CHAPTER 5

Diagnosis of Skin Disease

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Fundamentals of diagnosis

Disease definition

As for any other organ system, diagnosis of skin disease involves a history, examination and sometimes additional tests. The visibility of skin allows an instant diagnosis in some cases, or at least a ‘diagnostic label’ for the type of disease process being considered, using a variety of visual clues which include not only the individual lesional morphology but other factors such as the body site distribution, colour, scaling and arrangement of lesions. Such apparently effortless pattern recognition is actually quite complex when the individual components are analysed separately [1]. Further history, histopathology examination of skin biopsies, and other investigations, may be needed to refine the diagnosis or, in some instances, to identify a cause. The concept often held by non-dermatologists, that dermatology just involves having a ‘quick look’ at a patient, ignores issues around investigation and successful management (Fig. 5.1).

Whilst visual aspects are of great importance in dermatology diagnosis, other sensory modalities are also used in examination; for example, palpation may help in determining induration, quality of scaling and temperature changes [2], and even smell may be diagnostic in some instances. Some conditions may lack objective signs or may just have secondary changes (for example, due to scratching); in several eruptions, a knowledge of internal disease is required in order to make a diagnosis. This chapter briefly introduces aspects of the history, examination and other diagnostic manoeuvres.

Disease definition

Most skin diseases do not have a cause which is both identified and unique to that disorder. Conversely, many known causes of skin disease may play a part in several different types of disorder (for example, ultraviolet light may cause or contribute to sunburn, skin cancers, skin ageing and various patterns of photosensitivity; chromate may cause irritant contact dermatitis, caustic burns or allergic contact dermatitis at various body sites). Current definitions of most skin diseases therefore rely on the presence of a constellation of clinical, histopathological and sometimes immunopathological or genetic features. Even common and important diseases such as psoriasis have no strict and unique diagnostic criteria; indeed, some feel (and genetic studies are perhaps starting to support the thesis) that what has been accepted as ‘psoriasis’ should actually be more tightly classified morphologically [1] in order to help understand phenotypic heterogeneity [2]; it may be that this common dermatosis is several different diseases or is expressed according to different pathomechanisms.

The diagnostic stringency required for day-to-day clinical management may differ from that required in epidemiological and therapeutic research, in which it is clearly important to be sure that all studies are actually describing the same entity [3]. In some disorders which remain difficult to classify, such as parapsoriasis [4], numerous names may have been applied over the years and it may be difficult to know exactly what was meant in a previous publication. This problem applies even in atopic eczema/dermatitis, a very common disorder and generally considered a fairly straightforward diagnosis, and has significant implications for epidemiological research. Similarly, treatments and prognosis may vary between different types of cutaneous T-cell lymphoma (CTCL), but it is impossible to be certain about the types of CTCL that have been assessed in some studies.

Scientific advances are resolving some of these diagnostic and terminology issues, but many disease definitions in dermatology are still based on a constellation of clinically determined,
morphological cutaneous features. Some of these have distinct anatomical correlates (e.g. myxoid cyst), a specific external cause (e.g. scabies), or have a known genetic or biochemical defect (e.g. many genodermatoses). Many will have characteristic histological features, although—particularly in the case of inflammatory dermatoses—there are often areas of overlap between disease entities.

In other cases, there may be a number of different cutaneous features or multiorgan involvement which are associated together as a syndrome, as in systemic lupus erythematosus (SLE) or Behçet’s disease. A syndrome is usually defined by the simultaneous presence of a fixed combination of disease indicants, but these may not all be present in an individual case and may not require to be present concurrently; additionally, ‘overlap’ syndromes can occur where features of two or more related syndromes are present in the same patient. In such instances, making a diagnosis may rely on fulfilling a certain number of criteria—for example, the American Rheumatism Association (ARA) criteria for diagnosis of SLE [5]. This can be further refined by having major and minor criteria in order to achieve a given sensitivity and specificity. In some instances, such as the International Study Group diagnostic criteria for Behçet’s disease, a single diagnostic criterion must be fulfilled (recurrent oral aphthae) together with a given number of minor criteria [6]. In other instances, the number of criteria in each category which need to be fulfilled may vary—for example, in the diagnostic criteria for streptococcal toxic shock, the number of minor criteria that need to be fulfilled depends on the strength of the major criteria that are achieved [7]. All such diagnostic criteria may need to be updated to take into account new diagnostic techniques. However, it should be noted that many such criteria have been derived for confirmation of diagnosis for epidemiological or research reasons, rather than being a prerequisite for clinical diagnosis and management of individual patients. Thus, even for the same disorder, different diagnostic criteria may exist, with different purposes, complexity, levels of sensitivity and specificity, and validity; in atopic dermatitis, the criteria of Hanifin and Rajka are fulfilled by having three (of four) major criteria and three (of 22) minor criteria [8], whilst those of Williams and Pembroke proposed a single obligatory criterion (itchy skin) together with three (of five) additional features [9]. Clearly, some of the 22 minor criteria will have greater discriminatory value than others. Validation of such diagnostic criteria has been discussed in more detail elsewhere, using these examples [10].

Observer experience may also influence how well diagnostic criteria work in practice; the UK ‘seven-point’ checklist for suggesting melanoma as a diagnosis in pigmented lesions, whilst a useful tool to generate suspicion by patients and non-specialists [11,12], does not have sufficient sensitivity or specificity to allow risk to be assessed from the score criteria when they are used in the clinical situation of a primary care physician deciding that urgent dermatological opinion is required [13]. However, it is only by recording, challenging and refining such diagnostic criteria that advances will occur. This is particularly important for trainees and non-experts; for example, a diagnostic algorithm designed for use by rural health workers in under-developed countries was tested and had about 80% accuracy [14], a major benefit for care providers with essentially no access to ongoing education. At the other end of the scale, more sophisticated computer-assisted diagnostic algorithms can be constructed from detailed morphological and body site descriptions [15].

It is also important not to view such diagnostic criteria as static; for example, in Sweet’s syndrome (Chapter 50), proposed diagnostic criteria have been modified over a period of years, and criteria for drug-induced Sweet’s disease have been added. In other areas, proof of genetic mutations is redefining disease diagnosis—for example, in the classification of different types of epidermolysis bullosa [16–18]. Careful correlation of genotype and phenotype enables large diagnostic systems to be constructed, which aid diagnosis for subsequent patients [19,20] as well as assisting epidemiological research [21].

Having an accurate diagnosis is obviously important for patients, for prognosis, and may become important for more precisely targeted treatment [22,23]. It also enables construction of diagnostic coding systems, which are widely used in determining the cost of skin disease (largely relating to reimbursements for periods of care in insurance-led health-care systems, termed ‘diagnosis-related groups’ (DRGs [24,25]) or ‘health-related groups’), but which also aid epidemiological and therapeutic research. There is, however, concern about accuracy of coding, costing and case mix issues in such systems.

Diagnosis, and thus construction of valid databases, is influenced by many issues. Specifically, drug reaction surveillance generally relies on voluntary reporting [26,27], which may vary according to perceived severity, ‘newness’ or other unusual aspects. For example, searching the UK Committee on Safety of Medicines data for reports of toxic epidermal necrolysis (searched as TEN), most reports relate to lamotrigine [28] although historically this would not be the commonest cause of TEN—reporting may reflect increased use of a drug, ‘newness’ of the drug or severity of the reaction, active encouragement not to report well-known reactions, etc. Cutaneous reactions typically account for most adverse drug reaction reports, for example they comprise almost 30% in the French Pharmacovigilance database [27], but accurate
diagnosis of different types of drug eruption will often vary according to whether the reporting physician has dermatological experience or not. Similarly, in occupational reporting, the cases and situations encountered by occupational health physicians (mainly irritant dermatitis in larger industrial settings) will differ from those seen by dermatologists (more allergic contact dermatitis, including a greater emphasis on occupations such as hairdressing) [29–31]. Generally, systems that are designed to include other disciplines, such as the World Health Organization’s International Classification of Diseases (ICD) system, have been felt to be dermatologist ‘non-friendly’, and unhelpful for clinical and epidemiological dermatology [32], so some national bodies have created their own diagnostic indexing systems (such as the British Association of Dermatologists Dermatological Diagnostic Index System, DDISIS).

References
5. Tan EM, Cohen AS, Fries JF et al. Toxic shock syndrome, 1:

The history
Clinical diagnosis is paramount in dermatology, a discipline where histopathological and other techniques are often not routinely used, and which may only support a clinical diagnosis rather than being specific in their own right. However, whilst not necessarily required for rashes, histopathology for confirmation of the diagnosis, and for assessment of adequacy of excision, is important in the case of skin neoplasms—an increasing part of the work of dermatologists. Histopathological support for a diagnosis is often appropriate for some rashes (especially if systemic therapy is being considered).

In most cases, a carefully directed history is important for refining the diagnosis, for identifying further investigations (both to confirm a diagnosis and to determine the investigatory hypothesis that might help to identify a cause) and to address issues that may be important for optimal management. The amount of history required, and the sequence of history-taking and examination, may vary depending on the condition and on the referral information already provided to the dermatologist from a primary care provider. For example, a patient with hand dermatitis, especially if it is of possible occupational causation (Chapter 27), may need a detailed history about agents handled, hand washing and protective gloves that are used (Fig. 5.2).

Several national committees, consensus conferences, workshops and therapeutic guidelines have suggested minimum data sets for the medical history and morphological findings in skin diseases [1,2] as well as the information and investigations that are suitable for (especially systemic) therapies [3–5]; these are likely to become an important part of the clinical history along with the more fundamental issues pertaining to diagnosis, that are discussed below.
The presenting complaint

The following issues are likely to form part of the dermatological history, especially for dermatoses, in most consultations, although the emphasis on each will vary according to the diagnostic area.

Symptoms. Itch is the prime dermatological symptom, but may be variously described by different patients; there are individual differences in threshold and perception. Intense itch is typical in scabies, atopic dermatitis and lichen planus, whereas psoriasis and pityriasis versicolor usually cause less severe itch for the same degree of body surface involvement. Indeed, the degree of itch (as judged by the amount of scratching, and the general affect, and even without any other history), is potentially useful in distinguishing between atopic versus seborrhoeic dermatitis in infants.

Other symptoms include various qualities of pain, such as sharp pain (e.g. chondrodermatitis of the ear), burning (e.g. chilblains) or tenderness (e.g. erythema nodosum). The site may influence symptoms; for example, urticaria causes itch, but the same pathology affecting the palms often causes pain (because the oedema is deeper and the firmer tissues of the palm cannot distend easily). Both the quality and intensity of symptoms should therefore be recorded.

Symptoms usually parallel overt development of an eruption, but discordance can be diagnostically useful—for example, localized itch preceding herpetic vesicles (Fig. 5.3), or fever and malaise preceding erythema and swelling in cellulitis of the leg or erysipelas.

Duration, evolution, periodicity and previous episodes. The overall duration of a rash or localized lesion is usually apparent to the patient, although there are exceptions; basal cell carcinoma, for example, is often noticed only when it ulcerates, and the patient will therefore underestimate the duration of the lesion. Whether the onset of a rash was sudden or gradual may be diagnostically useful. The overall duration is also of diagnostic help for localized lesions. For example, a presumed keratoacanthoma that is still enlarging after a few months is probably a squamous cell carcinoma; lesions that turn black overnight do so due to intrallesional bleeding, not as a result of becoming a melanoma.

More precise details may require carefully phrased questions. In urticaria, the diagnostic feature is that individual lesions change from day to day (usually over a few hours), but the overall duration of the process may be years. Asking the patient about the duration of the eruption needs to distinguish between these two aspects. Similarly, if lesions are not present, then diagnosis may depend on the patient’s description, but there are pitfalls; weals are often described as ‘blisters’, a term which should not be taken at face value, and distinguishing between eruptions triggered by heat or sunlight often causes confusion. It is helpful to ask the patient whether any particular factors (e.g. dietary items, cosmetics, work chemicals, sunlight) appear to provoke (or alleviate) the condition.

Some dermatoses have a characteristic evolutionary sequence (e.g. pityriasis rosea, in which a solitary larger ‘herald patch’ precedes the widespread eruption by a few days, or ‘pre-pemphigoid’ eczematous lesions). Other disorders may demonstrate periodicity; for example, occupational contact dermatitis may improve at
weeks or holiday periods, and both photosensitivity and airborne contact allergy to plants may be seasonal.

Previous episodes of a similar type are likely to be relevant, but other skin problems may be important even if they do not appear to be the same process. For example, patients with type IV hypersensitivity to fragrance materials might at different times have eyelid rash due to cosmetics, axillary rash due to deodorants, widespread eczema due to soaps or clothing detergents or diffuse facial rash due to airborne perfume agents. In such cases the body site distribution may be confusing, but the sequence of sites affected should be determined, especially the site of initial involvement in the case of rashes.

Previous episodes are also potentially relevant for localized lesions (e.g. patients with two or three previous basal cell carcinomas have a high risk of another, so the level of suspicion may be greater in those with a positive previous history of these lesions).

**Previous therapy.** Previous treatment and response should be documented to guide future therapy, and to exclude the possibility of the diagnosis being obscured (for example, tinea incognito due to use of topical corticosteroids).

**General history**

**Medical history, medications and dietary history.** General medical conditions may have cutaneous features, and should be noted, especially in patients with rashes or generalized skin symptoms (see Chapter 62). Recent illnesses, even if apparently resolved, deserve special attention, as conditions such as urticaria, vasculitis, guttate psoriasis and erythema multiforme can be triggered by viral or bacterial infections in the weeks preceding the onset of the rash. Any recent or current systemic medication should be noted, including regular or intermittent self-medication or that received from relatives or friends, both as a possible cause of drug eruptions and to avoid interactions with treatment prescribed for the skin complaint. Topical therapies should also be considered, both in terms of their efficacy (or lack of), as well as because they may conceal or even cause a dermatosis. Allergies to medicaments or other agents may be important, as are drugs that might interact with anaesthetics or cause surgical bleeding.

Dietary history may be important in some individuals, especially those with intermittent urticaria or anaphylaxis. However, diet is often erroneously blamed for skin eruptions.

**Family history.** This may be important if a genodermatosis is suspected, in disorders with more complex inheritance (e.g. atopic dermatitis, psoriasis), and in some non-inherited disorders in which family contact is important (e.g. scabies, chickenpox).

**Occupation and leisure activities.** An occupational history may be of importance, both current and previous, particularly in individuals with eczema; a detailed account of processes and chemicals may be required, together with additional testing (Chapters 25–27). Hands are the most commonly affected site in occupational dermatitis, and it is useful to record details of hand protection (e.g. gloves, barrier creams) as well as the agents to which the patient is exposed. Hobbies less commonly cause problems, but may involve exposure to a variety of common allergens. Outdoor work or hobbies may also involve exposure to sun, cold or to plant allergens. An overview of some of these aspects is given in Table 5.1.

**Ethnicity and cultural aspects (Chapter 9).** Several disorders have a predilection to occur in specific racial groups—for example, the high frequency of sarcoidosis in black patients [1], or prurigo pigmentosa in the Japanese [2]. The morphology of common diseases may be altered by racial pigmentation, and normal pigmentary variations may be apparent. The severity of diseases may appear to be different between races or cultural groups; atopic eczema has been noted to be more frequent in children born in England of Asian or Caribbean origin [3,4]. Cultural differences may be diagnostically important, such as use of hair pomades and skin depigmenting agents, or may influence acceptance and understanding.

**Geographical factors.** Foreign travel, especially if recent, is a potentially important cause of dermatological disease. The place(s) visited may lead to specific likely diagnoses, and documentation should include any brief stopping-off countries. A long visit increases the risk of significant exposure to environmental agents, but dust-borne spores and insect vectors may be carried in aircraft and potentially alter the natural history of a disorder by allowing exposure outside the anticipated geographical distribution.

**Social and psychological factors.** The living conditions, economic status and standard of nutrition of the patient may be relevant both as a guide to diagnosis and to ensure compliance with the treatment advised. Specific examples of important social factors include the strong association between cigarette smoking and palmpoplantar pustulosis, and the multiple influences of excessive alcohol intake on the severity and therapeutic options in psoriasis. A sexual history is also required in some instances. The effects of skin problems on lifestyle, relationships, costs to the patient and costs to the community from work days lost are important, and it is helpful to know the patient’s main concerns. This applies particularly to chronic skin eruptions, but many patients with discrete lesions primarily want reassurance that they are not malignant. It is unlikely that many skin eruptions are due to ‘nerves’, but psychological factors can clearly be of importance in aggravating or perpetuating symptoms, and may be the primary abnormality in some instances (Chapter 64).

**References**

### 5.6 Chapter 5: Diagnosis of Skin Disease

#### Table 5.1 Some occupations and hobbies and their dermatological problems.

(Adapted from GM White and NH Cox, Diseases of the Skin, 2nd edn. London: Mosby, 2000: 12. See also ‘Occupational Dermatoses’, Chapter 27.)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Examples of dermatological implications that may occur</th>
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</table>
| Agricultural | Irritant dermatitis (e.g. to disinfectants, physical ‘wear and tear’) (Chapter 25)  
Contact allergy (e.g. rubber chemicals in gloves or footwear) (Chapter 26)  
Hazards from animals (e.g. tinea; Chapter 36)  
Hazards from plants (e.g. lichen allergy in forestry) |
| Gardening | Irritant or contact allergic dermatitis related to many plants  
Contact allergy to gloves  
Bites and stings; harvest mites etc. (Chapter 38) |
| Building trade and ‘do-it-yourself’ | Irritant dermatitis from cement (also causes chemical burns), plaster, solvents, preservatives, fibreglass  
Contact allergic dermatitis, especially from chromate in cement, epoxy resin, formaldehyde resins, colophony in soldering flux  
Mechanical—frictional palmar dermatitis from tools; vibration white finger related to use of some tools |
| Cars (trade or home) | Irritant dermatitis from solvents, paints, hand cleaners  
Contact allergic dermatitis from paints, resins, metals, rubber (gloves, tyres, tubing)  
Chemical leukoderma from rubber chemicals in tyre manufacture |
| Cooking (work or home) | Irritant dermatitis (detergents/hand washing, juices of meat, fruit and vegetables)  
Contact allergic dermatitis (or urticaire in some cases) from fruits, garlic, spices, meat, fish, gloves  
Physical—cuts, burns |
| Cleaning (work or home) | Irritant dermatitis from detergents  
Contact allergic dermatitis to fragrances or antimicrobials in detergents, polishes etc., or to gloves |
| Health workers | Irritant dermatitis from cleaning agents/hand washing  
Contact allergies—latex allergy (urticaire or dermatitis), medicament allergies (dentists—allergy to balsam flavourings, mercury, resins)  
Infections and infestations, e.g. scabies, especially nursing homes |
| Hairdressers | Irritant dermatitis from shampoos, bleaches etc.  
Contact allergic dermatitis from perfumes, dyes, bleaches, lanolin, antimicrobials; contact urticaire due to henna |
| Textiles (work or hobby) | Irritant dermatitis from solvents, bleaches, detergents/hand washing  
Contact allergic dermatitis—dyes, formaldehyde resins (finishes), mordants |
| Travel | Physical—photodermatoses, prickly heat  
Animals—bites, stings, seabather’s eruption, swimmer’s eruption, other marine invertebrate hazards  
Infections—cutaneous larva migrans, tungiasis, leishmaniasis, tropical viral exanthems  
Contact allergy—exotic plants, phytodermotaxis |

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### Examination of the skin

Most patients referred to the dermatologist have objective changes in the appearance or consistency of the skin. Even those who describe itch without rash often have dry skin or other features that can be elicited, such as dermographism. Most lesions and eruptions can either be diagnosed fully, or at least assigned to a diagnostic category, by clinical examination; indeed, clinical diagnosis is more precise than laboratory tests in many disorders. The ability to elicit and interpret cutaneous physical signs is therefore of fundamental importance in dermatological training.

The patient should always be examined in a good light, preferably daylight, and with magnification of lesions if necessary. Ideally, the entire skin should be examined in every patient, and particularly if the diagnosis is in doubt, as this may reveal lesions that are more easily identifiable and have not been modified by secondary changes. Adolescents and elderly people will often deny the existence of lesions other than those presented for examination, the former because they are unwilling to undress and the latter because they have not seen them.

In the examination of the skin, it is helpful to consider the morphology of individual lesions, their overall pattern and spatial relationship to each other, and their body site distribution. Each of these aspects is discussed more fully below. Specific attention to hair, nails and the mucous membranes is required. Careful description and use of nomenclature aids the monitoring of changes during follow-up, and any discussion with colleagues.

Touching the skin is important in most instances, and is discussed in more detail below. Gloves should be worn for examination of the mouth, genital/perineal region, or in the case of infective or infected dermatoses.

Additional, simple aids to clinical examination include use of Wood’s light, diascopy, dermoscopy, starch iodine testing to identify sweat duct orifices and hair microscopy.

### Individual lesions—nomenclature

The commoner descriptive terms applied to cutaneous lesions are listed below. These definitions are broadly in agreement with those recommended by the Nomenclature Committee of the International League of Dermatological Societies [1]. However, it is important to note that some of these definitions have been challenged subsequently [2–5]. A particular problem that many authors have glossed over is the dynamic aspects of skin disease. For example, some papules (less than 0.5 or 1 cm, depending on the source of the definition) are destined to grow larger and become nodules, whereas others (such as syringomas) rarely do so. Additionally, some eruptions may have essentially similar lesions but whose size may include both papules and nodules. Recording of actual size of lesions, or the range of sizes, is often a more useful clinical record [6].

### References

1 Winkelmann RK. Glossary of basic dermatology lesions: the International League of Dermatological Societies Committee on Nomenclature. Acta Derm Venereol Suppl (Stockh) 1987; 130: 1–16.

Glossary

alopecia—absence of hair from a normally hairy area.
apthha—a small ulcer of the mucosa.
atrophy—a loss of tissue from one or more of the epidermis, dermis or subcutaneous tissues. There may be fine wrinkling and increased translucency if the process is superficial.
burrow—a small tunnel in the skin that houses a parasite, such as the scabies acarus.
callus—a localized hyperplasia of the stratum corneum.
cellulitis—an inflammation of cellular tissue, particularly purulent inflammation of the deep dermis and subcutaneous tissue.
comedo (pl. comedones)—a plug of keratin and sebum in a dilated pilosebaceous orifice.
crusts (scabs)—crusts consist of dried serum and other exudates.
cyst—any closed cavity or sac (normal or abnormal) with an epithelial, endothelial or membranous lining and containing fluid or semisolid material.
cechymosis (bruise)—a macular area of haemorrhage more than 2 mm in diameter.
en cocarde (or 'cockade')—a rosette pattern of concentric rings, usually applied to naevi.
erosion—a loss of epidermis, which heals without scarring. It commonly follows a blister.
erythema—redness of the skin produced by vascular congestion or increased perfusion.
excoriation—loss of skin substance, specifically produced by scratching.
exfoliation—the splitting off of the epidermal keratin in scales or sheets.
fibrosis—the formation of excessive fibrous tissue.
fissure—any linear gap or slit in the skin surface.
fistula—an abnormal passage from a deep structure, such as a hollow viscus, to the skin surface or between two structures. It is often lined with squamous epithelium.
gangrene—death of tissue, usually due to loss of blood supply.
guttate lesions—small round or oval lesions distributed as a ‘shower’ of droplets. Usually applied to a form of psoriasis.
haematoma—a localized tumour-like collection of blood.
keralederma—a horny thickening of the skin.
lichenification—thickening of the epidermis (and to some extent also of the dermis) in response to prolonged rubbing.
macule—a circumscribed alteration in the colour of the skin. Authorities vary on the issue of scaling causing texture change within the definition.
maculopapular—rash consisting of both macules and papules.
milium—a tiny white cyst containing lamellated keratin.
nodule—a solid mass in the skin, which can be observed as an elevation or can be palpated. It is more than 0.5 cm in diameter. It may involve epidermis and dermis, dermis and subcutis, or subcutis alone. It may consist of fluid, other extracellular material (e.g. amyloid), inflammatory or neoplastic cells.
papilloma—a nipple-like mass projecting from the surface of the skin.
papule—a circumscribed palpable elevation, less than 0.5 cm in diameter. By careful examination it is often possible to determine whether the thickening involves predominantly the epidermis or the dermis and what type of pathological process is concerned. The only distinction between a papule and a nodule is the size, and this is artificial; some lesions characteristically occur at the smaller size of a papule, whereas others typically enlarge from a papule to become a nodule. Recording a finite size is more useful.
petechia (pl. petechiae)—a punctate haemorrhagic spot, approximately 1–2 mm in diameter.
plaque—an elevated area of skin, usually defined as 2 cm or more in diameter. It may be formed by the extension or coalescence of either papules or nodules as in psoriasis and granuloma annulare, respectively. Small plaque is sometimes used for such lesions 0.5–2 cm in diameter.
poikiloderma—the association of cutaneous pigmentation, atrophy and telangiectasia.
pustule—a visible accumulation of free pus. It may occur within a pilosebaceous follicle or a sweat duct or, less often, on glabrous skin. Most commonly due to infections (Fig. 5.3), but some eruptions typically cause sterile pustules.
pyoderma—any purulent skin disease.
scale—a flat plate or flake of stratum corneum. A collarette scale is a fine, periodically attached and centrally detached scale at the edge of an inflammatory lesion. Annular scaling is also seen in porokeratosis (Fig. 5.4). Furfuraceous or pityriasiform scales are fine and loose. Ichthyotic scales are large and polygonal. Scaling may accompany or follow many inflammatory disorders. Silvery scales are characteristic of processes involving parakeratosis, especially psoriasis. The silvery colour is due to reflection of light at the many air–keratin interfaces and can be altered by wetting the skin.

Fig. 5.4 Annular scaling in porokeratosis; subtle atrophy is also visible centrally.
scar—replacement by fibrous tissue of another tissue that has been destroyed by injury or disease. An atrophic scar is thin and wrinkled. A hypertrophic scar is elevated, with excessive growth of fibrous tissue. A cribiform scar is perforated with multiple small pits.
sclerosis—diffuse or circumscribed induration of the subcutaneous tissues. It may also involve the dermis, when the overlying epidermis may be atrophic. It is characteristically seen in scleroderma, but may occur as a sequel to or in association with many different processes.
sinus—a cavity or track with a blind ending.
target lesions—those are less than 3 cm in diameter and have three or more zones, usually a central area of dusky erythema or purpura, a middle paler zone of oedema, and an outer ring of erythema with a well-defined edge.
tumour—literally a swelling. The term is used to imply enlargement of the tissues by normal or pathological material, or cells that form a mass. It may be inflammatory or non-inflammatory, benign or malignant. The term should be used with care, as many patients believe it implies a malignancy with a poor prognosis.
uclc of skin)—a loss of dermis and epidermis, often with loss of the underlying tissues.
vegetation—a growth of pathological tissue consisting of multiple, closely set, papillary masses.
vesicles and bullae—visible accumulations of fluid within or beneath the epidermis. Vesicles are small (less than 0.5 cm in diameter) and often grouped. Bullae, which may be of any size over 0.5 cm, should be subdivided as multilocular (due to coalesced vesicles, typically in eczema) or unilocular.
weal—a transient area of dermal or dermal and hypodermal oedema, white, compressible and usually evanescent. It is the characteristic lesion of urticaria. It is often surrounded by a red, axon-mediated flare.

Shape of lesions, linear and annular lesions
The shape of each lesion and the pattern in which neighbouring lesions are arranged in relation to each other is often of great significance and may provide an easily recognizable clue to a rapid visual diagnosis. The main shapes, with examples, are listed in Table 5.2 and illustrated in Figs. 5.5–5.10. The mechanism or anatomical factor dictating the shape can sometimes be inferred, as in the case of many linear lesions (Table 5.3) or the vascular patterning leading to livedo (Fig. 5.5); in other instances, such as many annular lesions (Table 5.4) and reticulate lesions (Fig. 5.6), the explanation for the pattern is less clear.

A specific cause of a linear lesion is the Koebner or isomorphic phenomenon [1]. This term is applied when localized, non-specific trauma locally provokes lesions of a dermatosis which is usually spontaneously present elsewhere, and usually in a relatively ‘active’ or eruptive phase. It is particularly characteristic of psoriasis (Fig. 5.9, see also Chapter 20) and lichen planus, but occurs in several other dermatoses (Table 5.3). Less common dermatoses in which this may occur include erythema multiforme [2], Sweet’s disease and scleromyxoedema [3]. The trauma may be mild, and is usually a scratch or similar, although light or heat may do the same. Occasionally, one disease may be responsible for the localization of another, such as granuloma annulare developing at sites of herpes zoster, or psoriasis developing at sites of contact dermatitis; this has been termed the isotopic response [4]. Development of lesions of pyoderma gangrenosum or Behçet’s disease at sites of injection of serum or saline (or even just pinprick or venepuncture) is known as pathergy.

Some annular shapes result from centrifugal extension of an infection from the point of inoculation (e.g. linea corporis with dermatophyte fungi or erythema chronicum migrans in Borrelia burgdorferi infection). In others, a spreading neoplastic or inflammatory process leaves central scarring or ulceration, for example superficial basal cell carcinoma and discoid lupus erythematosus. In eruptions in which an allergic process is probably involved, the annular configuration is attributed to the refractory state of the central area. In some conditions, annular shapes can be related to the vascular network (see livedo, Chapter 49, and Fig. 5.5). Some involve an iatrogenic component, for example warts recurring at the margin of a blistered cryotherapy site. However, in many diseases, such as lichen planus, sarcoidosis or psoriasis, there is no satisfactory explanation for the occurrence of annular lesions. In clinical evaluation of annular lesions, it is particularly helpful to consider surface features such as scaling as an aid to identifying epidermal involvement and thus narrowing the differential diagnosis.

Table 5.2 Main shapes of skin lesions. (Adapted from GM White and NH Cox, Diseases of the Skin, 2nd edn. London: Mosby, 2000: 6.)

<table>
<thead>
<tr>
<th>Shape Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discoid (nummular)</td>
<td>A filled circle</td>
</tr>
<tr>
<td>Petaloid</td>
<td>Discoid lesions which have merged together</td>
</tr>
<tr>
<td>Arcuate</td>
<td>Incomplete circles</td>
</tr>
<tr>
<td>Annular</td>
<td>Open circles with different central skin compared with the rim</td>
</tr>
<tr>
<td>Polycyclic</td>
<td>Circles which have merged together</td>
</tr>
<tr>
<td>Livedo</td>
<td>Chicken-wire criss-cross pattern</td>
</tr>
<tr>
<td>Reticulate</td>
<td>Fine lace-like pattern</td>
</tr>
<tr>
<td>Target</td>
<td>Multiple concentric rings</td>
</tr>
<tr>
<td>Stallate</td>
<td>Star-shaped</td>
</tr>
<tr>
<td>Digitate</td>
<td>Finger-shaped</td>
</tr>
<tr>
<td>Linear</td>
<td>Straight line</td>
</tr>
<tr>
<td>Serpiginous</td>
<td>Snake-like</td>
</tr>
<tr>
<td>Whorled</td>
<td>Swirling pattern</td>
</tr>
</tbody>
</table>

References
Table 5.3 Anatomical and causative factors in linear lesions (Figs 5.7–5.9). (Adapted from C.M. Lawrence and N.H. Cox, Physical Signs in Dermatology, 2nd edn. London: Mosby, 2002: 21.)

<table>
<thead>
<tr>
<th>Determinant of pattern</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood vessels</td>
<td>Thrombophlebitis, Mondor’s disease (linear thrombophlebitis on the trunk)</td>
</tr>
<tr>
<td></td>
<td>Eczema related to varicose veins</td>
</tr>
<tr>
<td></td>
<td>Temporal arteritis</td>
</tr>
<tr>
<td>Lymphatics</td>
<td>Lymphangitis</td>
</tr>
<tr>
<td></td>
<td>Sporotrichosis, fish tank granulomas</td>
</tr>
<tr>
<td>Dermatome</td>
<td>Herpes zoster, zosteriform naevus, zosteriform Darier’s disease, zosteriform metastases</td>
</tr>
<tr>
<td>Nerve trunks</td>
<td>Lepero (thickened cutaneous nerves)</td>
</tr>
<tr>
<td>Developmental, Blaschko lines</td>
<td>Pigmentary demarcation line, linea nigra</td>
</tr>
<tr>
<td>Skin stretching</td>
<td>Striae due to growth spurt (on lower back)</td>
</tr>
<tr>
<td>Infestation</td>
<td>Scabies, larva migrans (both usually serpiginous)</td>
</tr>
<tr>
<td>External factors</td>
<td>Plants: Phytophotodermatitis</td>
</tr>
<tr>
<td></td>
<td>Allergens: Elastoplast, nail varnish (neck), necklace, waistbands, etc.</td>
</tr>
<tr>
<td></td>
<td>Chemical: Caustics, e.g. phenol</td>
</tr>
<tr>
<td></td>
<td>Thermal: Burns</td>
</tr>
<tr>
<td></td>
<td>Physical: Trauma to previously normal skin (keloid scar, bruising, dermatitis artefacta, amniotic constriction bands)</td>
</tr>
<tr>
<td></td>
<td>Trauma to skin with a pre-existing dermatosis (purpura, cryoglobulinaemia, amyloid, vasculitis)</td>
</tr>
<tr>
<td></td>
<td>Blisters (epidermolysis bullosa, porphyrias)</td>
</tr>
<tr>
<td></td>
<td>Koebner phenomenon (psoriasis, lichen planus, lichen nitidus, vitiligo, lichen sclerosus, pityriasis rubra pilaris)</td>
</tr>
<tr>
<td></td>
<td>Inoculation (warts, molluscum contagiosum)</td>
</tr>
<tr>
<td></td>
<td>Other mechanism (scar sarcoïd)</td>
</tr>
<tr>
<td>Other determinants</td>
<td>Linear scleroderma (limb, central forehead)</td>
</tr>
<tr>
<td></td>
<td>Senear–Caro ridge (on hands in psoriasis)</td>
</tr>
<tr>
<td></td>
<td>Dermatomyositis (dorsum of fingers; Gottron sign)</td>
</tr>
<tr>
<td></td>
<td>Interstitial granulomatous dermatitis (rope or cord sign)</td>
</tr>
<tr>
<td></td>
<td>Flagellate pigmentation due to cytotoxic drugs (e.g. bleomycin)</td>
</tr>
</tbody>
</table>

Table 5.4 Examples of lesions that are characteristically annular or often include annular morphology (Fig. 5.10).

- Infections
  - ‘Ringworm’ dermatophyte infections
  - Impetigo
  - Erythema chronicum migrans
  - Syphilis (secondary, tertiary)
  - Leprosy
- Inflammatory
  - Psoriasis
  - Seborrhoeic dermatitis
  - Atopic dermatitis (some)
  - Halo eczema (Meyerson’s phenomenon)
  - Subacute cutaneous lupus erythematosus
  - Lichen planus
  - Sarcoïdosis
  - Granuloma annulare
  - Actinic granuloma
  - Erythema multiforme
  - Urticaria
  - Serum sickness and serum sickness-like eruption
  - Linear IgA disease/chronic bullous dermatosis of childhood
  - Bullous pemphigoid
  - Subcorneal pustular dermatosis
  - Erythema annulare centrifugum
  - Jessner’s lymphocytic infiltrate
  - Erythema marginatum rheumaticum
  - Pityriasis rosea (herald patch)
- Vascular
  - Purpura annularis telangiectoides
  - Neoplastic
    - Superficial basal cell carcinoma
    - Mycosis fungoides
    - Other cutaneous lymphomas
- Keratinization disorders
  - Porokeratosis

**Pattern of lesions**

The arrangement of individual lesions may create a characteristic pattern, such as the grouping of vesicles in herpes simplex—this pattern is so striking that it is applied to other lesions which do not share the same aetiology (herpetiform mouth ulcers).

Useful terminology to describe patterns includes:

- **Agminate**—clustered; used to describe lesions such as acne agminata, where granulomatous lesions cluster around the lids (Fig. 5.11), or agminate naevi, an unusual clustering of melanocytic naevi.

- **Grouped or clustered**—characteristic of some infections (herpetic vesicles, molluscum contagiosum, plane warts), flea bites, as well as endogenous lesions such as lichen planus, leiomyo-mata, lymphangiomata circumscriptum (Fig. 5.12).

- **Satellite**—a cluster of lesions around a larger central lesion. May occur due to local lymphatic spread of neoplasm such as melanoma (Fig. 5.13); may occur in chronic bullous disease of childhood/linear IgA disease.

- **Confluent**—lesions merging together, locally or widespread, e.g. pityriasis versicolor.

- **Scattered, disseminated and exanthematous**—for example, many drug eruptions, viral exanthemata, as well as some extrinsic causes (Fig. 5.14).

- **Spared**—patterns of sparing may also be diagnostically important, e.g. islands of sparing occur within the otherwise often confluent orange–red erythema of pityriasis rubra pilaris, sparing within skin folds in papuloerythroderma of Ofuji, or areas shielded by clothing or a wristwatch may be overtly spared in photosensitivity (Fig. 5.15).

- **Symmetrical**—often endogenous (e.g. psoriasis) and asymmetrical, often of exogenous cause (e.g. tinea).
Fig. 5.5 Livedo. This is a ‘chickenwire’ patterning that is determined by the arrangement of the skin vasculature. (a) Resolving erythema infectiosum (fifth disease). (b) Diffuse dermal angiomatosis of the breast. (c) Cutaneous polyarteritis nodosa—a ‘broken’ livedo is typical in this disorder and in some disorders of microvascular occlusion.

Fig. 5.6 Examples of reticulate lesions. (a) In some cases this may be confined to specific localized lesions, as in buccal lichen planus. (b) In other cases it may describe an overall morphology of an eruption such as confluent and reticulate papillomatosis.
Examination of the skin  5.11

Fig. 5.7 Some examples of linear lesions. (a) Growth striae. (b) Lichen striatus. (c) Dermographism. (d) Linear epidermal naevus. (e) Linear excoriations in dermatitis artefacta.
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Fig. 5.8 Lymphangitis. Inflammation in distal superficial lymphatic vessels is reticulate, but becomes more linear as it spreads up a limb in deeper, larger lymphatic channels.

Fig. 5.9 Koebner phenomenon in psoriasis.

Fig. 5.10 Annular lesions. (a) Annular granuloma annulare. (b) Erythema annulare centrifugum, a superficial lesion with scaling. (c) Annular scale in porokeratosis. (d) Annular lesion of tinea corporis. (e) Annular lichen planus. (f) Characteristic annular arrangement of blisters in chronic bullous disease of childhood. (g) Subacute cutaneous lupus erythematosus; annular lesions on the trunk are common.
Fig. 5.10 Continued
**Fig. 5.11** Acne agminata; this is merely a historical term for grouped lesions.

**Fig. 5.12** Grouped lesions. (a) Dermatitis herpetiformis, a cluster of lesions on the knee. (b) Grouped pigmented areas in a speckled lentiginous naevus. (c) Grouped vesicles in herpes simplex. (d) Grouped lesions within a mosaic plantar wart.
The overall distribution of lesions in many common dermatoses may be so characteristic that it is of great assistance in clinical diagnosis, even though the mechanism in most instances is not understood. Examples of body site predilection of dermatoses are provided in Table 5.5. Some of these are explained by anatomy, sites of contact, etc. (see below), but even some demarcations that presumably have an anatomical basis are not fully understood, for example Wallace’s line on the foot or the equivalent on the hand (Fig. 5.16). Some, for example those at flexural sites (Table 5.6), are often modified in appearance by moist occlusion. Important factors in determining the distribution of dermatoses include the following:

**Anatomical factors**
- blood supply, e.g. venous eczema
- skin appendages, e.g. acne, hidradenitis
- type of skin, e.g. eruptions may be localized to the glabrous skin of palms and soles
- neural, e.g. herpes zoster
- developmental, e.g. disorders which follow lines of Blaschko (Chapter 15)
- regional variation in the skin surface microenvironment, e.g. erythrasma is usually localized to flexures
- others, e.g. polychondritis is restricted to sites where there is cartilage, affecting ears, nose, joints (and trachea)

**External factors**
- solar exposure, e.g. photosensitivity disorders, squamous cell carcinoma
- chemical exposure, e.g. contact dermatitis
- infective, e.g. orf

**Colour of skin and of lesions**
Normal skin colour is due to melanin, phaeomelanin, haemoglobin, oxyhaemoglobin and carotenoids (Chapter 58). The colour of the skin is greatly modified by the scatter of light, which is responsible, for example, for the whiteness of scale and the blueness of any melanin deep in the dermis, although colour contrast with surrounding skin also alters perception of the colour of skin and subcutaneous structures [1]. The range of colours that may be seen

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**Fig. 5.13** Satellite lesions—in this case, local metastases around a primary nodular melanoma.

**Fig. 5.14** Scattered lesions. The predominantly ‘buckshot’ pattern here is typical of ‘strimmer’ or ‘weedwacker’ dermatitis, in which photosensitizing plant products have been spattered onto the skin and produced localized photosensitivity. A useful clue to diagnosis is that, in addition, some of the individual lesions have a linear morphology (seen here as a poorly defined linear band crossing the elbow joint) representing direct contact with a causative plant stem.

**Fig. 5.15** A drug-induced phototoxic eruption. There is a striking pattern of sparing of skin covered by a sandal.
Table 5.5 Some examples of disorders that have predilection for specific body sites.

<table>
<thead>
<tr>
<th>Body site</th>
<th>Type of disorder</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp</td>
<td>Hair disorders/alopecia</td>
<td>Alopecia areata, androgenetic alopecia</td>
</tr>
<tr>
<td></td>
<td>Inflammatory dermatoses</td>
<td>Psoriasis, seborrhoeic dermatitis, lichen simplex</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Pilar cysts, organoid naevus, squamous cell carcinoma, atypical fibroxanthoma, cutaneous metastases</td>
</tr>
<tr>
<td>Eyelids</td>
<td>Inflammatory dermatoses</td>
<td>Atopic dermatitis, contact allergy (cosmetics, nickel), seborrhoeic blepharitis, angioedema, dermatomyositis</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Basal cell carcinoma, xanthelasma</td>
</tr>
<tr>
<td>Ears</td>
<td>Inflammatory dermatoses</td>
<td>Seborrhoeic dermatitis, psoriasis, atopic dermatitis, relapsing pachydermatosis</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>Pseudomonas ('malignant') otitis externa</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Actinic keratosis, squamous cell carcinoma, chondrodermatitis nodularis, atypical fibroxanthoma, angiomyloid hyperplasia with eosinophilia, gouty tophi</td>
</tr>
<tr>
<td>Face</td>
<td>Inflammatory dermatoses</td>
<td>Acne, atopic dermatitis, seborrhoeic dermatitis, rosacea, lupus erythematosus, lupus pernio, photosensitivity</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Herpes zoster, erysipelas, impetigo</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Naevi and freckles, actinic keratoses, basal and squamous cell carcinomas, keratoacanthoma, lentigo maligna</td>
</tr>
<tr>
<td>Lips</td>
<td>Inflammatory dermatoses</td>
<td>Dermatitis (atopic, contact), cheilitis (angular, actinic), angioedema, contact urticaria, erythema multiforme</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Herpes simplex, viral warts</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Vascular lesions (venous lake, pyogenic granuloma), squamous cell carcinoma</td>
</tr>
<tr>
<td>Hands</td>
<td>Inflammatory and other dermatoses</td>
<td>Dermatitis (dyshidrotic, pompholyx, contact), psoriasis and palmoplantar pustulosis, keratoderma, erythema multiforme, photosensitivity (dorsal hand), collagen vascular disorders and vasculitis, granuloma annulare</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Paronychias, onychomycosis, scabies (especially fingerwebs), viral warts</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Actinic keratoses, squamous cell carcinoma, subungal melanoma</td>
</tr>
<tr>
<td></td>
<td>Nail disorders</td>
<td>Koilonychia, pachyonychia congenita, many others</td>
</tr>
<tr>
<td>Limbs</td>
<td>Inflammatory and other dermatoses</td>
<td>Psoriasis (elbows, knees), atopic dermatitis (limb flexures), discoid eczema, venous eczema and ulceration (lower leg), astmatotic eczema (lower leg), lichen simplex (lower leg), lichen planus (flexor forearms, shins), dermatitis herpetiformis (knee, elbow), granuloma annulare (elbows), erythema nodosum (legs), vasculitis (legs), papular urticaria/flea bites (lower leg)</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Bowen’s disease (lower leg), dermatofibroma</td>
</tr>
<tr>
<td>Feet</td>
<td>Inflammatory and other dermatoses</td>
<td>Dermatitis (pompholyx, contact, juvenile plantar), psoriasis and palmoplantar pustulosis, vasculitis and arterial disease, callosities/corns</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Dermatophyte fungal infection (skin and nails), pitted keratolysis, verrucae</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Eczema poroma, subungal exostosis</td>
</tr>
<tr>
<td>Axillae (see also Table 5.6)</td>
<td>Inflammatory dermatoses</td>
<td>Psoriasis, contact dermatitis, hidradenitis suppurativa, acanthosis nigricans, fibroepithelial polyps, freckles in neurofibromatosis (Crowe’s sign)</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Staphylococcal boils, erythromas</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Apocrine hidrocystoma</td>
</tr>
<tr>
<td>Genital</td>
<td>Inflammatory and other dermatoses</td>
<td>Psoriasis/Reiter’s syndrome, lichen planus and lichen nitidus (penis), lichen sclerosus (penis, vulva), lichen simplex (scrotum, vulva), fixed drug eruption (penis), Zoon’s balanitis (glans penis), plasma cell ulvitis, other vulval dermatoses</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
<td>Sexually transmitted diseases, genital warts, molluscum contagiosum</td>
</tr>
<tr>
<td></td>
<td>Localized lesions</td>
<td>Epidermoid cysts (scrotal), squamous cell carcinoma (penis, vulva)</td>
</tr>
</tbody>
</table>

Fig. 5.16 A keratoderma showing abrupt discontinuation at Wallace’s line.

in individual skin lesions is enormous (Table 5.7). Although many red, scaly rashes tend to resemble each other, many dermatoses have their own distinctive colour which aids recognition—for example, the orange and yellow–orange palms of pityriasis rubra pilaris and carotenaemia, respectively. Some colours can be logically explained—for example, the purple of lichen planus is due to the redness of inflammation combined with the blue-brown of melanin within the dermis.

Examination of pigmented skin requires a degree of practice, as the physical signs may be modified. Erythema is seen as a dark area, macular or diffuse. Dermal oedema lightens the skin and weals appear pale. Papules may be pale or dark according to the degree of oedema or the presence of acanthosis or hyperkeratosis, which mask pigment. Purpura may be difficult to detect, but may appear jet-black in lighter-pigmented skin. Post-inflammatory depigmentation and hyperpigmentation are exaggerated
### Table 5.6  
Some disorders that have a predilection for flexural sites. (Adapted from GM White and NH Cox, Diseases of the Skin, 2nd edn. London: Mosby, 2000: 24. See also Chapter 71.)

<table>
<thead>
<tr>
<th>Type of Disorder</th>
<th>Disorder</th>
<th>Comment (all refer to major flexures unless specified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory dermatoses</td>
<td>Psoriasis</td>
<td>Common in flexures, typically red and shiny rather than the usual white scale (Chapter 20); may be termed the ‘inverse pattern’ if mainly flexural distribution</td>
</tr>
<tr>
<td>Seborrhoeic dermatitis</td>
<td>Usually with lesions elsewhere also; central face, scalp etc.</td>
<td></td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>Irritant or allergic; may affect the vault of the axilla (e.g. deodorants) or axillary folds (e.g. clothing dermatitis) (Chapters 25 and 26)</td>
<td></td>
</tr>
<tr>
<td>Intertrigo</td>
<td>Especially inframammary; may be due to simple maceration, but also secondary infection may occur (staphylococcal, streptococcal, candidial)</td>
<td></td>
</tr>
<tr>
<td>Napkin rash</td>
<td>Many causes, the commonest are irritant and candidal (see Chapter 17)</td>
<td></td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Not often mainly flexural, but may cause confusion as flexural and genital lesions are often brown in colour and/or annular in morphology, rather than the usual purplish plaques, and may lack the anticipated pruritus</td>
<td></td>
</tr>
<tr>
<td>Hidradenitis suppurativa</td>
<td>Affects axillae, groin, inframammary area (Chapters 30 and 42)</td>
<td></td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>Cutaneous lesions affect especially the perineum (Chapter 71)</td>
<td></td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>Affects elbow and knee flexures, uncommonly the major flexures other than in infants when the process may be generalized (Chapter 24)</td>
<td></td>
</tr>
<tr>
<td>Bullous diseases</td>
<td>Pemphigus vegetans</td>
<td>Rare, mainly flexural (Chapter 40)</td>
</tr>
<tr>
<td>Hailey-Hailey disease</td>
<td>Inherited, variable (Chapter 39)</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>Dermatophytes</td>
<td>Especially male groin; usually associated with tinea pedis (Chapter 36)</td>
</tr>
<tr>
<td>Erythrasma</td>
<td>Brownish colour, fluoresces under Wood’s light (Chapter 30)</td>
<td></td>
</tr>
<tr>
<td>Trichomycosis axillaris</td>
<td>Coated hair shafts (Chapter 66)</td>
<td></td>
</tr>
<tr>
<td>Candidosis</td>
<td>Especially in napkin rash or bedbound elderly adults, commoner in diabetes; satellite pustules are characteristic (Chapter 36)</td>
<td></td>
</tr>
<tr>
<td>Bacterial</td>
<td>Various types—follicular infections (furuncles), perianal abscesses, secondary infection of intertrigo, Gram-negative toe-web infections etc. (Chapter 30)</td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>Multiple itchy flexural nodules are highly suggestive of the relatively chronic nodular variant—penile lesions are also common in this pattern (Chapter 38)</td>
<td></td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>Often acral, but the laterothoracic type may include axillary involvement, and a bathing trunk pattern involves groin flexures; often purpuric</td>
<td></td>
</tr>
<tr>
<td>Localized lesions</td>
<td>Fibroepithelial polyps (skin tags)</td>
<td>A common normal variant</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>Axillary freckling is seen (Crowe’s sign) (Chapter 15)</td>
<td></td>
</tr>
<tr>
<td>Fox–Fordyce disease</td>
<td>An apocrine occlusion dermatosis (Chapter 44)</td>
<td></td>
</tr>
<tr>
<td>Pseudoxanthoma elasticum</td>
<td>Inherited defect of elastic tissue, most apparent on the neck and axillae (Chapter 45)</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Hyperhidrosis and other sweat apparatus disorders</td>
<td>Mainly axillae (Chapter 44)</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>May be endocrine-related or paraneoplastic (Chapters 19 and 62)</td>
<td></td>
</tr>
<tr>
<td>Acrodermatitis enteropathica/zinc deficiency</td>
<td>Severe napkin rash and perianal rash in an infant (Chapter 17); acquired version in adults; necrolytic migratory erythema of glucagonoma syndrome may have the same pattern (Chapter 62)</td>
<td></td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
<td>May present as severe napkin rash (Chapter 17)</td>
<td></td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>Often affects shielded sites, may be limited to main flexures ± buttocks</td>
<td></td>
</tr>
<tr>
<td>Granular parakeratosis</td>
<td>Rare—hyperkeratotic, mainly adult female axilla</td>
<td></td>
</tr>
<tr>
<td>‘Inverse’ pattern of drug eruption</td>
<td>See Chapter 75</td>
<td></td>
</tr>
</tbody>
</table>

Compared to paler skin—for example, after herpes zoster, syphilis, leprosy, lichen simplex and many other conditions. Normal pigmented variation between body sites is also more apparent in darker skin, and may cause confusion (for example, dark crease lines on the relatively pale palms); pigmented demarcation lines may also be visible (Futcher’s and Voigt’s lines) [2].

### References

### Palpation of the skin

Palpation of rashes or localized lesions imparts additional information about texture, consistency, thickness, tenderness and temperature [1]. It has been shown, using a trained ‘blinded’ observer, that the scaling of psoriasis and eczema can be distinguished by palpation alone [2]. Gentle scratching or rubbing alters visibility of scaling and may elicit dermographism. The main ‘touch’ modalities in examining the skin are:

- **Simple palpation**—to determine texture, etc., as above.
- **Blunt pressure**—e.g. to detect oedema, assess capillary refill, identify the dermal defect that occurs in anetoderma.
- **Linear or shearing pressure**—to elicit dermographism, or Nikolsky’s sign in pemphigus (Chapter 40).
- **Squeezing or pinching**—to determine localization and consistency of lesions, e.g. a pinch of skin can be lifted up over a subcutaneous nodule, whereas squeezing a tethered intradermal process such as a dermatofibroma produces dimpling (Fig. 5.17).
Table 5.7 Colours of skin lesions. (Adapted from CM Lawrence and NH Cox, Physical Signs in Dermatology, 2nd edn. London: Mosby, 2002: 21.)

<table>
<thead>
<tr>
<th>Colour</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>Melanin, e.g. some naevi, melanoma</td>
</tr>
<tr>
<td></td>
<td>Exogenous pigments, e.g. tattoos, pencil/ink</td>
</tr>
<tr>
<td></td>
<td>Exogenous chemicals, e.g. silver nitrate, gold salts</td>
</tr>
<tr>
<td></td>
<td>Deeply situated blood or melanin, e.g. angiomas, blue naevus</td>
</tr>
<tr>
<td>Blue-grey</td>
<td>Inflammatory diseases, e.g. orf</td>
</tr>
<tr>
<td></td>
<td>Drug-induced pigmentation, e.g. phenothiazines, minocycline</td>
</tr>
<tr>
<td>Dark brown</td>
<td>Melanin near the skin surface, e.g. most melanocytic naevi</td>
</tr>
<tr>
<td></td>
<td>Exogenous pigments, e.g. dithranol (anthralin) staining</td>
</tr>
<tr>
<td>Pale brown</td>
<td>Melanin near the skin surface, e.g. lentigo, freckles</td>
</tr>
<tr>
<td>Muddy brown</td>
<td>Melanin in the superficial dermis, e.g. post-inflammatory pigmentation</td>
</tr>
<tr>
<td>Purple</td>
<td>Vascular lesions, e.g. angiomas</td>
</tr>
<tr>
<td></td>
<td>Other disorders where telangiectasia is a prominent feature, e.g. lupus pernio (chronic sarcoidosis), dermatomysis</td>
</tr>
<tr>
<td>Dusky blue</td>
<td>Reduced amounts of oxygenated haemoglobin, e.g. poor arterial supply, central causes of cyanosis, methaemoglobinemia</td>
</tr>
<tr>
<td>Violaceous and lilac</td>
<td>Lichen planus, edge of plaques of morphea, connective tissue disorders, e.g. dermATOMYSIS</td>
</tr>
<tr>
<td>Pink-red</td>
<td>Many exanthemata and common disorders, such as psoriasis</td>
</tr>
<tr>
<td>Red-brown</td>
<td>Inflammatory dermatoses, e.g. seborrhoeic eczema, secondary syphilis</td>
</tr>
<tr>
<td></td>
<td>Haemosiderin, e.g. pigmented purpuric dermatoses</td>
</tr>
<tr>
<td>Scarlet-red</td>
<td>Lesions with a strong arterial supply, e.g. pyogenic granuloma, spider naevus</td>
</tr>
<tr>
<td></td>
<td>Altered haemoglobin, e.g. carbon monoxide poisoning</td>
</tr>
<tr>
<td>Orange</td>
<td>Haemosiderin, e.g. lichen aureus</td>
</tr>
<tr>
<td></td>
<td>Inflammatory disorders, e.g. pityriasis rubra pilaris</td>
</tr>
<tr>
<td>Yellow-white/yellow-pink</td>
<td>Xanthomatous disorders</td>
</tr>
<tr>
<td>Yellow-orange</td>
<td>Carotenaemia (ingested carotene, myxoedema)</td>
</tr>
<tr>
<td>Yellow-green</td>
<td>Jaundice</td>
</tr>
<tr>
<td>Green</td>
<td>Exogenous pigment, e.g. copper salts</td>
</tr>
<tr>
<td>White-ivory</td>
<td>Lichen sclerosus et atrophicus, morphea</td>
</tr>
<tr>
<td>White (or pale pink, depending on vascularity)</td>
<td>Vitiligo, naevus anaemicus, arterial insufficiency, chemical depigmentation on vascularity</td>
</tr>
</tbody>
</table>

Stretching—may produce blanching of vascular lesions, and helps in visualizing lesions such as ‘submarine’ comedones, the elastomas of Buschke–Ollendorf syndrome and the glassy edge of a superficial basal cell carcinoma.

Rubbing—may cause release of chemicals, e.g. rubbing a mastocyteoma causes urtication and a flare due to histamine release (Darier’s sign), rubbing a neuroblastoma causes surrounding pallor due to catecholamine release.

Scratching and picking—scratching scale in psoriasis makes the scale appear more silver in colour by introducing air–keratin interfaces; more vigorous scratching or picking off the scale produces small bleeding points (Auspitz’s sign). Neither of these is specific to psoriasis. Removal of crusts overlying nodules may demonstrate the extent of the lesion, and additional diagnostic features, more accurately.

References

Additional simple clinical examination

Wetting the skin with water or mineral oil (which lasts longer) fills air spaces in scale and allows underlying features to become more visible. In some instances, this just enhances underlying redness—for example, in psoriasis. In other instances, diagnostic features may become apparent to the naked eye (such as Wickham’s striae in lichen planus) or with the aid of additional magnification (e.g. use of a dermatoscope to examine pigmented lesions). Soaking of the skin may make the lesions of pitted keratolysis more apparent.

Application of heat or cold may identify specific physical urticarias. Whole-body warming may confirm cholinergic urticaria. Even whole-body cooling has been used, to identify dysarthria as being due to Raynaud’s phenomenon of the tongue.

Pinprick sensation may be lost in leprosy, and decreased light touch sensation (using specific graded monofilaments) can predict diabetes-related neuropathic ulceration.

Paring the skin allows distinction between a wart and a corn, or may confirm the presence of old blood in talon noir or a haematoma.

Smell may be useful—for example, in suspecting anaerobic wound infection, or in diagnosis of rarities such as trimethylaminuria.

Simple microscopy may be diagnostic for hair shaft abnormalities and for distinguishing between hair casts and head lice egg cases (nits), and is used to detect cutaneous fungal disease. Dermoscopy, an in vivo form of magnification, is discussed on p. 5.20.
Table 5.8 Uses of Wood’s light.

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fungal infection</strong></td>
<td>Tinea capitis—green fluorescence associated with Microspora species and favus (see also Chapter 36)</td>
</tr>
<tr>
<td></td>
<td>Pityriasis versicolor—yellow</td>
</tr>
<tr>
<td><strong>Bacterial infections</strong></td>
<td>Erythrasma, acne—coral pink (porphyrins)</td>
</tr>
<tr>
<td></td>
<td><em>Pseudomonas pyocyanea</em>—yellowish green (pyocyanin)</td>
</tr>
<tr>
<td><strong>Infestations</strong></td>
<td>Scabies—fluorescein solution fills the burrows and can be viewed with Wood’s light</td>
</tr>
<tr>
<td><strong>Porphyrias (see also Chapter 59)</strong></td>
<td>Urine, faeces and occasionally blister fluid fluoresce in porphyria cutanea tarda; teeth in erythropoietic porphyria; blood in protoporphyria</td>
</tr>
<tr>
<td><strong>Pigmentary disorders</strong></td>
<td>Vitiligo is accentuated (see text), dermal pigment becomes less apparent</td>
</tr>
<tr>
<td></td>
<td>Detection of ash leaf macules in tuberous sclerosis</td>
</tr>
<tr>
<td><strong>Drugs and chemicals</strong></td>
<td>Detection in tissues, e.g. staining of teeth or sebum from tetracyclines and of the nails from mepacrine</td>
</tr>
<tr>
<td></td>
<td>Detection of fluorescent contact or photosensitizers on the skin, or in cosmetics and industrial agents, e.g. ballpoint-pen ink, eosin, furocoumarins, halogenated salicylanilides, pitch ingredients</td>
</tr>
<tr>
<td></td>
<td>Fluorescein can be added to topical medications to investigate sites of application or of manipulation (e.g. in the investigation of dermatitis artefacta)</td>
</tr>
<tr>
<td><strong>Tumours</strong></td>
<td>Red fluorescence can occur in some malignant tumours and other lesions of the skin, especially squamous cell carcinomas</td>
</tr>
<tr>
<td></td>
<td>Conversion of aminolaevulinic acid to protoporphyrin IX occurs within tumours as the first step in photodynamic therapy and can be detected with Wood’s light</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>Lipofuscins in sweat from patients with chromhidrosis can be identified by Wood’s light examination of stained clothing</td>
</tr>
<tr>
<td></td>
<td>Research use of fluorescent ‘markers’ for the investigation of cutaneous penetration and epidermal turnover</td>
</tr>
<tr>
<td></td>
<td>Detection of mineral oil on the skin in the assessment of barrier creams</td>
</tr>
</tbody>
</table>

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**Additional clinical investigations**

**Diascopy**

Pressing a glass slide or (more safely) a stiff, clear, colourless piece of plastic onto the skin compresses blood out of small vessels, to allow evaluation of other colours. Diascopy is of particular value in detecting granulomatous nodules, which have a translucent brownish colour known as ‘apple jelly’ nodules (e.g. in lupus vulgaris). In naevus anaemicus, a localized area of vasoconstriction, other pigments are unaltered—diascopy of adjacent skin therefore reveals an identical colour to that of the ‘depigmented’ area. By contrast, diascopy of skin adjacent to vitiligo, in which there is loss of melanin, demonstrates that the vitiligo remains paler. Application of medium pressure to a spider naevus can compress radiating arterioles and allow visualization of pulsatile flow in the feeding vessel.

**Wood’s light**

This is a source of ultraviolet light from which virtually all visible rays have been excluded by a Wood’s (nickel oxide) filter. Applications of Wood’s light are listed in Table 5.8 [1,2].

Variations in epidermal pigmentation are more apparent under Wood’s lamp than under visible light, whereas variations in dermal pigment are less apparent [3]. Thus, for example, it can be used to distinguish vitiligo from naevus anaemicus. Vitiligo is due to loss of epidermal melanin, and the depigmented areas are greatly exaggerated under Wood’s light; naevus anaemicus is due to localized dermal vasoconstriction with normal overlying epidermal pigmentation, and the pallor completely disappears under Wood’s light. The ash-leaf macules of tuberous sclerosis are much more prominent under Wood’s lamp [3].

Many organisms produce chemicals that fluoresce under Wood’s light [4, 5] including *Propionibacterium acnes* [6], and *Corynebacterium minutissimum*, the bacterium responsible for erythrasma (Fig. 5.18), and conversion of aminolaevulinic acid to protoporphyrin occurs in several tumours and other skin lesions, leading to the technique of photodynamic diagnosis [7] as well as photodynamic therapy (Chapter 78). Fluorescein can be added to topical agents in studies of their use—for example, to detect areas that are missed during sunscreen application [8]. Wood’s light can also be used to view *ex vivo* specimens, such as blood or urine in porphyrias [9], or even inanimate objects, such as clothing from patients with chromhidrosis [10].

There are pitfalls of using Wood’s light:

- It is useful to diagnose tinea capitis acquired from cats or dogs, but most fungi do not fluoresce, so a negative test does not exclude the diagnosis.

- There is some reflection of light from any scaly dermatosis, which may be confused with the relatively subtle colour change of pityriasis versicolor.

- Optical brighteners in detergents fluoresce strongly—white shirts and coats may be a considerable distraction.

- Erythrasma fluoresces pink due to porphyrins—it is a reasonable frequent finding that the expected fluorescence is negative if the affected skin has been washed prior to a clinic appointment.

**References**

Clinical microscopy, dermoscopy and other imaging systems

Microscopy is an important laboratory technique, discussed briefly later. However, microscopy in a clinical setting also has several uses.

Dermoscopy

This technique, also known as dermatoscopy or epiluminescence microscopy, is an extension of the use of simple magnification. Dermoscopes have built-in illumination, and are applied to the skin surface with a film of oil on the lesion to enhance visibility of subcorneal structures. The technique is mainly used in the diagnosis of doubtful pigmented lesions (Chapter 54). The images may be viewed directly, photographed or recorded digitally for subsequent or sequential analysis. A structured system of analysing the colours and appearances of the structural elements (pigment network, globules and dots, horn cysts and pseudofollicular openings and the vascular patterns visualized) may increase the accuracy of diagnosing malignant melanoma [1]. Scoring systems such as the ABCD dermoscopy score (assessing asymmetry, border colour and dermatoscopic structures) [2] and a ‘seven-point check list’ [3] have been devised. Computerized image analysis is being developed to aid in distinguishing benign melanocytic lesions from melanoma [4]. Dermoscopes can also be useful in distinguishing haemangiomas, angiokeratomas, pigmented basal cell carcinomas and seborrhoeic keratoses from melanocytic lesions. More novel uses include the identification of scabies burrows and mites, diagnosis of tungiasis and other parasitic infections.

Other imaging systems for localized lesions

Spectrophotometric image analysis of pigmented lesions (SIAscopy) allows the assessment of eight narrow-band spectrally filtered images of the skin over an area of 24 × 24 mm with radiation ranging from 400 to 1000 nm. The value of this technique as an adjunct to clinical examination and dermoscopy has produced differing opinions [1–3]; it has also been used in diagnosis of non-melanoma skin cancers [4], and used with an algorithmic approach to diagnosis [5].

In vivo confocal laser scanning microscopy (CLSM) represents a novel imaging tool that allows the non-invasive examination of skin cancer morphology in real time at a ‘quasi-histopathological’ resolution, viewing microanatomical structures and individual cells. It may show promise in the assessment of suspected melanoma [6].

Identification of scabies mites

Scabies mites can be extracted from the end of a burrow using a needle, with microscopy to confirm the diagnosis. The technique can be useful to convince sceptical sufferers of their infestation. Alternatively, application of mineral oil [1] or 5% potassium hydroxide to an affected interdigital space, followed by light scalpel scraping, reveals the acarus or its eggs. The faecal pellets (scybala) of the mite are also diagnostic, but are dissolved by potassium hydroxide; they remain intact in oil. Burrows can also be removed by a very superficial shave technique, and can be made more apparent by application to the skin of either black ink, or fluorescein with Wood’s light visualization. Dermoscopy (see above) can also be used—the mite appears as a dark triangle shape—or higher-resolution microscopy with a standard light microscope [2]. Outwith the scope of this section, scabies can also be identified using polymerase chain reaction (PCR) to detect mite antigens [3].
Other simple microscopy procedures

Simple light microscopy is helpful in evaluating hair shaft abnormalities (this, and more complex electron microscopy, are discussed in Chapter 66).

Microscopy of skin scrapings for fungi is discussed in Chapter 36. Scraping the base of a herpetic vesicle with simple Giemsa staining may reveal giant cells (Tzanck smear); molluscum contagiosum can be identified in a similar fashion. Examination of skin pustule smears after fixation and haematoxylin and eosin staining may be useful in the rapid diagnosis confirmation of infantile eosinophilic folliculitis and incontinentia pigmenti; in both conditions, the pustules are filled with eosinophils.

Skin surface biopsies using tape-stripping or adhesive microscope slides pressed onto the skin allow observation of cells of the stratum corneum and of bacteria, fungi such as Pityrosporon species, and Demodex mites [1–3]. Plastic polymer (Silflo) skin surface impressions may be useful for the study of eccrine gland pore size and numbers.

References

Fine-needle aspiration of lymph nodes (FNA)

Aspiration of lymph node tissue using a 25- or 27-gauge needle allows cytological assessment of lymph nodes and is useful in the staging of metastatic malignant melanoma and squamous cell carcinoma of the skin, as well as the assessment of lymph nodes in suspected lymphoma. In patients with palpable lymph nodes and melanoma, the technique has been shown to have high specificity and sensitivity [1] (Fig. 5.19). Combining the technique with flow cytometry can help in the differentiation of lymphoma from reactive and dermatopathic lymphadenopathy [2].

References

Commonly used laboratory tests

Numerous special investigations are used to refine a dermatological diagnosis, or for disease or therapy monitoring. Many of these are discussed specifically in relevant chapters—for example, testing for photosensitivity (Chapter 29) or for contact allergy (Chapter 26). The commonest tests which involve additional laboratory processing of samples are as follows:

• Blood tests for haematology or biochemistry. These are used in numerous situations, both diagnostically and for assessing the impact of a skin disease or for monitoring systemic therapy. Many infective disorders or acute inflammatory conditions are associated with neutrophilia or with abnormal results of inflammatory markers such as erythrocyte sedimentation rate or C-reactive protein; eosinophilia is also a feature of several dermatological conditions (briefly listed in Table 5.9, and discussed in more detail in Chapter 62).

• Blood tests for immunological studies. For example, in the diagnosis of connective tissue diseases (Chapter 51), IgE and radioallergosorbent test (RAST) in atopic and allergic diseases (Chapters 13 and 24).

• Histology of skin biopsy (Chapter 10). This may include special staining methods, direct immunofluorescence studies and immunocytochemistry. ‘Rush’ frozen sections may be necessary—for example, during micrographic surgery or in the urgent diagnosis of some blistering conditions [1].

Table 5.9 Some ‘dermatological’ causes of eosinophilia (more than $0.44 \times 10^9/L$ eosinophils).

| Atopic disorders, especially asthma and eczema |
| Parasitic infestations |
| Worms (intestinal or systemic) |
| Scabies |
| Allergy to food or drugs |
| Tryptophan myalgia syndrome |
| Collagen vascular disease (especially polyarteritis nodosa and variants), dermatomyositis and eosinophilic fascitis |
| Malignancy, especially Hodgkin’s disease and eosinophilic leukaemia |
| Bullous disorders |
| Dermatitis herpetiformis |
| Pemphigus |
| Pemphigoid |
| Erythema neonatorum |
| Hypereosinophilic syndrome |
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- Other immunological and microscopy studies for bullous diseases, e.g. immunoblotting (Chapter 40) and electron microscopy (Chapters 16 and 39).
- Bacteriological and mycology samples (Chapters 30–37). May include samples for microscopy and culture, serological tests, PCR tests (e.g. for mycobacteria).
- Cytological examination. Usually in the context of FNA from lymph nodes, discussed above.

Reference

Radiological and imaging examinations

These have an important role in dermatology, but less than in many other specialties, because the skin can so readily be seen and felt. Ultrasound [1,2], magnetic resonance imaging (MRI) [3–5], radio-isotope scans and even positron emission tomography (PET) [6,7], are all used in clinical dermatological practice, mainly in relation to detection of lymphadenopathy or other metastatic skin cancer. High resolution ultrasound is increasingly important in documentation of nodal enlargement and tumour infiltration, and can be used to guide biopsies. Other uses of radiological procedures in dermatology include, for example, for the accurate assessment of the thickness of lesions in scleroderma, the extent of infection in severe forms of cellulitis (and distinction, using MRI, from necrotizing fasciitis), and assessment of local invasion of tumours. Various imaging techniques are also important in the management of diseases such as neurofibromatosis, where there may be central nervous system involvement, or in the assessment of muscle change in dermatomyositis. Lymphoscintigraphy may be a useful functional assessment of the lymphatic system of the swollen lower limb (Chapter 48). Doppler assessment of the peripheral lower limb arteries is an essential bedside technique prior to the use of high-compression bandaging in the management of venous leg ulcers (see Chapter 47); use of standard electronic sphygmomanometer systolic pressure measurements is not accurate in measurement of peripheral arterial pressures [8].

References

8 Aboyans V, Lacroix P, Doucet S et al. Diagnosis of peripheral arterial disease in general practice: can the ankle-brachial index be measured either by pulse palpation or an automatic blood pressure device? Int J Clin Pract 2008; 62: 1001–7

Skin testing

Substances may be introduced into the skin by a variety of techniques to study pathological and immunological [1] reactions under controlled conditions. Such tests are extremely valuable, but details of the type of test and the time at which it is read must correspond to the pathological process under consideration. Interpretation of the relevance of tests, either positive or negative, must always be correlated with the clinical picture. All too often, evidence adduced from tests is either meaningless or misleading.

Absorption of many substances through the intact skin is poor and variable, but direct application to the surface of the skin is used for patch testing. The epidermal barrier may be overcome either by removing it or by introducing the material directly into the dermis. The following techniques for skin testing are most commonly used.

Techniques for skin testing

**Epicutaneous tests—patch tests**

Patch tests are usually used to detect contact allergy of the delayed hypersensitivity type. They are usually read at 48–72 h and again up to 1 week, but can also be read at 15–30 min to detect contact urticaria. At times, patch testing may usefully be combined with scratch testing. Details of these techniques are discussed in Chapter 26.

**Intradermal injection**

The injection is made into the superficial layer of the dermis through a fine-bore (26- or 27-gauge) needle with its bevel pointing upwards. The quantity that may conveniently be injected varies from 0.01 to 0.1 mL. Precise measurement of smaller quantities is difficult and requires syringes with especially well-fitting plungers and a micrometer screw gauge. For routine clinical purposes, an approximation is sufficient—either 0.05 mL or the amount that just causes a visible weal (0.01–0.02 mL).

The optimal time for reading the reaction naturally varies with the pharmacological agent or the type of immunological reaction. Most such tests are read at either 15–20 min or at 48 h, but it may be important to read the tests at other times, for example at 4–12 h or after 4 days. The response to be observed at 15 min—for example, after an injection of histamine or after immediate-weal allergy tests—is a weal with a surrounding flare (Fig. 5.20). The weal is a more accurate measure than the flare. When the test is read at 48 h—for example, in the tuberculin reaction—the sizes of the indurated papule and of the erythematous reaction should be observed.

The site of the test is of some importance [2,3]. In general, the whole skin surface is capable of responding to skin tests, but there are regional variations. The back and the flexor aspects of the forearms are most conveniently used. The skin on the ulnar aspect of the forearm is more sensitive than the radial, and the proximal
more sensitive than the distal. These differences are not of sufficient magnitude to affect routine testing, but must be taken into account by using symmetrical areas for controls in any accurate quantitative testing.

A test solution must always be compared with a control solution injected in a comparable site at the same time. A positive test may be taken as one that is significantly different from the control. Assessment of what is significant is difficult, and varies with the enthusiasm of the tester. If a difference of less than 5 mm is accepted, reproducible results may not be obtained on retesting [4].

The measurement of a weal is usually made by diameter, although more sophisticated methods, such as volume measurements and Doppler flow, have been used [5]. If the weal is not circular, an approximation may be made by averaging maximum/minimum diameters, or more accurately the area may be calculated by the formula $D_1 \times D_2 \times \pi/4$, where $D_1$ and $D_2$ are the maximum and minimum diameters [6]. For irregular weals, a tracing may be made on squared paper. Pseudopodia should be noted, but for measurement of diameter they are ignored. Attempts to assess the volume of a weal are less satisfactory for routine use.

The size of the weal is not directly proportional to the dose of the active agent, but varies also with the total volume of fluid injected. An approximation of a linear relationship may best be achieved, often only over a narrow range, by plotting the response against the log dose. For accurate quantitative observations, weal diameters below 4 mm or above 15 mm cannot be relied upon.

Antihistamines may greatly inhibit the immediate weal tests. In the case of very long-acting agents, this effect may last as long as 3 weeks. They have no appreciable effect on delayed hypersensitivity patch tests. Moderate to large doses of corticosteroids, in contrast, may somewhat inhibit patch tests, although smaller doses—for example, prednisone 10 mg daily—are not necessarily a contraindication to testing. Steroids do not greatly inhibit the immediate weal tests. When a patient feels faint, any immediate weal test may be completely inhibited.

**Prick test**
This is a modification of the intradermal injection. A small quantity of the test solution is placed on the skin and a prick is made through it with a sharp needle. This should be superficial and not sufficient to draw blood. The quantity has been estimated as $3 \times 10^{-6}$ mL [3]. The size of the weal and flare are measured after 15 min (Fig. 5.20). This test gives reproducible results and is convenient for much routine allergy testing. Because of the discrepancy in quantities injected, the testing solutions are made up at different strengths for prick testing and intradermal testing. The intradermal injection of prick-test solutions may be dangerous.

**Scratch test**
The scratch test resembles the prick test. A linear scratch about 1 cm long, but not sufficient to draw blood, is made through the epidermis. This test gives less reproducible results than the prick test.

**Modified prick test**
Here, a drop of the test solution is placed on the skin. A needle is then inserted very superficially and almost horizontally into the skin and lifted to raise a tiny tent of epidermis. This test is slightly more sensitive than the ordinary prick test, but gives no more reproducible results.

**Skin-window technique** [7,8]
The surface of the skin over an area a few millimetres square is scratched off with a scalpel, the test solution applied and the area covered with a coverslip. This is removed at various intervals—for example, 3 h, 6 h, 12 h, 24 h and 48 h—and immediately replaced by another coverslip. The cells on the coverslip are stained with ordinary haematological stains. The cellular response at varying time intervals can be assessed.

References

Immediate weal tests
These tests are used for detecting IgE antibodies. The passive transfer test may be used to detect circulating IgE, but is not recommended because of the risk of serum hepatitis or human immunodeficiency virus (HIV). These antibodies play a role in hay fever, asthma, atopic dermatitis and anaphylactic reactions. They occur especially, but not exclusively, in patients with a personal or family background of atopy. Positive skin tests to a wide variety
of antigens are extremely frequent in these patients and must always be correlated with the history. They are principally used in the assessment of hay fever and asthma and have a limited place in the management of atopic dermatitis (Chapter 24). They are disappointing in the diagnosis of urticaria. False-positive and false-negative reactions are common.

Severe systemic reactions and, very rarely, fatalities may occur after correct use of standard testing solutions, and epinephrine (adrenaline) and hydrocortisone injections should always be at hand when skin tests are performed [1,2].

Alternative methods of detecting and measuring circulating antibodies are the RAST and the enzyme-linked immunosorbent assay (ELISA). RAST correlates well with skin testing [3,4]. It is particularly useful (i) in testing very young children; and (ii) with allergens associated with risk on prick testing (e.g. drugs).

The autologous serum test is a technique used in the investigation of chronic idiopathic urticaria whereby the patient's own serum is injected intradermally. It is regarded as being positive if at 30 min there is a weal 1.5 mm larger than at the saline control injection site. Positive reactions are indicative of functional auto-antibodies against the high-affinity IgE receptor FceRI, or against IgE [5] (Chapter 22).

Delayed (4–8 h) tests
The clinical interpretation of tests that are positive at 4–8 h can be difficult. Sometimes, these represent an Arthus reaction, but ideally this should be confirmed histologically. Other such tests represent a delayed variant of the immediate weal (15-min) test.

Intradermal tests for the detection of delayed sensitivity to bacterial, fungal and viral antigens

The tuberculin test. Testing for evidence of tuberculosis has achieved new importance in dermatology, in part because of an increasing incidence of tuberculosis associated with HIV infection, and also because screening is a necessary part of the work-up before use of antitumour necrosis factor biological drugs (for example, in psoriasis). A positive result to the standard strength (10 tuberculin units, TU) is an indication of previous mycobacterial infection, but not necessarily by Mycobacterium tuberculosis (especially if the reaction is weak or doubtful). Reactions to 1 TU (1/100 dilution of purified protein derivative (PPD)) are, however, significant. In sarcoidosis, reactions may be wholly negative, or only positive to 100 TU. The minimum size of a positive reaction is taken as 5 mm. An intermediate (24-h) reaction sometimes occurs.

Comparable doses of PPD may vary according to their source. Misleading negative reactions may occur in anergic patients. Tuberculin tests are discussed further in Chapter 31.

The Heaf test. Used in mass testing and in children. It is roughly equivalent to, or perhaps slightly more sensitive than, a dilution of 1:100 old tuberculin [6].

Candida antigen is used in a similar manner to the tuberculin test. Depressed reactivity occurs in sarcoidosis and other immunosuppressed conditions. Negative reactions in normal subjects are, however, not uncommon and depend on age and locality.

Trichophytn detects past infection by Trichophyton species. Its value is limited.

The lepromin test. This is discussed in Chapter 32.

Histoplasmin, coccidioidin and similar antigenic tests are of most value in areas where these diseases are not endemic. The Frei test and cat scratch fever antigen are of some value in the UK, where the relevant diseases are comparatively rare. A positive reaction is then significant. Conversely, Brucella antigen and toxoplasmin are of limited use in dermatological practice.

Delayed-type bacterial antigen tests [7–9]. These are not widely used, partly because their specificity and interpretation are difficult to assess. They consist of standard preparations of bacterial extracts, each probably containing a mixture of antigenic components, which may produce an immediate, or delayed 48-h reaction or an even later reaction. The normal 48-h response is a papule showing, histologically, a tuberculin-type reaction of lymphocytic type. Occasionally, however, especially in cases of vasculitis, an acute leukocytoclastic reaction occurs within 6–8 h [8] and is fully established at 24–48 h. Sometimes, the reaction is severe enough to produce a sterile abscess. It is tempting to believe that these reactions may be of some significance in conditions such as erythema multiforme, erythema nodosum (streptococcal), allergic vasculitis and, perhaps, pustular psoriasis. However, the antigens at present in use are relatively impure and the reactions may be non-specific. Further careful immunological studies are required.

Long-delayed (6-week) intradermal reactions. These comprise the Kveim test and the Mitsuda test. They are read at 6 weeks, but biopsy is essential with the Kveim test. Kveim test antigen is no longer available in the UK.

References
Oral provocation tests

The administration of a drug, food or chemical by mouth may sometimes be called for to confirm the diagnosis of an eruption or to establish its exact cause. Such tests are used in the following situations.

1 To determine the cause of a drug eruption or to isolate one from a number of drugs or ingredients of a compound drug. It is applicable only when the drug given and the dose chosen are unlikely to provoke a severe reaction in the patient. It may be a valuable method of proving the cause of a fixed drug eruption but should rarely, if ever, be used if the reaction has been of a generalized or acute nature. The subject is discussed in more detail in Chapter 75.

2 In the course of the investigation of food allergens [1–3]. The reintroduction of specific foods, one at a time, is an established part of exclusion, elimination and challenge diets. It is important that the role of the suspect food is subsequently confirmed by reintroducing it in a disguised form to avoid identification by the patient. The procedure is applicable to patients with atopic eczema (Chapter 24), chronic or recurrent urticaria (Chapter 22) and possibly to some other dermatological conditions that have an allergic basis. However, it must be carried out with care and is only valuable if the tests are properly controlled and the patient is cooperative and well motivated.

3 In establishing the role of additives in chronic urticaria or angio-oedema (Chapter 22). Tartrazine, benzoates and antioxidants have been especially implicated [4–6]. Although oral provocation with increasing test doses of these substances is theoretically simple, the same reservations apply, and the administration of the diets and the ‘blind’ challenge require time, patience and motivation. Audit has shown that these tests appear to benefit the patient at low cost, but their scientific validity remains uncertain [7].

The role of oral nickel and chromate in the behaviour of endogenous hand eczema has been studied [8,9]. Some authors have produced flares of vesicular hand eczema after oral administration of nickel, but others have been unable to reproduce these results when interspersing test doses with placebo capsules.

Oral provocation with balsam of Peru was used in a series of 221 patients [10]. Flares of an existing dermatitis occurred in 45 patients, only 17 of whom had shown positive patch-test reactions to this substance. Subsequent dietary restriction of flavourings was said to clear or ‘markedly improve’ the dermatitis in half the patients.

Sublingual food tests are unreliable [11].

References


Telemedicine

Considerable clinical experience is needed in order to make correct dermatological diagnoses, and since trained dermatologists are in relatively short supply even in many developed countries, telemedicine—remote consultation via an electronic link—may become an attractive option. It is particularly useful in remote or rural areas where there are no specialists.

Dermatologists have for many years conducted long-range consultations by telephone or by mailing histology slides or clinical photographs, but the unique feature of telemedicine is the two-way electronic network that now allows immediate interactive communication between the patient, the primary care physician and the specialist (so-called real-time teleconsultation). Different parts of the patient can be viewed at various magnifications, and the specialist can ask supplementary questions and advise on the most suitable biopsy sites if necessary. Such teleconsultations may be extremely valuable for obtaining international specialist opinion. A less satisfactory, but relatively time-efficient approach is the ‘store and forward’ system, whereby history details and images taken remotely are reviewed later by a distant specialist. Both for the primary care physician and specialist, teleconsultation time exceeds the duration of face to face consultation [1]. This does not allow simultaneous supplementary history and directed image choice, which may hamper appropriate management.

Several trials have shown that telemedicine can be effective, with high levels of satisfaction reported by patients, GPs and hospital specialists [2–4] though good photographic technique and lighting are essential for optimal results. It may be useful for tumour triage as well as assessing inflammatory dermatoses [5]. A personal encounter between specialist and patient may offer additional advantages, such as enhanced information about the patient’s personality, with more patient participation in decisions and a placebo effect, which can lead to greater compliance [6]. The ability to palpate and smell can also give valuable diagnostic information (p. 5.17) but telemedicine clearly has considerable potential for dermatological diagnosis. With the ubiquity of high resolution mobile phone cameras, an increasing number of patients bring images of themselves, and this may be valuable in assessing evanescent eruptions. Mobile phone teledermatology may help in triage [7,8].

References