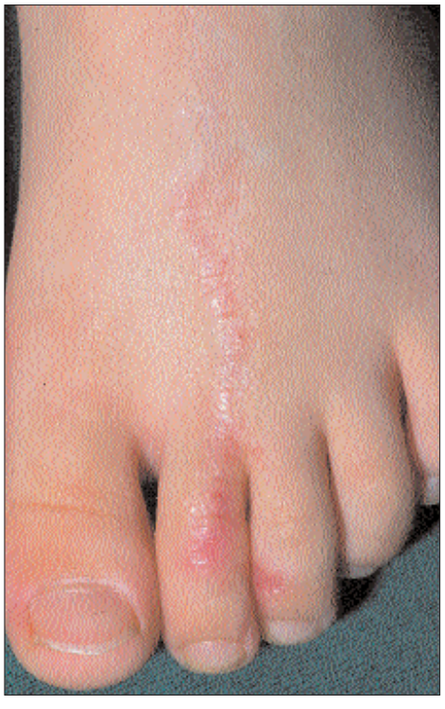
1.23 Dermatitis herpetiformis classically shows herpetiform lesions (vesicles grouped together like a cold sore) on elbows, knees, buttocks, and shoulders.

- Configuration: first, does the condition affect the body symmetrically or not? Second, is there a pattern to the condition, such as linear, where lesions are in a line or annular, where they form a ring; are the lesions in groups or isolated (**1.24**, **1.25**)? When describing an isolated lesion, the physician should check if there are surrounding lesions and if so, do they form a pattern.
- Morphology: the form of the rash or lesion should be described, its size, colour, and any associated features. If the rash has different forms within it, each form should be described separately, using the terms described in the previous section. A general physical examination of the patient should not be overlooked, especially where the skin condition is a manifestation of systemic disease.

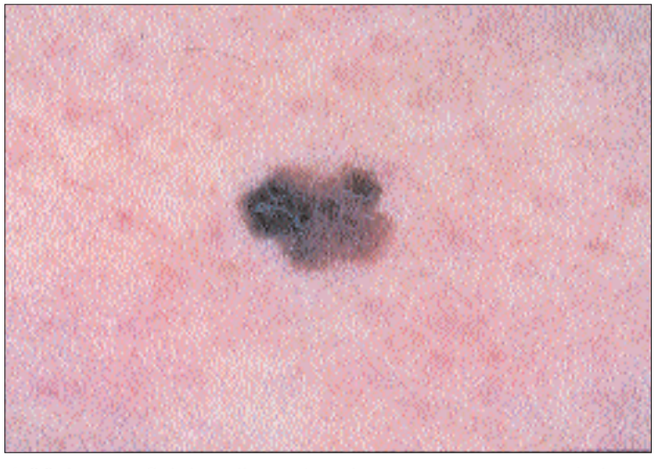
For a lesion that is changing, use of the **ABCDE** criteria can be a useful tool for suspecting malignancy (**1.26**, **1.27**). This rule has been validated in scientific studies in the prediction of malignant melanoma. Although it has not been validated for nonmelanoma skin lesions, it is a useful approach to all skin lesions that are reported as changing.



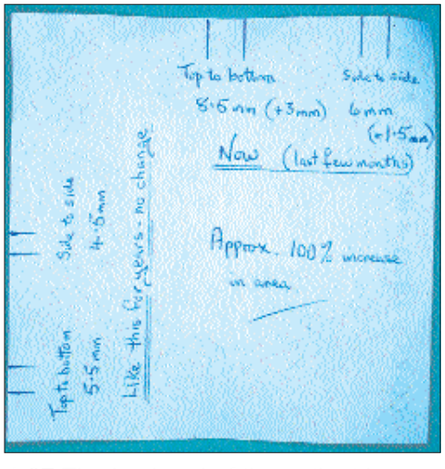
1.24 Herpes simplex infection of the palm.



1.25 Lichen striatus.



1.26 A superficial malignant melanoma on a woman's leg. It is **A**symmetrical, the **B**order is irregular, there is **C**olour variation, its **D**iameter is ≥6 mm, and it is **E**nlarging (**1.27**).



1.27 The husband of the patient in **1.26** regularly measured the lesion.

Malignancy should be suspected if one or more of the following criteria are fulfilled:

- Asymmetry: is the lesion asymmetrical in shape?
- Border: does the lesion have an irregular border?
- Colour: is the colour of the lesion irregular or changing?
- Diameter: is the diameter >6 mm?
- Enlargement: is the lesion growing, either vertically or horizontally along the skin surface?

Investigations

The skin can be viewed using a dermatoscope, a handheld device that magnifies the field of view ×10. This is especially useful when looking at pigmented lesions (see Chapter 4). Where a fungal infection is suspected, skin scrapings, collected using brisk strokes of a scalpel blade across the affected area, may be sent for analysis by microscopy and culture (**1.28**). Likewise, fluids within blisters or exuding from a lesion may be collected using a swab or syringe and analysed for the presence of bacteria or viruses.

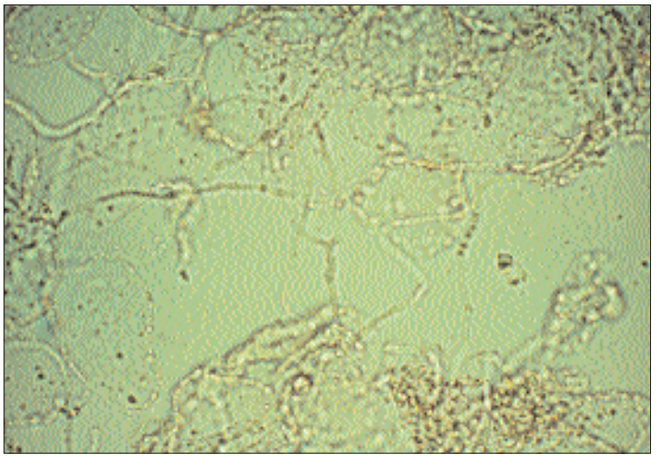
An invasive investigation of skin disease is the removal of affected skin for analysis. Commonly, a core of skin measuring up to 6 mm in diameter is removed using a circular blade called a punch biopsy. Biopsies can be analysed in a number of ways including histology, culture, and immunofluorescence, which is a useful tool when considering the aetiology of immuno-bullous skin disease.

Patch testing is useful in suspected contact dermatitis (*Table 1.1*). Skin, usually on a patient's back, is exposed to different allergens; each is placed onto a separate disc and held in contact with the patient's skin using tape (**1.29**). These so-called patches are left in place for 2 days and then removed. The skin is inspected after a further 2 days for any reactions (**1.30**). Skill is required to discern irritant from allergic reaction. Various contact dermatitis groups set the number of standard chemicals used, although additional chemicals may be 'patched' if the history is relevant.

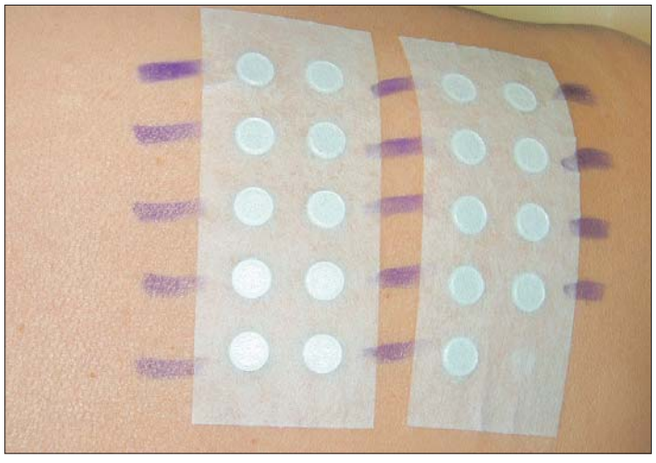
Skin prick tests are used to examine for atopy, latex allergy, and food allergy. A drop of allergen in solution is placed on the patient's forearm. The skin is pricked with a lancet through the drop and excess solution is then removed. Skin is inspected after 20 minutes (**1.31**). Skill is again required in interpretation of these tests. These tests are not commonly used because of the limited information afforded by them.

Table 1.1 Indications for patch testing

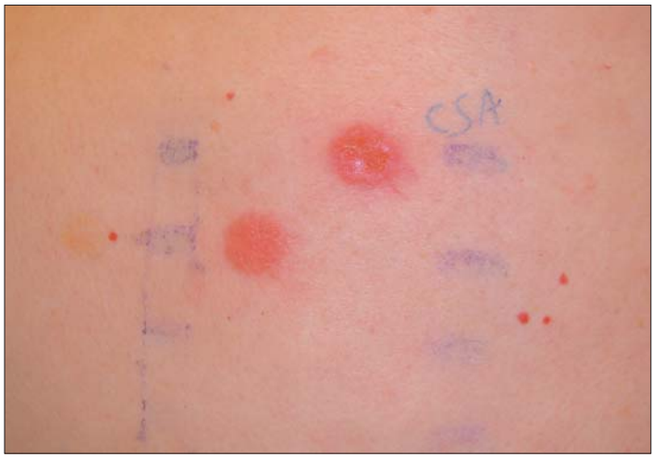
- Treatment-resistant eczema
- Chronic hand eczema
- Gravitational eczema
- Occupational contact dermatitis



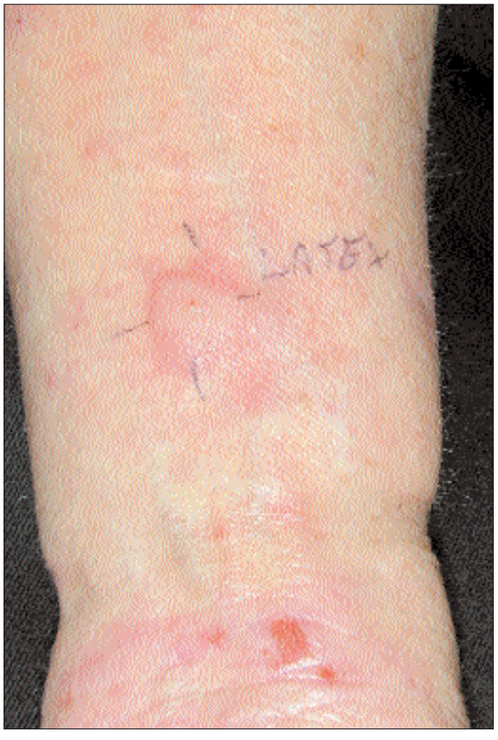
1.28 Fungal spores and hyphae seen on microscopy.



1.29 Patch tests in place.



1.30 Positive allergic reactions at day 4.



1.31 A positive prick test to natural rubber latex allergy.

Further reading

Burns T, Breathnach S, Cox N, Griffiths C (2004). *Rook's Textbook of Dermatology* (7th edn). Blackwell Science, Oxford.

McKee PH, Calonje E, Grauter SR (2005). *Pathology of the Skin* (3rd edn). Elsevier Mosby, Philadelphia.