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ESSENTIALS As in most medical specialties, the diagnosis of skin disease relies on careful history taking, and a thorough examination, supported in some cases by appropriate investigation. Astute physicians will also be aware that management outcomes are improved by taking account of the impact of skin disease on patients' lives, whether through discomfort, disfigurement, or disability. This chapter, how- ever, is chiefly concerned with aspects of history taking and examin- ation that inform the diagnostic process. History taking There are certain key points in the history of skin disease that should be specifically elicited, and these are summarized in Box 23.2.1. These should include a description of the events surrounding the onset of skin lesions: when and where the eruption started, and how it progressed. Neoplasms are likely to be relatively asymp- tomatic and persistent, whereas inflammatory disorders can itch, scale, or ooze, and frequently fluctuate. The rapidity of fluctuation is helpful; urticaria and eczema are both intensely itchy, but are dis- tinguished by the fluctuation of the individual lesions of urticaria over hours, rather than days or weeks as in eczemas or psoriasis. The site of onset might also give a clue to the diagnosis and cause of a rash. The history should include an enquiry into general health, both past and present, and of skin disease, including specific enquiry about the personal and family history of psoriasis and the atopic disorders eczema, asthma, and hay fever. If more than one house- hold member is affected this might indicate heredity or contagion. Occupation, travel, or residence abroad, leisure activities, and hobbies might indicate exposure to the sun, irritant or sensitizing chemicals, or infections. Many patients will already have tried top- ical treatment before presentation, either self-medicated or phys- ician prescribed, and the response to these, whether beneficial or adverse, can be helpful in diagnosis. Drug-induced skin disease is important, and a full history of drugs taken for other disorders is essential. Examination Dermatology differs from other specialties because the disease is visible to the naked eye, and the lesions can also be touched and palpated. However, it is necessary to know what to look for and to understand what is seen and felt. To examine the skin

properly the patient should ideally be undressed, and examined in a good light, preferably daylight. Distribution Before concentrating on the appearance of the individual lesions, much can be deduced from their distribution. The distribution of lesions in many common dermatoses is so characteristic that it fre- quently aids diagnosis. In some diseases, the pattern might reflect regional variations in skin structure (e.g. acne vulgaris favours areas rich in pilosebaceous units, such as the face and upper torso). Other disorders are distributed according to exposure to external causative agents (e.g. points of contact with irritants/allergens or sun exposure) (Fig. 23.2.1). Gravity and stasis underpin the distribution of varicose eczema on the lower legs. The sluggish blood flow of stasis also favours immune-complex deposition, and explains the frequency of vasculitis lesions on the lower legs (Fig. 23.2.2). In other instances the factors affecting distribution are not necessarily fully understood but, nonetheless, observation of the distribution can be crucial to diagnosis. Is the skin disease localized or generalized? Is it symmetrical? What specific sites are involved? It is important to examine not only the skin itself, but also the hair and nails, and the mucous membranes (particularly inside the mouth). Symmetry Although the basis for the body symmetry of rashes is not fully understood, the presence or absence of symmetry serves as a useful pointer in diagnosis. Rashes showing bilateral symmetry are frequently suggestive of endogenous skin disease. The most common inflammatory dermatoses—atopic eczema and psoriasis, having a strong hereditary component in their pathogenesis—are regarded as endogenous or constitutional dis- eases, and both show striking symmetry in the distribution of
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 their lesions (Fig. 23.2.3). Symmetry is not confined to the major heritable skin diseases; several skin diseases are regarded as re- actions to underlying triggers. Although these might not have a genetic basis, they behave like intrinsic disorders and, as such, frequently show symmetry. Examples of these are most drug eruptions, viral exanthema, erythema multiforme provoked by a cold sore or other trigger, and dermatitis herpetiformis (the rash of gluten sensitivity). By contrast, rashes and lesions caused by exogenous factors such as the random behaviour of a biting insect, contact with allergenic or irritant substances, or with infections like bacterial impetigo are commonly, but not necessarily, asymmetric. A foot dermatitis that affects only one foot should prompt investigation for fungal infection. Site Certain conditions have a predilection for characteristic sites, and knowledge of the favoured sites is diagnostically important. Psoriasis favours the extensor surfaces of elbows and knees, and also affects the scalp, nails, and gluteal cleft. By contrast, atopic eczema favours the flexures (Fig. 23.2.3b), for example, antecubital and pop- liteal fossae, and other sites. This distinguishes it from seborrhoeic eczema, which prefers the scalp and ears, central face (eyebrows, nasolabial folds), mid chest, and groins. Lesions provoked by sunlight predominate on exposed skin (e.g. skin cancers, idiopathic or drug-induced photosensitive rashes, lupus erythematosus). In some sun-induced rashes there might be a sharp cut-off under clothing, or sparing of shielded sites (e.g. under the chin and behind the ears). Contact derma- titis to airborne pollens, such as those of the Compositae family (Fig. 23.2.1), or volatile allergens such as epoxy resin glues, will not spare these shielded sites, but might show a similar cut-off at the collar. The distribution of some important diseases is shown in Fig. 23.2.4. Morphology Many skin diseases have characteristic lesion morphology, although scratch marks, ulceration, and secondary infection can modify the appearance. A good light is essential, and a hand lens is helpful. Touch and palpation give important information about the thick- ness, depth, consistency, and tenderness of lesions, and

whether the surface is rough or smooth. Ideally, a primary lesion should be sought for deciding lesion type, one that has not been damaged by picking, scratching, or prior application of creams or anything else likely to eradicate important clues. To aid the clear and unambiguous description of lesions, certain terms are used, the most important of which are listed in Table 23.2.1. The lesion type, colour, and surface characteristics should be recorded, the aim being to try to glean as much information as possible about the underlying pathology. Redness (erythema) Fig. 23.2.1 Eczema confined to exposed skin. In this case, it is resulting from contact dermatitis to an airborne allergen (Compositae pollen), but a similar cut-off under clothing can occur with photosensitivity. Box 23.2.1 Outline of dermatological history • History of present skin condition — Duration — Site of onset — Details of spread or enlargement — Does it fluctuate or persist? — Provoking or aggravating factors — Symptoms (e.g. itch, burning, soreness, pain, bleeding, weeping, oozing, blisters, odour) — Impact on quality of life • Past history of skin disorders • Past and present general medical history — Ask specifically about asthma and hay fever • Family history — Ask specifically about eczema, asthma, and hay fever (the atopic disorders), and psoriasis • Social history — Occupation, travel, and leisure activities — Particularly enquire about sun exposure and burning episodes • Medication used to treat present skin condition — Topical or systemic — Physician prescribed or over the counter • Drugs taken for other disorders — Allergies to medication, or contact allergens Fig. 23.2.2 These purpuric lesions are palpable rather than flat, indicating vasculitis. The distribution on the lower legs is common.

section 23 Disorders of the skin 5598 resulting from vasodilatation of the upper dermal vasculature will blanch on pressure, and indicates inflammation. If purpuric lesions are present, attention should be paid to whether they are entirely flat (macular) or are palpable, the latter indicating a more profound degree of vascular pathology than mere leakage, and sig- nifies the presence of vasculitis (Fig. 23.2.2). The presence and nature of scale is a physical sign of great im- portance. Keratin is the principle protein product of the epidermis, and constitutes up to 90% of the stratum corneum. Any disease, whether inflammatory, infective, or neoplastic, that affects the epidermis will disrupt keratin production, resulting in scaliness. The importance given to scale is indicated by the large number of synonyms used by dermatologists to describe it (scaly, keratotic, hyperkeratotic, keratinized, warty, verrucous). Scale can be par- ticularly thick and loosely adherent in psoriasis, making it ap- pear light in colour (silvery scale), or is sometimes dense and compacted. Very acute inflammation of the epidermis will also result in ves- iculation and oozing, as in the case of acute eczemas and superfi- cial bacterial infections, or might result in an influx of neutrophils leading to pustule development in bacterial and candidal infec- tions, and in some forms of psoriasis. The presence of epidermal signs (scale, vesicles, ooze, pustules) indicates that the pathology is chiefly or solely superficial, and differentiates these diseases from those that are chiefly dermal. Deep-seated dermal or sub- cutaneous inflammatory or neoplastic infiltrates are more likely to form lumps or swellings, which can distort the epidermis from below, but may not actually disrupt it, so that the surface is more likely to be smooth with skin markings preserved. This distinction between epidermal and dermal diseases is not of course absolute, and many disorders affect both, but this artificial separation helps to focus the examiner on the question: Where is the pathology? The appearance of some lesions might be so characteristic that occasionally they permit an immediate confident diagnosis, an ex- ample being lichen planus when present in its most typical form, with shiny, flat-topped, mauve-coloured papules with surface white streaks (Wickham’s striae). Other lesion types might not permit immediate diagnosis, but are still sufficiently distinctive as to be a useful starting point for a differential diagnosis, an example being

vesicles and bullae (blisters). Common causes of blisters include burns, acute eczemas, viral infections such as Herpes spp., and in- fection with Staphylococcus aureus (bullous impetigo). Rarer causes of blisters include erythema multiforme, immunobullous diseases (e.g. pemphigoid, pemphigus), and some porphyrias. Lesion shape and grouping Additional diagnostic clues are afforded by the lesion shape and the way they are grouped. Distinctive lesion shapes are annular, target- shaped, and linear. Annular lesions imply inflammation spreading out centrifu- gally from a central focus, with clearance in the centre. This pat- tern is characteristic of dermatophyte fungus infection of skin (tinea corporis or ringworm; Fig. 23.2.5), which, being a superfi- cial infection, is accompanied by subtle scaling, particularly at the margin. Granulomas in the dermis form a characteristic ring in granuloma annulare. These lesions are palpable, but the overlying epidermis is smooth. Reactive erythemas frequently assume an an- nular shape (also known as annular or toxic erythema; Fig. 23.2.6). The margin is red, slightly elevated, and can be very slightly scaly. Annular erythemas evolve at a variable rate; the slow enlargement of erythema chronicum migrans (the eruption of early Lyme disease) occurs at a rate of a few centimetres per day, rather than over hours, and eventually fades within a few weeks. Reactivation of inflamma- tion at the centre of annular erythema produces target lesions char- acteristic of, but not exclusive to, erythema multiforme. The close clustering of individual lesions into groups is some- times distinctive. The grouping of vesicles in herpes simplex (Fig. 23.2.7) is so characteristic that other diseases which show (a) (b) Fig. 23.2.3 Both atopic eczema and psoriasis show classical epidermal signs (scaliness), but have different distributions. Symmetry is characteristic of many endogenous skin diseases. (a) Extensive psoriasis. The symmetry of psoriatic lesions may be dramatic and striking. (b) Itchy, scaly, inflamed skin in a symmetrical flexural pattern. This is typical of atopic eczema.

23.2 Clinical approach to the diagnosis of skin disease 5599 Cosmetic, medicament, and clothing Make-up Necklace Deodorants Otitis externa Mouth Rubber gloves Jean buttons Shoe: chrome rubber dyes Pruritus ani Discoid lesions can be in any distribution but they tend to be symmetrical and coin-sized Interdigital Genitalia Axillary folds Hands Nickel ear-rings a m e z c e cie o h rr o b e S a m e z c e cip o t A a m e z c e tc a t n o C Erythema multiforme Discoid eczema Eyes Feet seib a c S ytivitis n e s o t o h P si m r o fite p re h sitita m re D Nipples Wrists Psoriasis Mouth Genitalia a e s o r sisairytiP s u n alp n e h ciL Fig. 23.2.4 Distribution of common skin diseases.

section 23 Disorders of the skin 5600 similar lesion grouping are referred to as herpetiform (e.g. derma- titis herpetiformis). The grouping of lesions within a dermatomal distribution is seen in shingles, and reflects reactivation of the varicella–zoster virus from dorsal root ganglia. In some conditions, a scratch or other injury localizes lesions in a linear fashion because the lesions have a predilection for dam- aged skin. This is known as the Koebner phenomenon, and is seen in psoriasis, lichen planus, and warts. Other lesions are roughly linear because they follow linear anatomical structures (e.g. super- ficial thombophlebitis and ascending lymphangitis). The shape of many congenital hamartomas might be determined by the migra- tion of skin cells during embryogenesis, or from genetic mosaicism. Lesions might be roughly linear in shape, or assume bizarre patterns of lines and whorls (Blaschko’s lines, named after the dermatologist who described the patterns in epidermal naevi). Brushing against the foliage of phototoxin-containing plants in sunlight produces painful linear lesions with blisters (phytophotodermatitis) and long- lasting streaks of pigmentation. Very straight-edged lines and rec- tilinear shapes might raise the suspicion of artefactually induced lesions (dermatitis artefacta). Special investigations Although it is frequently possible to diagnose a rash or lesion from its appearance, in some cases additional

investigations are required. Table 23.2.1 Terminology of skin lesions Lesion Definition Description Macules Flat (nonpalpable) lesion Minimal changes in surface markings or texture; may merely be areas of redness, purpura, or melanin Papules and plaques Papules are small, circumscribed, palpable raised lesions Plaques are larger diameter palpable lesions, often resulting from the confluence of papules Palpable lesions may arise either from thickening of the epidermis, or from infiltration/oedema of the upper dermis, or a combination Nodules Circumscribed palpable masses, usually >1 cm Usually consist of infiltrating cells (inflammatory or neoplastic) filling the dermis and/or subcutaneous tissue Cysts Circumscribed palpable lesions containing fluid or semisolid material Clinically resemble nodules, but are fluid filled rather than solid (unlike vesicles and blisters, which are superficial, unlined, and contain visible fluid) Vesicles and bullae (blisters) Visible accumulations of fluid Vesicles are small, bullae are >1 cm; they frequently coexist Urticaria or wheal Angio-oedema Urticaria is dermal oedema (can be any size) Angio-oedema is deep-seated dermal oedema extending into subcutaneous tissue Petechiae and purpura Leakage of blood in the skin, which does not blanch on pressure Petechiae (pinhead size) Purpura (a few mm diameter) Ecchymosis (larger haemorrhagic areas) Fig. 23.2.5 Fungal infection (tinea corporis). By contrast with the endogenous diseases, this eruption is asymmetrical. The annular shape is typical. Dermatophyte fungus infections are usually very superficial, so the epidermal sign of scaliness is marked. Fig. 23.2.6 Annular erythema (reactive or toxic erythema). The annular shape may suggest a fungal infection, but the overlying epidermis is smooth or only slightly scaly, indicating that the pathology lies chiefly in the dermis. The margins of these rings are elevated by dermal infiltration with inflammatory cells and oedema.

23.2 Clinical approach to the diagnosis of skin disease 5601 Skin scrapings for fungal mycelia Scales removed by gentle scraping with a scalpel blade are treated with potassium hydroxide to clear keratin and other obscuring debris, and examined by light microscopy for fungal hyphae. Culture on a suitable medium identifies the fungal species. Biopsy Biopsy is indicated in the evaluation of skin tumours, in the case of rashes in which there is clinical uncertainty, or when it is essen- tial to document the diagnosis before treatment (e.g. lymphomas). The lesion or area of rash chosen for biopsy should be reasonably representative, and not be modified by scratching, picking, sec- ondary infection, or treatment. The standard procedure is to re- move a small ellipse of skin, including some underlying fat, under local anaesthesia. A punch biopsy of 4 mm diameter is frequently sufficient and convenient in a clinic setting, but is less suitable for evaluating deep pathology such as panniculitis. Small lesions (e.g. papules, small nodules, and blisters) can be entirely excised within a small ellipse. Complete excision is preferable to an in- cisional biopsy for the evaluation of tumours. If a blister is to be biopsied, this should be a recent one (no more than 24 h old), so that the blister depth can be judged before epithelial regener- ation takes place. For standard histopathology the skin is placed in formalin. Dermoscopy The dermoscope is a hand-held instrument with a powerful halogen beam that illuminates and magnifies (10×) intraepidermal and some subepidermal structures, including the superficial vascular plexus. A smear of water, alcohol, or mineral oil applied to the surface of the lesion eliminates surface reflections and make the horny layer more translucent. Dermoscopy is principally used as a noninvasive tool for the evaluation of melanocytic lesions by assessing the pattern of the pigmentary network, certain features of which correlate with malignancy. It is also useful for assessment of other nonpigmented skin tumours, such as haemangiomas and basal cell cancers, and has an increasing use in the evaluation of nonneoplastic conditions, for example, for visualizing the mites in suspected scabies. Immunofluorescence tests Immunofluorescence tests using fluorescein-labelled antibodies can detect skin-bound immunoglobulins or complement, and are used in the diagnosis of the

immunobullous diseases such as pemphigus, pemphigoid, and dermatitis herpetiformis (see Chapter 23.4). The direct immunofluorescence test requires a skin biopsy frozen im- mediately in liquid nitrogen, and detects immunoreactants already bound to antigenic components of the patient’s skin. The indirect test is performed using patient serum or blister fluid incubated with a substrate of normal skin or other epithelia before the application of a fluorescein-tagged antiglobulin. The indirect test is used to detect circulating antibodies directed against skin antigenic components. Woods light examination Examination of the skin with an ultraviolet A lamp (360 nm, Wood’s light) can help to accentuate pale areas, for example, the symmet- rical irregular areas of depigmentation in vitiligo (see Chapter 23.8) or the hypopigmented ash-leaf macule of tuberous sclerosis (see Chapter 24.17). It can also demonstrate green fluorescence in some fungal infections of hair (e.g. Microsporum canis), or pink fluores- cence in teeth and urine indicating porphyrin accumulation. FURTHER READING Coulson IH, Cox NH (2010). Diagnosis of skin disease. In: Burns T, et al. (eds) Rook’s textbook of dermatology, pp. 5.1–6.1. Blackwell, Oxford. Fig. 23.2.7 Grouping of vesicles typifies herpes simplex virus infection.

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