# 23.6 Dermatitis eczema

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ESSENTIALS Eczema is a characteristic pattern of skin inflammation that has many subtypes, with some induced by external factors such as ir- ritants or skin sensitizers. Atopic eczema is due partly to a genetic susceptibility, which programmes altered immune responses and skin physiology, together with reactions to exogenous allergens and microbes, but several eczema patterns do not appear to have ex- ternal causes. The key points in the recognition of eczema are that the skin is red- dened, may be thickened as a result of the inflammatory infiltrate and oedema, and the affected areas have ill-defined margins that break up into tiny red papules. Acute or severe eczema bubbles, blisters, and weeps. The distribution of the rash may be diagnostic, both of the type of eczema and the key causal factors. Management requires identification and avoidance of provoking factors. The inflammation is treated with topical steroids of different potencies, supplemented with moisturizers. Newer therapies include topical calcineurin antagonists, with a range of systemic therapies being used to control the most severe types of disease. Introduction The term eczema is used to describe a pattern of skin inflam- mation characterized clinically by ill-defined areas of redness (erythema) made up of tiny individual papules (bumps). At the edges of eczema lesions the individual papules often become vis- ible, which accounts for the lack of sharp definition (Fig. 23.6.1). Eczemas are characteristically very itchy. Microscopically, ec- zematous inflammation shows infiltration of T lymphocytes in both the dermis and epidermis, and the generation of oedema in the dermis, but also particularly in the epidermis. The oedema separates the epidermal cells from each other like the air spaces in a sponge (called spongiosis), but the oedema may coalesce into blisters, giving the appearance of a bubbly surface; these may leak or rupture producing serous oozing and crusting. There are many different types of eczema, some

with known causation and others remaining cryptic. Classification There is no completely accepted classification of eczema, but it can be helpful to group eczemas in relation to what is known of their aeti- ology: those with mainly exogenous causation, often called dermatitis rather than eczema, and those with no known external causes (en- dogenous eczemas) (Box 23.6.1). The exogenous eczemas are never- theless the consequence of interactions between external factors and host susceptibility, which may be largely genetically determined. Contact dermatitis/eczema This form of dermatitis/eczema is induced by external agents of dif- ferent physicochemical types: substances with irritant properties that are not immunogens, those that induce T-cell-mediated allergic contact sensitivity, and ultraviolet light. Irritant contact dermatitis Aetiology/pathogenesis Irritants are substances that inflict toxic damage on the epidermis. There are many types of irritant, but from a practical point of view they can be classified as surfactants (soaps/detergents), solvents (petrol, paraffin, oils), caustics (acids, alkalis, chemicals such as phenol), and miscellaneous chemicals that include nonanoic acid and dithranol (used in the treatment of psoriasis). Irritants vary greatly in their potency and hence the level of exposure required to induce an inflammatory response in skin. Individuals also vary greatly in their intrinsic resistance or susceptibility to the effects of irritants. A single exposure to mild irritants such as soaps and de- tergents is often insufficient to cause a clinically apparent irritant ef- fect, which usually requires multiple exposures having a cumulative effect. The general effect of irritants is a perturbation of the epidermal microenvironment, which is detected as a danger signal. This re- sults in the activation of essential components of the innate immune response. Keratinocytes produce a variety of cytokines, including interleukin (IL)-8, IL-18, and tumour necrosis factor-α; epidermal Langerhans' cells become activated and up to 30% may migrate 23.6 Dermatitis/eczema Peter S. Friedmann, Michael J. Arden-Jones, and Roderick J. Hay

 into the dermis; the dermal microvasculature expresses increased levels of the adhesion molecules ICAM1, E-selectin (ELAM1), and VCAM1; and there is infiltration of lymphocytes and often neutro- phil leucocytes. Repeated exposure may augment the microscopic response until it becomes clinically apparent inflammation. Most of the changes resulting from cumulative irritant insult are indistin- guishable from those that follow the specific immunologically me- diated process of allergic contact dermatitis. Epidemiology Irritant dermatitis is a major occupational skin disease. A survey in Sweden indicated that of 16 600 people who responded to a ques- tionnaire about hand eczema, 11% had experienced eczema in the last year. Thirty-five per cent (35%) of cases were irritant hand ec- zema, 19% allergic contact dermatitis, and 22% atopic hand eczema. In northern Germany, a large study from 1990 to 1999 examined compensation claims for occupational skin disease. The annual incidence of occupational irritant dermatitis was 4.5 cases per 1000, compared with 4.1 cases per 10 000 of allergic contact dermatitis. Under most circumstances the hands are the body site most likely to come into contact with irritants. One notable exception is the napkin area of infants, which may be in prolonged contact with alkaline (ammoniacal) urine or faecal material, and can develop irritant napkin dermatitis as a result. The rash is erythematous with poorly defined margins, ac- companied by scaling or fissures, and if more severe or acute, by eczematous blisters. The dorsa of the hands are usually more se- verely affected than the palmar surfaces, which probably reflects the thicker stratum corneum permeability barrier of the palms (Fig. 23.6.2). Once an irritant dermatitis has been initiated it seems to require very little and only occasional exposure to irritants to maintain a chronic dermatitis. Many patients who try to protect themselves by wearing rubber gloves find that when the hands become sweaty inside the gloves, this actually irritates and aggra- vates the dermatitis.

Those with a past or present history of atopic eczema are sig- nificantly more susceptible to developing irritant dermatitis from surfactants and solvents. This may reflect an impaired stratum cor- neum barrier and/or summation/synergism of the irritant effects and low-level subclinical inflammation of atopic eczema. Treatment The most important principle is avoiding further contact with irri- tants. The medical treatment is as for other eczemas, as outlined in ‘Treatment of atopic eczema’later on in this chpter. Allergic contact dermatitis Aetiology Contact hypersensitivity is an acquired immune response in which T lymphocytes recognize and react to the causative molecules. Contact allergens are mostly small xenobiotic molecules, although under some circumstances proteins can act as contact sensitizers. Several factors are involved in determining whether an individual will develop contact sensitivity to a given molecule. These include the intrinsic immunogenicity of the chemical, the dose to which the individual is exposed, and the individual’s susceptibility to sensitization. Fig. 23.6.1 Poorly defined margins of eczema. Box 23.6.1 Classification of eczema Exogenous Contact dermatitis • Irritant • Allergic • Photoinduced Atopic eczema Seborrhoeic eczema/dermatitis Photodermatitis Endogenous Asteatotic eczema; dyshidrotic eczema; varicose eczema Fig. 23.6.2 Dorsal hand involvement in dermatitis.

 Sensitizing potency of chemicals Of the thousands of chemicals in the environment, some are clearly highly potent immunogens capable of sensitizing everyone, while others may be defined as moderate, weak, or even nonsensitizers. For small molecules to become recognizable by the T-cell receptor, they have first to act as haptens, which become bound to protein carriers. The hapten–carrier complex will be processed by den- dritic antigen-presenting cells such as epidermal Langerhans’ cells. Processing involves loading haptenated peptides into the major histocompatibility molecules (mainly MHC class II, but in some in- stances also Class I) on the surface of the antigen-presenting cell. The sensitizing potency of chemicals is generally proportional to their protein-binding reactivity. Some compounds (haptens) are intrinsically protein reactive, others (prohaptens) are con- verted to protein-reactive metabolites through the actions of phase I xenobiotic metabolizing enzymes such as the cytochrome P450 family. The overall phenotype of xenobiotic detoxification systems, including P450 and other antioxidant systems, may be an important contributor to an individual’s susceptibility to sensitization. They may either detoxify reactive compounds and prevent immunogen- icity, analogous to high acetylator status and resistance to drug al- lergy, or, possibly through the failure of normal detoxification, may generate protein-reactive immunogenic intermediates. Lessons from experimental work The use of 2,4-dinitrochlorobenzene (DNCB) as an experimental contact sensitizer in healthy human volunteers has revealed that the human immune system obeys very reproducible dose-response relationships. Groups of individuals received different sensitizing doses of DNCB (62.5–1000 μg) on a 3 cm diameter circle of forearm skin. In proportion to the log of the sensitizing dose, there was a classical sigmoid dose-response curve for the proportion of indi- viduals showing clinical sensitization, as detected by positive elicit- ation challenges applied four weeks later, with 100% being sensitized by 500 μg or more. Furthermore, as the sensitizing dose increased, there was a log-linear increase in the strength of the response to the elicitation challenge; in other words, as the sensitizing dose in- creases on a log scale, so proportionately more people are sensitized, and to a greater extent. For a chemical to induce allergic contact sensitization it must penetrate the stratum corneum. Most sensitizers are lipophilic and hence penetrate readily, but metals such as nickel, cobalt, and chromate are water soluble. Hence a major factor in augmenting sensitization by metals is mechanical penetration of the stratum cor- neum, as in body piercing. The induction of contact sensitization involves the

activation of hapten-specific T cells, which undergo clonal expansion resulting in the establishment of immunological memory. The next time the sensitizer is in contact with the skin it will be recognized by the memory T cells, which respond by releasing interferon-γ and other proinflammatory cytokines. This recruits other T cells to the site in a non-antigen-specific fashion. The combination of cells and cyto- kines generates the oedema and swelling accompanied by itch that is characteristic of allergic contact dermatitis. Individual susceptibility Very little is known of how individual susceptibility is controlled. There are clearly individuals who develop contact sensitivity to environmental substances more easily than others. Thus individuals who developed contact sensitivity to three or more unrelated chem- icals could be sensitized experimentally by 2,4-dinitrochlorobenzene to a much greater degree than individuals with no pre-existing con- tact allergy. Individuals with only one contact sensitivity were inter- mediate in reactivity. These differences are not qualitative, but reflect the high-responder end of the normal distribution of responsive- ness. The corollary of this is that there is a low-responder end of the normal distribution—individuals who appear resistant to the spon- taneous development of contact sensitivities, and who give the lowest responses to any given sensitizing dose of 2,4-dinitrochlorobenzene. There do not appear to be any major human leukocyte antigen as- sociations with increased susceptibility to contact sensitization. As indicated here, one level at which susceptibility may be determined is that of intermediate metabolism, which can either detoxify or gen- erate reactive intermediates. A second level, which has been shown at least with regard to nickel sensitivity, is the fundamental control of immunological tolerance, mediated by regulatory T lymphocytes. Prevalence Allergic contact sensitization and dermatitis are common; about 10% of women are sensitive to nickel. The total prevalence of contact dermatitis among the population of many countries is estimated at between 6 and 11%. The incidence of occupational contact derma- titis has been estimated to be around 0.5–1.9 cases per 1000 full-time workers per year (Chapter 10.2.1). Clinical features of allergic contact dermatitis Allergic contact dermatitis can vary from a low-grade minor nuisance—the pierced earlobes that become mildly inflamed and itchy if the earrings are left in for too long—to catastrophic and disabling acute blistering and weeping with severe oedema of the sites to which the sensitizer was applied. The key points in diagnosis are the recognition that the inflammatory process is eczematous in nature, and that the distribution on the body raises the suspicion that there is an exogenous source. Thus contact dermatitis from nickel in the metal studs and buttons of denim jeans has a character- istic distribution around the lower abdomen and hips (Fig. 23.6.3). However, in strongly sensitized individuals nickel in most metal ob- jects, such as money, keys, cutlery, and door handles, can transfer from the fingers to other places, resulting in ill-defined eczematous Fig. 23.6.3 Allergic contact dermatitis to nickel.

 areas on the face and abdomen. The relationship of these distant areas to contact sensitivity may be much less obvious. Common sensitizers in everyday products include metals; dyes (paraphenylenediamine and other azo dyes) used for ha ir and clothing; preservatives (often formaldehyde releasers, as well as methyl- or chloromethyl-isothiazolinone) found in many personal products; rubber accelerators found in rubber gloves and glue/ce- ment used in shoe manufacture; colophony, extracted from pine resin and used to facilitate adhesion, as in the rubbery adhesive of sticking plasters, but also in mascara and felt-tipped pens; and fra- grances used in personal and domestic products. Confirmation of causality Contact allergens are applied to the skin of the back in patch tests. Patients are normally screened by an initial application of 40 substances (some individual, others as mixtures of a class) re- ferred to as the European standard battery. These compounds have been selected by the International Contact

Dermatitis Research Group and the European Environmental and Contact Dermatitis Research Group because they represent the groups of the most fre- quent sensitizers. The patch tests are applied on aluminium disc chambers held in place with hypoallergenic adhesive tape for 48 h, after which the chambers are removed and the skin assessed. Each compound or mixture is used at the highest concentration that does not normally induce a nonspecific irritant reaction. Many centres read the patch tests a second time at 72 or 96 h after appli- cation; this is said to reduce the number of false-positive tests that may result from irritant effects, and may detect responses that are slower to evolve. The final interpretation of causality depends not only on the pres- ence of a positive patch test, but also on the demonstration of rele- vance in terms of the person actually being exposed to the culprit, and it making contact with them in the areas where there is clinical dermatitis. The use of patch tests in elucidating the presence of con- tact allergy in patients with hand dermatitis is of great importance, as there may be major implications for the person in terms of their occupation. Treatment The general approach is first to identify the causal agent(s) through careful history taking, examination, and patch tests, and then avoid it. The treatment of the eczematous inflammation is summarized in ‘Treatment of atopic eczema’ later on in this chapter. Atopic dermatitis/eczema Definitions The atopic state is defined when an individual’s immune system re- sponds to certain antigens by producing antibodies of the IgE class rather than the IgG class. There is considerable disagreement among dermatologists, paediatricians, and allergists over how best to define atopic eczema/dermatitis. Dermatologists define it as a diffuse sym- metrical eczematous eruption that is characterized by onset in early life (infancy or childhood), and typically affects flexural sites such as the antecubital and popliteal fossae, and the hands and face. There is characteristically a personal and/or family history of allergic syn- dromes of asthma or rhinitis. The main point of controversy is whether it is found only in in- dividuals who are atopic. Among European dermatologists, atopic dermatitis is classified as extrinsic (associated with IgE-mediated allergies of mucosal systems) or intrinsic (usually of onset in adult life and not associated with the formation of allergen-specific IgE or clinical mucosal allergies). The extrinsic type accounts for around 80–95%, and the intrinsic type for 5–15% of cases of atopic eczema. Incidence, prevalence, and natural history of atopic eczema/dermatitis Over the last 40 years there has been a steady increase in the frequency of the atopic state and all the associated allergic syndromes of eczema, asthma, and rhinitis. While assessments for different national groups vary somewhat, it is now estimated that one-third of the population of the Western World is atopic. In the United Kingdom, up to 15% of children will develop atopic eczema by the age of 12 years. The maximum incidence is during the first two years of life. Atopic ec- zema is usually the first of the atopic syndromes to develop, whereas asthma comes later, and rhinitis last—a sequence that has been called the atopic march. There are several patterns to the natural history, the most common being early onset and spontaneous remission during childhood. Atopic eczema affects up to 0.5% of the adult population. In some of these, the eczema has been present from early childhood, while in others it recurs after a period of remission. Clinical features The distribution of atopic eczema varies with age. In pre-crawling infants, it is often a diffuse symmetrical erythema with dryness af- fecting the head and neck, torso, and even the limbs. Once a baby starts crawling, the eczema is usually distributed on the extensor surfaces of the arms, knees, and ankles, all of which are in phys- ical and frictional contact with the floor surface on which the child is crawling. As the child becomes ambulatory, the eczema tends to be distributed in the flexural areas, particularly the antecubital and popliteal fossae (Fig. 23.6.1). In some adults, the eczema may be localized predominantly or exclusively to the head, neck, and upper chest, a pattern possibly re- lated to the distribution of the saprophytic skin microbe Malassezia. In addition to the flexural pattern, there is

a pattern comprising circular or discoid patches of eczema, sometimes called nummular (coin-shaped), scattered on the torso and limbs. This pattern is not well associated with allergic sensitization (Fig. 23.6.4). The extent of skin involvement is one of the indicators of the overall severity, others being the degree of redness, the presence of weeping/oozing and crusting, as well as the presence of excoriation. The main symptom of eczema is itch, which can be very intense; a child can work itself into a complete frenzy of scratching, which can be almost as distressing for the parents/carers because of the diffi- culty of relieving the symptom. Pathogenesis of atopic eczema The pathogenesis of atopic eczema is still remarkably obscure. There is clearly genetic programming of susceptibility, with the atopic state being determined in a polygenic manner. Twin studies show that in monozygotic twins there is a 75% concordance rate, while it is only 21% in dizygotic twins. However, what causes the susceptibility to become manifest as disease is unknown. Many

 observations have been made of abnormalities in the physiological functions of the skin and the immune system, but it is not clear how they fit together. The dominant hypothesis is that the atopic state is primarily a dysregulation of the immune system, in which characteristics of the fetal immune system aimed at avoiding immune rejection between the mother and fetus somehow fail to mature into the adult im- mune responses designed to give protection against the extrauterine world. Thus in the fetus, T-helper cells differentiate towards the Th2 phenotype (Chapter 4.3). Following delivery, as the postnatal in- fant is colonized by microbes and exposed to endotoxin-producing pathogens, there is a change in the drivers of T-cell differentiation, resulting in the redirection of T-helper cells towards the Th1 pheno- type. Lack of exposure to endotoxins from enteral pathogens is re- garded as a major factor in the increase in the incidence of the atopic phenotype; the so-called hygiene hypothesis. So in early postnatal life, the immune response of atopic individuals is directed via the Th2-derived cytokines IL-4, -5, and -13 to generate IgE, causing the activation of mast cells and eosinophils. This pattern of immune re- sponse correlates with the development of clinical atopic allergies, but it is not clear what causes the orientation to either the skin or mucosae. Additional factors that may contribute to the altered immune response include constitutive overproduction of prostaglandin E2 and IL-10 by monocyte-macrophages, which favours Th2 dif- ferentiation. There is also evidence of constitutive overactivity of the cAMP-degrading enzyme phosphodiesterase 4. This results in the attenuation of intracellular signalling mediated via cAMP, but the consequences of this on the immune system or skin are not yet known. Three main alterations have been detected in the skin itself. The first suggests an impaired contribution to innate immune re- sponses. Thus, atopic eczematous skin produces decreased quan- tities of the antimicrobial peptides β-defensins, which have homologies with chemokines such as IL-8. This appears crucial in the increased susceptibility of atopic eczematous skin to infection by a range of microbes (see ‘Microbes’, next). The second alteration is the observation of a strong genetic association with mutations in the filaggrin gene. Filaggrin is a crucial component involved in the formation of the stratum corneum permeability barrier. This finding has not been confirmed in all populations studied, but it raises the important concept that altered permeability of the epi- dermis may be a primary factor in the development of atopic ec-zema. The third observation is that the skin of atopic dermatitis sufferers is actually able to help programme the adaptive T-cell- mediated immune response towards the Th2 bias that character-izes atopics. When a previously unencountered immunogen such as the experimental contact sensitizer 2,4-dinitrochlorobenzene is delivered to the immune system via the epidermal route, the sub- sequent T-cell response to 2,4-dinitrochlorobenzene is strongly Th2 orientated. This is in

marked contrast to the T-cell response of nonatopics after topical exposure to 2,4-dinitrochlorobenzene, in which case a nearly pure Th1 response is generated. A key factor in the epidermal capacity to direct the T-cell response appears to be the production of thymic stromal lymphopoietin (TSLP) by the atopic epidermis. This cytokine activates dendritic cells to drive T cells towards the Th2 type. The current working hypothesis is that atopic eczema, like other forms of eczematous inflammation, is a T-cell-mediated inflamma- tion. However, the range of cells and mediators contributing to the pathogenesis is more complex than for other types of eczema. Thus, at the microscopic level, atopic eczema is characterized by the infil- tration of CD4 + T cells, and eosinophils. In acute lesions, degranu- lated mast cells can be seen. A factor thought to be of importance is the presence of IgE on the epidermal Langerhans' cells. Antigen- specific cell-bound IgE is thought to facilitate the presentation of very low levels of antigen to T cells, so-called antigen focusing. Atopic eczema is regarded as multifactorial; some of the recognized triggering or aggravating factors include airborne and dietary aller- gens, microbial colonization and infection, emotional factors, and climatic factors (temperature and humidity). There are probably other as yet unrecognized factors. Role of allergy There are two sides to allergy in atopic eczema: the demonstration of allergic sensitization by skin tests, and the ascertainment of the clinical significance of allergy in the provocation of an individual's eczema. There is clear evidence that immunological sensitization, reflected by the presence of specific IgE, occurs not only early in life, but even in utero. The pattern of allergen-specific IgE changes during the first two years of life from predominantly food-directed to air- borne allergen-directed IgE. Allergy to environmental airborne and/or food allergens is an im- portant triggering factor in some, but not all individuals. There are major difficulties in determining which patients have clinically sig- nificant allergies contributing to driving the eczema. Different types of allergic response can be demonstrated with skin tests. Thus im- mediate, type I, weal and flare responses can be elicited by prick tests in 80–95% of people with eczema. If allergens are administered by intradermal challenge, up to 30% will exhibit both immediate and late phase (6–12 h) responses. If allergens are administered by ap- plication as patch tests, depending on whether or not the stratum corneum permeability barrier is breached by prior stripping with cellophane tape, eczematous responses that replicate the clinical and histological features of eczema can be generated in up to 80% Fig. 23.6.4 Discoid eczema.

 of patients. Also, if the patch-test challenge sites are inspected at the appropriate time, immediate (15 min) weal and flare responses are seen, and sometimes late phase (6 h) responses. The practical difficulty is in determining whether these positive skin tests correlate with clinically significant allergic provocation. Most patients have current or previous mucosal allergies of asthma or rhinitis, and immediate reactions in prick tests generally correlate well with the allergic provocation of those symptoms, rather than the eczema. However, very strongly positive prick-test responses to a given allergen often indicate that the allergen will aggravate the ec- zema. Positive patch tests with atopic allergens are reported to occur only in individuals with current or past eczema, and not in people with mucosal allergies and no eczema. Again, a strong patch-test re- sponse to a given allergen often indicates that the allergen has a sig-nificant role in provoking the eczema. Historical enquiry into which agents clearly exacerbate the eczema is usually unrewarding. One approach to establishing clinical relevance is allergen avoidance. Allergen avoidance This is only seriously practicable for house-dust mites, and foods. There is controversy in the literature as to the value of allergen avoidance measures. Tan et al. showed highly significant beneficial effects, whereas two other studies failed to show any benefit. The difference between the studies was the rigour of the dust-mite ex- clusion measures. Tan

encased all the bedding components (duvet, pillows, and mattress) in sealed encasements, treated the carpets with a spray combining acaricidal and allergen-denaturing activity, and used a high-power high-filtration vacuum cleaner. Gutgesell used bedding encasements and a vacuum cleaner, and Oosting et al. only used bedding encasements. In fact in Tan's study, the combin- ation of allergen-denaturing spray and vacuum cleaning resulted in a great reduction in the allergen load in the carpets, but the overall effect was not significantly better than that from the simple vacuum cleaner alone. So it is hard to explain why there are such differences in the results of the three studies. Dietary allergen exclusion has been explored in many studies, with the best effects being reported for infants and small children. Microbes Atopic eczema is highly susceptible to colonization and infection by coagulase-positive staphylococci. This was thought to result from the high relative humidity at the skin surface; even though the skin is dry to the touch the permeability barrier is defective, and there is a high transepidermal water loss. It is now known that an additional factor in the poor resistance to staphylococci is deficient production of the antimicrobial peptides β-defensins. Colonization by staphylococci that produce superantigens may lead to a general exacerbation of the eczematous inflammation. Infection by staphylococci results in folliculitis and/or acute exacer- bations of eczema with weeping and crusting. Also, the development of fissures of the eyelids and/or ear lobes is usually a sign of staphylo- coccal infection. Eczema is also susceptible to infection with herpes viruses, either herpes simplex or varicella–zoster. Eczema herpeticum is a poten- tially very serious condition that may lead to ocular damage, herpes encephalitis, or pneumonitis. The head and neck pattern of eczema is thought to be pro- voked by the ubiquitous skin-surface yeast Malassezia. Evidence is circumstantial, but is derived from the therapeutic response fol- lowing treatment with imidazole antifungal agents. Treatment of atopic eczema The general approach is to: (1), avoid any provoking factors (i.e. ir-ritants, contact sensitizers, or atopic allergens); (2), suppress inflam- mation with topical steroids (Box 23.6.2); and (3), give supporting symptomatic treatment. Allergen avoidance If clear allergic provoking factors can be identified then avoid- ance measures can make a significant contribution to the control of atopic eczema. Dust-mite avoidance must be done properly; ideally, all three elements of the bedding (mattress, top covers, and pillows) should be encased in bags of the appropriate dust- proof material. However, these are often hot and intolerable, and replacing duvet/quilts with cotton cellular blankets that can be washed frequently is an alternative. Similarly, acrylic pillows, and duvets can be subjected to hot washing and tumble drying every three months. The avoidance of dietary provocations is often practised, particu- larly in babies and children, on an empirical basis. This should only be continued if good evidence that it is contributing can be obtained by provocation challenge. Infection Staphylococcal infection requires antibiotics; it is better to use sys- temic antibiotics for 7–10 days than topical forms, to reduce bac- terial resistance. In patients with recurrent skin infection, the use of moisturizers containing antiseptic agents in the bath or applied directly to the skin is helpful. Itch The mediators of itch in atopic eczema are not known, but the con- tribution of histamine is minimal. Although antihistamines are often given, it is more likely that the sedating effects of older anti- histamines such as chlorpheniramine or trimeprazine make them better at symptom relief than nonsedating modern forms. Skin inflammation A crucial part of topical therapy is the use of emollient moistur-izers (Box 23.6.2). These are available as liquid oils, thin creams, Box 23.6.2 Treatment of eczema Moisturizers/emollients • Liquid oils or creams • Greasy ointments Topical steroids • See Box 23.6.3 Topical calcineurin antagonists • Tacrolimus • Pimecrolimus Systemic drugs • Azathioprine • Ciclosporin Additional treatments • Antibiotics if infected • If wet/oozing, potassium permanganate soaks (1/10 000)

section 23 Disorders of the skin 5636 and thick ointments, with varying degrees of water miscibility. The application of moisturizers that the patient finds agreeable can have excellent anti-itch and soothing effects, thus reducing scratching and hence contributing to controlling the eczema. The technique of wet wrapping can be very helpful, particularly in ba- bies and small children. This involves the initial application of a moisturizer to the limbs and torso, followed by the application of a double layer of tubular bandages, the inner layer being wetted with tepid water. Topical steroids are the mainstay of treatment of the skin in- flammation (see Box 23.6.3). In many patients, the chronic use of topical steroids may be ineffective or can result in steroid-induced side effects of striae, skin atrophy, and telangiectasia. In this case, the topical calcineurin antagonists tacrolimus or pimecrolimus are indicated. If these are ineffective, a range of systemic drugs may be used. These include azathioprine, ciclosporin, methotrexate, and mycophenolate mofetil. Systemic steroids are reserved for acute rescue therapy of acute flares, but should not be used for long-term therapy. Other forms of dermatitis/eczema Seborrhoeic eczema Seborrhoeic eczema is a response to the ubiquitous saprophytic skin yeast Malassezia. The rash comprises erythematous dry areas, most classically affecting the nasolabial folds, scalp, and ears. The most minimal form of seborrhoeic eczema is dandruff; if it is more active the scalp becomes itchy and finally inflamed, with red scaly areas most typically around the hair margin. There may be circular co- alescing areas on the central chest and/or upper back. Seborrhoeic eczema can mimic psoriasis, and indeed there is an entity termed sebopsoriasis, which behaves like psoriasis, but is in the distri- bution of seborrhoeic eczema. Most people experience minimal seborrhoeic eczema at some time. It is not known what causes the relationship with the fungus to change so that it induces an inflam- matory reaction. People infected with HIV are prone to developing florid seborrhoeic eczema. Treatment The main treatment is with antifungal agents such as imidazoles in shampoo and topical forms; for severe cases, systemic agents such as fluconazole may be used. For very symptomatic cases, low-potency topical steroids in combination with antifungal agents can be used to gain control, after which imidazole antifungals are usually sufficient for long-term control. Dyshidrotic (pompholyx) eczema This is an intensely itchy eruption affecting the palms and/or soles. It is characterized by tiny vesicles and blisters (pompholyx), which initially appear as small grey dots. The affected areas then become reddened, with hyperkeratotic scale that can fissure leading to painful splits. This is often a very chronic eczematous condition. It is thought that there is an associated disturbance of the structure or function of the sweat glands in the affected areas, hence the term dyshidrotic. Differential diagnosis It is important to exclude the presence of allergic contact dermatitis by careful history taking and diagnostic patch tests. It is also im- portant to avoid irritants such as soaps; greasy moisturizers should be used as substitutes. Potent topical steroids are normally required, but often the condition is only poorly controlled. Systemic agents such as azathioprine may be required for the long-term control of severe cases. Asteatotic eczema Asteatosis indicates lack of oil/grease, a condition that develops gradually with increasing age, and that preferentially affects the lower legs. The epidermal surface becomes dry, and cracks develop in the scale. These cracks can become red and itchy, a characteristic appearance called eczema craquelé, one pattern of asteatotic eczema (Fig. 23.6.5). The other main pattern is a more typical eczematous inflammation, usually distributed on the lower legs in association with a generalized dryness and hyperkeratosis. Treatment The main component of treatment is replacement of the epidermal oils by the application of greasy moisturizers. In the acute phase, moderate-potency topical steroids in an ointment base may be re- quired to bring the symptoms under control. Varicose eczema Following deep venous thrombosis in the leg veins, the valves in the veins are damaged, causing a rise in the venous pressure gradient down the legs. Any cause of venous

hypertension may Box 23.6.3 Topical steroids Category 1: mild • Hydrocortisone Category 2: moderate • Clobetasone butyrate Category 3: potent • Betamethasone valerate Category 4: super potent • Clobetasol propionate Fig. 23.6.5 Asteatotic eczema.

23.6 Dermatitis/eczema 5637 reverse the direction of flow, channelling returning blood into the superficial veins. The raised pressure transmitted to the small veins and postcapillary venules results in plasma transudation, deposition of fibrin (which produces sclerosis and skin teth- ering), and leakage of erythrocytes, generating haemosiderin. The haemodynamic changes alter the nutritional provision to the skin. As part of this, perhaps by analogy with the processes underlying asteatotic eczema, there may develop a rather diffuse eczematous process. If the skin's nutritive blood supply is sufficiently com- promised the tissue may break down, resulting in venous ulcer disease (Chapter 23.12). Differential diagnosis It is common for allergic contact dermatitis to develop on the lower legs affected by venous ulcers. The contact allergy is in response to ingredients of the many medicaments and impregnated bandages that are applied as part of the treatment. Treatment The most important component of therapy is external compression with stockings or bandages. This can improve the haemodynamics and restore the direction of venous return, with associated improve- ment in nutritive skin blood flow. The eczema is treated with mois- turizers and a range of topical corticosteroids. Ultraviolet-induced eczema or photodermatitis Some people develop eczema in areas exposed to sunlight, mainly the face, neck, and dorsa of hands. There are two types of this photodermatitis; an apparently spontaneous reactivity to light, and chemically sensitized photoallergy. Many drugs can act as photoallergens, becoming converted to allergens by the combined effect of ultraviolet (UV) radiation and as yet undefined metabolic factors in the individual. Well-known examples are thiazide diur- etics and quinine. The causal role is demonstrated by photopatch tests, in which the suspect chemical is applied to the back in du- plicate; one test site is irradiated with long-wavelength ultraviolet (UVA), and the other is simply occluded. The role of photoallergy is shown by a positive response only at the UV-irradiated test site. Even in people who develop apparently spontaneous photo dermatitis, there is often the suspicion that plant-derived substances such as sesquiterpene lactones from the chrysanthemum family may be involved. Treatment This involves minimizing exposure to sunlight by wearing thick clothing and hats. Sunblock creams are only helpful if they are very thick and opaque. Potent topical steroids and even systemic agents such as azathioprine may be required. FURTHER READING Calnan CD, Fregert S, Magnusson B (1976). The International Contact Dermatitis Research Group. Cutis, 18, 708–10. Cavani A, et al. (2003). Human CD25+ regulatory T cells maintain immune tolerance to nickel in healthy, nonallergic individuals. J Immunol, 171, 5760–8. Coenraads PJ, Smit J (1995). Epidemiology. In: Rycroft RJG, et al. (eds) Textbook of contact dermatitis, 3rd edition, pp. 133–50. Springer- Verlag, Berlin. David TJ, et al. (2000). Dietary factors in established atopic dermatitis. In: Williams HC (ed) Atopic dermatitis: the epidemiology, causes and prevention of atopic dermatitis, pp. 193–201. Cambridge University Press, Cambridge. de Jongh GJ, et al. (2005). High expression levels of keratinocyte anti- microbial proteins in psoriasis compared with atopic dermatitis. J Invest Dermatol, 125, 1163–73. Dickel H, et al. (2002). Importance of irritant contact dermatitis in oc- cupational skin disease. Am J Clin Dermatol, 3, 283–9. Diepgen T (2000). Is the prevalence of atopic dermatitis increasing? In: Williams HC (ed) Atopic dermatitis: the epidemiology, causes and prevention of atopic dermatitis, pp. 96–109. Cambridge University Press, Cambridge. Diepgen TL, Coenraads PJ (1999). The epidemiology of occupational contact dermatitis. Int Arch Occup Environ Health, 72, 496–506. Friedmann PS (1991). Graded continuity, or all or none—studies of the human immune response. Clin Exp Dermatol,

16, 79–84. Friedmann PS (2006). Contact sensitisation and allergic contact dermatitis: immunobiological mechanisms. Toxicol Lett, 162, 49–54. Friedmann PS, et al. (1993). Early time course of recruitment of im- mune surveillance in human skin after chemical provocation. Clin Exp Immunol, 91, 351–6. Gerberick GF, et al. (2000). Local lymph node assay: validation assess- ment for regulatory purposes. Am J Contact Dermatitis, 11, 3–18. Gutgesell C, et al. (2001). Double-blind placebo-controlled house dust mite control measures in adult patients with atopic dermatitis. Br J Dermatol, 145, 70–4. Kusel MM, et al. (2005). Support for 2 variants of eczema. J Allergy Clin Immunol, 116, 1067–72. Lachapelle JM (1995). Histopathological and immunohistopathological features of irritant and allergic contact dermatitis. In: Rycroft RJG, Menne T, Frosch PJ (eds) Textbook of contact dermatitis, 3rd edition, pp. 91–102. Springer-Verlag, Berlin. Lintu P, et al. (2001). Systemic ketoconazole is an effective treatment of atopic dermatitis with IgE-mediated hypersensitivity to yeasts. Allergy, 56, 512–17. Meding B (1990). Epidemiology of hand eczema in an industrial city. Acta Derm Venereol Suppl (Stockh), 153, 1–43. Miles EA, et al. (1996). Peripheral blood mononuclear cell proliferative responses in the first year of life in babies born to allergic parents. Clin Exp Allergy, 26, 780–8. Mudde GC, Bheekha R, Bruijnzeel-Koomen CA (1995). Consequences of IgE/CD23-mediated antigen presentation in allergy. Immunol Today, 16, 380–3. Newell L, et al. (2013). Sensitization via healthy skin programs Th2 responses in individuals with atopic dermatitis. J Invest Dermatol, 133, 2372–80. Ohmen JD, et al. (1995). Overexpression of IL-l0 in atopic derma- titis: contrasting cytokine patterns with delayed-type hypersensi- tivity reactions. J Immunol, 154, 1956–63. Oosting AJ, et al. (2002). Effect of mattress encasings on atopic derma- titis outcome measures in a double-blind, placebo-controlled study: the Dutch mite avoidance study. J Allergy Clin Immunol, 110, 500–6. Palmer CN, et al. (2006). Common loss-of-function variants of the epi- dermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. Nat Genet, 38, 441–6.

section 23 Disorders of the skin 5638 Patrick E, Maibach HI (1995). Predictive assays: animal and man, and in vitro and in vivo. In: Rycroft RJG, Menne T, Frosch P (eds) Textbook of contact dermatitis, 3rd edition, pp. 705–47. Springer- Verlag, Berlin. Raghupathy R (2001). Pregnancy: success and failure within the Th1/ Th2/Th3 paradigm. Semin Immunol, 13, 219–27. Schultz Larsen FV (1993). The epidemiology of atopic dermatitis. Monogr Allergy, 31, 9–28. Strachan DP (1989). Hay fever, hygiene, and household size. BMJ, 299, 1259–60. Tan BB, et al. (1996). Double-blind controlled trial of effect of housedust-mite allergen avoidance on atopic dermatitis. Lancet, 347, 15–18. Warner JA, et al. (1996). Prenatal sensitisation. Pediatr Allergy Immunol, 7, 98–101. Willis CM, Stephens CJM, Wilkinson JD (1993). Differential pat- terns of epidermal leukocyte infiltration in patch test reactions to structurally unrelated chemical irritants. J Invest Dermatol, 101, 364–70.

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