

Review article

The therapeutic concept of “patient management” in atopic eczema

Ring J, Brockow K, Abeck D. The therapeutic concept of “patient management” in atopic eczema.

Allergy 1996; 51: 206–215. © Munksgaard 1996.

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Accepted for publication 8 January 1996

Atopic eczema (or atopic dermatitis) is a chronic pruritic inflammatory skin disorder characterized by a typical age-related distribution and skin morphology (1). Atopy can be defined as familial hypersensitivity of skin and mucous membranes to environmental substances, associated with increased IgE production and/or altered nonspecific reactivity (2). Over the last decades, the incidence of atopic eczema has dramatically increased worldwide (3). Atopic eczema for which a multifactorially determined polygenic background is discussed (4, 5) is one of the most common skin diseases, usually starting in childhood. While some affected people outgrow their eczema, it may last for decades in others, and it may be complicated by the development of respiratory atopic diseases (6, 7). The health systems of all countries are burdened with the heavy economic load of direct and indirect costs of treatment and social morbidity (8). Although the pathogenesis of atopic eczema is not known, knowledge of components of immune and inflammatory responses in patients with atopic eczema has increased over the last decade (9, 10). However, there is still a wide gap between experimental progress and everyday clinical practice. There is much frustration among patients, parents, and doctors with regard to therapeutic approaches. Here, we describe our concept of “patient management” for atopic eczema, integrating aspects of diagnosis, therapy, and prevention.

Patient integration and motivation as key to success

Social (problems in school, illness, loss of work) as well as psychological factors (anxiety, doubt, guilt

(what have I done wrong?) and disfiguring appearance) put an enormous burden on patients with atopic eczema and their parents (11). Previous disappointments may provoke uncomfortably aggressive behavior. The success of any therapeutic effort in atopic eczema is substantially dependent on the integration of patients (in the case of children, also the parents) into the therapeutic concept and their active cooperation. As a prerequisite, patients must be informed thoroughly of the nature and course of the disease, its pathophysiologic factors, and the therapeutic options. They must accept that there is no simple (“miracle”) treatment available that leads to complete healing; at the same time, they must be informed that relapses can be effectively controlled by individual therapy considering specific skin conditions and provoking factors (12). Disease-related underlying factors should be ruled out in all patients with chronic or severe atopic eczema. In these cases, admission to a specialized dermatology department seems advisable for standardized diagnostic procedures and therapeutic training (13). After individual provocation factors have been analyzed and subsequently excluded, further guidance on specific avoidance procedures and maintenance therapy should follow in an outpatient setting. Allergologic evaluation should be repeated on a yearly basis (especially for children) since changes in sensitization patterns are not infrequent (14).

Diagnosis and avoidance of environmental provocation factors in atopic eczema

In atopic eczema, diagnostic and therapeutic approaches are intimately connected. Diagnosis

Table 1. Important provocation factors in atopic eczema

1. Unspecific provocation factors
Irritants (Table 2)
Microbial skin colonization or infection
<i>Staphylococcus aureus</i>
<i>Pityrosporum ovale</i>
Herpes simplex (eczema herpeticum)
Psychic stress, emotional factors
Bacterial and viral infections
2. Specific provocation factors (individual hypersensitivity)
IgE-mediated allergy
Food
House-dust mite
Animal dander
Pollen
Microbial colonization?
Contact allergy
Pseudoallergy (idiosyncrasy) and intolerance
Preservatives in food
Citrus fruits

comprises not only identification of the disease and its characteristics (especially chronic or chronically relapsing pruritic flexural eczema with positive personal or family history of atopic diseases, and additional features such as atopic stigmata and altered reactivity) (15–17), but also detection of provoking factors. On the basis of genetic predisposition, environmental influences can provoke or aggravate atopic eczema. These influences are called provocation, triggering, eliciting, or flare factors (18–20) and can be divided into unspecific (irritative-toxic) and specific (individual hypersensitivity) factors (Table 1). Avoidance often can prevent exacerbation, reduce the need for therapy, or even directly improve skin conditions. Patients with atopic eczema form a heterogeneous group with individually differing provocation factors.

Avoidance and therapy of unspecific provocation factors

Irritants. Patients with atopic eczema show an increased susceptibility to irritative factors of the skin (21, 22). These include effects from clothing, cleansing, skin care, cosmetics, etc. Generalized noneczematous dry skin, more appropriately termed "rough skin" (23), is a consistent finding in atopic eczema and is accompanied by changes in the biophysical or biochemical properties of the stratum corneum, including increased transepidermal water loss or disturbances of skin-surface lipids (24, 25). This results in a defective barrier function, leading to enhanced susceptibility to various irritants (26). Education about these factors is crucial. General guidelines are given in Table 2.

Microbial colonization. In a subgroup of patients with atopic eczema, eczematous skin lesions seem to be triggered by microbial factors, e.g., *Staphylococcus aureus*, which has a peculiar ability to colonize the skin of patients with atopic eczema. Although found as part of the normal microflora in most adult persons, *Pityrosporum ovale*, a lipophilic yeast, is thought to cause atopic eczema in the head and neck area (so-called head and neck dermatitis) (20, 27). In these cases, an antimicrobial treatment regimen may be beneficial.

Although this hypothesis is often debated, *Candida albicans* and *Trichophyton* species have not been convincingly shown to have much impact on atopic eczema (28–30). Yet, cutaneous colonization may be treated because of possible irritative effects. In our experience, antimycotic therapy of gastrointestinal *C. albicans* colonization rarely results in the alleviation of symptoms.

Table 2. Unspecific irritants for patients with atopic eczema and recommendations

	Not recommended	Recommended
Clothing	Wool, synthetic fibers Coarse fabric Occlusive nonabsorptive garment	Cotton Light clothing Nonocclusive clothing
Washing	Solvents, detergents, soap Too hot or too frequent bathing or showering Intense scrubbing with towel	Mild syndets for intertriginous areas only Brief lukewarm oil baths Patting with soft towel Application of lubricants to half-wet skin
	Disinfectants (e.g., chlorine) Too hot water Use of fabric conditioner Wet working conditions	Avoidance Cold or lukewarm water only Avoidance; rinsing thoroughly Avoidance of these conditions
Occupation	Dust, dirt, sand, mineral oil Mechanical trauma	
Others	Sweating, exposure to heat Plastic mattresses and pillowcases Cigarette smoke	Moderate temperature Avoidance Avoidance

Bacterial and viral (e.g., respiratory tract) infections often unspecifically aggravate atopic eczema especially in children (31). Therefore, antibacterial or surgical treatment may be indicated to eliminate an acute or chronic microbial focus (e.g., chronic tonsillitis). Eczema herpeticum is a complication of atopic eczema as a result of skin infection by Herpes simplex virus. Distinct, monomorphic, round, small erosions in disseminated distribution dominate the clinical picture. Treatment with intravenous acyclovir completely clears the symptoms within a few days. Disseminated mollusca contagiosa are often found in children with atopic eczema and should be treated with curettage after occlusive application of local anesthetics for 30 min or under brief general anesthesia.

Psychosomatic influence. Psychic stress is a well-known provocation factor in atopic eczema. Emotional disturbances (good or bad) can aggravate atopic eczema in a subgroup of patients (32). Many patients feel chronically anxious and incapable of controlling anger (33). Various psychologic treatments such as behavioral techniques aimed at eliminating scratching by positive reinforcement, as well as aversion or stress management, have proven successful in the management of this chronic disease (34). Hypnotherapy has produced both immediate and long-term improvement in objective and subjective parameters in adults and children with atopic eczema resistant to conventional treatment (35). Psychosomatic approaches to the treatment of atopic eczema should be supported if the doctor or the patient feel that there is a need for this.

Others. UV therapy is often used as an adjunctive treatment of atopic eczema, but in a small subgroup of patients with atopic eczema it may be a provocation factor and should be avoided (36). Lack of sunlight, psychologic factors, and low humidity may contribute to the unspecific deterioration of atopic eczema often seen in the winter months (37). Approximately one-third of female patients report premenstrual deterioration of the eczema. Pregnancy may also aggravate the symptoms in some patients, while in others an improvement may be seen. These observations strongly suggest that hormonal changes also have an influence on atopic eczema (38).

Avoidance and therapy of specific provocation factors (individual hypersensitivity)

Specific provocation factors (hypersensitivity) can be divided into allergic (abnormal immune response) and pseudoallergic (nonimmunologic mechanisms) reactions (39). In infancy, allergic

reactions to food are frequent, while aeroallergens become more important later (40). The frequency of food allergy is a point of controversy. According to the literature, prevalences vary by 0–84%, reflecting differences in selection of patients, test methods, and evaluation of positive reactions, and are a cause of confusion in this field (41). The chance of sensitization and positive reactions depends on age and on the severity of atopic eczema. Sampson and coworkers tested 320 patients with extensive atopic eczema and found positive food challenges in 63% (skin symptoms 75%, gastrointestinal symptoms 41%, respiratory symptoms 36%) (14). The most common food allergens were those of milk, egg, wheat, seafood, and peanut. Citrus fruit and food preservatives are the cause of the most important and often underestimated nonallergic provocation factors (42). For diagnosis of food allergy, a detailed history has to be taken and sensitizations have to be detected by skin tests and/or determination of specific IgE antibodies (e.g., RAST) (39). Skin tests with native foods (e.g., “prick-prick” test) often seem to be more reliable than with commercial extracts (43). In patients with high IgE values, RAST may sometimes show false-positive reactions through unspecific binding of IgE (44). Positive reactions in the skin prick test and RAST (sensitizations) have to be critically evaluated for their clinical relevance, because not every sensitization is relevant to the actual skin condition. In doubtful cases, oral provocation tests should be performed under standardized conditions; e.g., in hospitalized patients (41).

Therapy consists of elimination of the relevant allergens. Undirected extensive elimination diets without allergologic rationale are of questionable benefit and may be associated with severe risks to the patients (malnutrition, prolonged hospitalization, life-threatening reactions after reintroduction) (41). Prophylactic dietary manipulations in infants and their mothers may be justified for high-risk infants. Allergen avoidance during pregnancy has shown no beneficial effect (45, 46). Although randomized prospective definite studies are lacking, exclusive breast-feeding for 6 months is recommended to reduce exposure to food allergens (41). Although maternal avoidance of cow's milk, egg, soybean, and peanut during lactation has shown beneficial effects in respect to the development of atopic eczema, food and respiratory allergies remained unaffected (47, 48). The disadvantages of such a diet should not be overlooked, and the experimental nature should be discussed with the parents. Advice by a dietitian is needed if extensive intervention in the diet is planned. An increased risk of development of atopic eczema has been observed in children who were exposed to a diverse

solid food diet during the first 4 months (49, 50). These findings suggest a possible protective influence of delaying solid food feeding at least in postponing atopic eczema (51).

Aeroallergens can aggravate atopic eczema (52). In taking the history, one should look for worsening of skin conditions in relation to contact with house-dust mite, animals, and pollens. In many patients, sensitization to aeroallergens can be detected by skin prick test and RAST. A problem in evaluating the relevance of aeroallergens to atopic eczema is the lack of available provocation tests that exactly imitate normal situations. In cases in which the patient's history and sensitization do not form a conclusive picture, the atopy patch test (APT) may aid evaluation of the relevance (53–55). Although the definite mechanism of the reaction is still not known, this experience helps to bridge the gap between IgE-mediated hypersensitivity to high-molecular-mass allergens and an eczematous response. The comparison of test reactions in the literature is difficult due to variations in test conditions (preparations used, pretreatment with tape stripping, state of the skin) (56, 57). The development of standardized test conditions is urgently required (58).

Most controversial in this respect has been the role of house-dust mites (HDM) in exacerbation of atopic eczema. It is attractive to assume the influence of this almost ubiquitous antigen, because sensitization to HDM is frequently detected. T cells that can recognize the HDM antigen have been detected in some patients (59). There is also a positive correlation between the magnitude of exposure to HDM and the frequency of the disease (60). Positive APT reactions in patients with sensitivity to HDM confirm the possible role of this allergen (56–58). There are reports of improvement of skin conditions after HDM reduction (53, 54, 61, 62). Although secondary events cannot definitely be ruled out, they justify avoidance procedures in patients with a suggestive history and/or positive test reactions. Indoor HDM load should be determined with commercially available test kits measuring guanine or mite allergen. Avoidance procedures include encasing mattresses, pillows, and blankets in impermeable synthetic material and hot washing (>57°C) of all bedding once a week. Removal of carpets and upholstered furniture are somewhat extensive procedures which may be added to destroy the habitat of mites. Acaricides such as natamycin seem not to be effective in reducing mites for a longer period (60). Allergen desensitization is not a standard therapy for atopic eczema. Further studies have to evaluate the benefit of this therapy. Recently, desensitization with allergen antigen complexes has shown encouraging results (63).

Some patients report deterioration of skin conditions after contact with animals. In patients with atopic eczema, sensitization to animal dander is frequently found. Cat, dog, and horse danders are effective allergens, and contact should best be avoided prophylactically. As standardized provocation tests do not exist, the relevance of sensitization has to be evaluated with the aid of APT in individual cases (53, 54, 58). Pollens and molds may aggravate atopic eczema in some patients (54, 64, 65). Although atopic eczema generally tends to improve during the spring and summer season, exacerbation may occur in relation to a heavy pollen emission. Vacations in an aeroallergen-poor climate (sea level or high altitudes above 1500 m) often bring relief to these patients (37).

In patients with atopic eczema, contact allergy may be caused by the ingredients of topical preparations (especially vehicles, preservatives, fragrances). Patch testing should be performed during the initial checkup and if the therapy does not result in adequate improvement of skin conditions. In recent years, contact dermatitis caused by topical steroids has been reported with increasing frequency (66, 67). Corticoid allergy should be always kept in mind in cases in which treatment seems to aggravate the skin condition, resulting in increased pruritus. Cross-reactions in contact dermatitis to steroids are well known and have been intensively studied (68, 69).

Dermatologic basic therapy plus exacerbation-oriented therapy

The therapeutic approach to atopic eczema distinguishes between dermatologic basic therapy to be continued during remission periods and acute therapy of exacerbation of atopic eczema, including its complication by microbial superinfection (Table 3).

Dermatologic basic therapy

Dry or rough skin, the characteristic sign of atopic eczema, creates itch, followed by scratching of the skin which perpetuates the inflammatory eczematous reaction (70). Against this background, the regular use of topical basic therapy, consisting of drug-free emollients (sometimes together with urea) and bath oils in atopic eczema, is essential in dealing with this chronic skin disease.

The emollient of choice. The use of an emollient has always to be adapted to the skin condition and follows the principal rules of topical dermatotherapy (71, 72). In the choice of the emollient, both seasonal (during the summer months, emollients

Table 3. Conventional treatment protocol for atopic eczema

Dermatologic basic therapy
Basic skin care with emollients
-Drug- and additive-free
-Adapted to skin condition
Oil baths
-Spreading type preferable
(+/-) Supportive procedures
-Addition of moisturizers
-Topical antiseptics
-Topical tar products (temporary)
Anti-inflammatory therapy
Steroid-free basic therapy
-Wet dressings
Topical glucocorticosteroids
-Step-down therapy
-Interval therapy
Systemic antihistamines
-Nonsedating
-Sedating
Systemic antibiotics
Adjuvant therapy
UV therapy
-UVA-UVB
-UV-A1
Unsaturated fatty acids
- γ -Linolenic acid

with reduced lipid content are preferable) and intraindividual differences between various body areas have to be taken into account. However, nowadays, most pharmaceutical companies engaged in skin care provide a wide range of drug-free emollients of different galenical composition, allowing an individual skin condition-based adjuvant basic therapy. It is the common experience of many patients with atopic eczema that a special emollient is often effective only for a limited period of time and then has to be replaced by a different one according to the altered skin condition.

Drug-containing emollients. The addition of moisturizers may result in an improvement of the water-binding capacity of the human horny layer. Among the natural moisturizing factors, urea has proven to be one of the most effective substances in the topical therapy of dry eczematous skin. Urea has proved to exhibit antipruritic, keratolytic, and antimicrobial effects (73). The penetration of urea is vehicle-dependent with a more intensive and more prolonged increase of the water-binding capacity seen for urea-containing lipophilic emulsions of the W/O-type (74). The irritative "stinging" effect of urea-containing products is also vehicle-dependent in this way, allowing the topical use of higher urea concentrations in lipophilic vehicles. In our opinion, urea is usually not well tolerated in children up to the age of 5 years. If used at all in children, low-urea concentrations (up to 3%) should first be tested on

a restricted area before beginning widespread application. In the USA, lactic acid is frequently used as another moisturizer.

Bath oils. Oil baths are the simplest and most effective method of lubrication for large areas of skin and, together with the use of emollients, they form the main component of the dermatologic basic therapy in atopic eczema. In principle, two types of bath oils, dispersible, emulsifier-containing bath oils and spreading bath oils, are distinguished, the latter allowing the deposit of more lipids on the skin, particularly on areas located deep in the water (75). Emulsifier-containing bath oils have the disadvantage of a high hydrophilic-lipophilic balance value and are hygroscopic, resulting in a water withdrawal from the stratum corneum instead of the desired increase of stratum corneum hydration (76). Therefore, bath oils of the "spreading" type are preferred in atopic eczema (77), especially because in daily practice many patients apply the bath oil directly on the skin without bathing. How often an oil bath should be taken is controversial; our recommendation is every second or third day. Daily bathing in an emollient oil bath has been shown to have adverse effects in children with atopic eczema (78). However, this has not been shown for the daily application of a bath oil of the more favorable spreading type.

Additional supportive treatment modalities of dermatologic basic therapy. In patients with microbial triggering of atopic eczema, regular topical skin care with the antiseptic chlorhexidine in a concentration of about 3% for several weeks has proved useful in our hands and by others (79). The use of topical antibiotics should be restricted because of resistance problems and the risk of sensitization (80). In addition, dyes such as gentian violet (0.3%) are capable of both eliminating *S. aureus* and improving skin conditions (Brockow et al., unpublished data). Their use is recommended in localized impetiginized eczema (wet and excoriated lesions are nearly always positive for *S. aureus*).

Although head and neck dermatitis responds to oral ketoconazole therapy (81), a combination of a topical antimycotic (miconazole) and a hydrocortisone combination together with a ketoconazole shampoo were not shown to be superior to hydrocortisone cream and placebo shampoo (82).

In chronic phases, especially for the treatment of lichenified lesions, tar-containing topical agents are effective (83). However, the carcinogenic potential of their polycyclic aromatic hydrocarbons is problematic (72, 84); therefore, we cannot recommend long-term application of tar-containing products.

Anti-inflammatory therapy in exacerbation of atopic eczema

Recurrent exacerbation is a consistent feature of atopic eczema, and measures taken should always aim to return to dermatologic basic therapy. The possibilities are innumerable, consisting of topical and/or systemic treatment modalities (Table 3).

Topical corticosteroids as the drug of choice for acute exacerbation. Corticosteroids act as anti-inflammatory and immunosuppressive agents, and their efficacy in atopic eczema is well documented. As a result of the well-known serious side-effects that long-term corticoid treatment can produce, a general aversion among the population to its use exists. In response to this, the pharmaceutical industry has expended much effort in the development of strong topical glucocorticosteroids with a reduced side-effect profile. Among these new drugs are prednicarbate (85), mometasone furoate (86), and methylprednisolone aceponate (87). For the efficacy of the drug used, the choice of the appropriate vehicle is most important and must follow the principal rules of topical dermatotherapy (71, 72). A potent steroid in an ointment base may not be effective for exudative lesions since the glucocorticosteroid cannot penetrate into the epidermal and dermal layers. Once-daily application of a class II or stronger steroid is sufficient, repeated application showing no more benefit (72). The combination with an antiseptic has not been shown to provide an additional therapeutic effect even in heavily *S. aureus*-colonized exudative lesions (88). Application regimens for steroids may follow various rules. The so-called step-down therapy begins with a very potent glucocorticosteroid (usually class III), which is replaced by a lower potency as soon as the skin improves. Subsequent reduction of the amount of steroids by decreasing application frequency down to dermatologic basic therapy is widely favored (67); this is the principal method in our department. Others prefer to retain one potent steroid during the whole treatment period and argue that a lower potency will not be effective if the skin improves due to insufficient penetration through the recovered epidermal barrier (72). There are no controlled studies comparing these two therapeutic modalities. In our view, the use of systemic glucocorticosteroids in the treatment of atopic eczema is dispensable.

Wet dressings for generalized acute erythrodermic atopic eczema. An immediate cooling effect, a reduction in weeping lesions, a rapid improvement of skin inflammation, and a marked reduction of distressing pruritus are the main advantages of the application of lipophilic wet dressings. This is best

done by applying a lipophilic cream (the addition of a TCS may be possible in intensive inflammation) and then wet (soaked in lukewarm water) pajamas and bed rest for about 15–20 min. This method is used with great success in our dermatologic department in the first few days after admission of patients with acute atopic eczema exacerbation. Although this method is usually limited to the hospital situation, "wet-wrap" dressings have been successful in the treatment of chronic severe atopic eczema in the community (89, 90).

Antihistamines during periods of acute exacerbation. Pruritus is usually the most distressing feature of atopic eczema. This applies especially to periods of acute exacerbation. In our hands, the use of sedating antihistamines supports the efforts of any topical treatment at night and is usually well tolerated by patients (91). The role of nonsedating antihistamines in reducing the pruritus of atopic eczema is controversial (92). However, third-generation, non-sedating antihistamines with additional antiallergic effects (loratadine, cetirizine) may be useful in special subgroups of patients with atopic eczema.

Systemic antimicrobial therapy. Exudative lesions are usually heavily colonized by *S. aureus*. Systemic antistaphylococcal antibiotics such as flucloxacillin, dicloxacillin, or a second-generation cephalosporin are indicated in many patients with atopic eczema, resulting in prompt improvement (19). The use of erythromycin is no longer recommended because of increasing bacterial resistance to this drug (93).

Adjuvant therapy

Phototherapy of atopic eczema. In the search for alternatives to steroids in the treatment of aggravated atopic eczema, phototherapy has emerged. In a recent comparison of different treatment modalities, a combination of UVA and UVB or selective UV phototherapy (SUP) was found to be superior to UVA or UVB alone (94, 95). However, in most cases, these phototherapeutic modalities are not sufficient to achieve complete remission, and are usually used as an additional, steroid-saving treatment in chronic atopic eczema.

PUVA has proved effective both in adults (96) and in children (97), but its frequent use in atopic eczema is limited due to the uncertainty of long-term cancerogenic effects. In recent years, a new approach using UV-A1 treatment in cases of acute aggravated atopic eczema (98) has attracted much attention. In some cases, therapy allows the complete withdrawal of TCS treatment. The therapeutic effect of UV-A1 therapy is dose-dependent, a dosage of 50 J/cm² being superior to one of 10 J/cm² (99).

However, many questions remain unanswered in relation to long-term effects and side-effects.

Fatty acid supplementation. Whether the oral administration of evening primrose oil (containing linoleic acid and γ -linolenic acid) can modulate cutaneous arachidonic acid metabolism, resulting in clinical improvement of atopic eczema, is a controversial issue (100, 101). In our department, we offer this treatment modality to children with atopic eczema and assess its further prescription after a 6-month period.

Therapeutic possibilities in patients not responding to conventional therapy, and future therapeutic modalities

In a minority of patients, the efforts described above are not sufficient to induce permanent improvement. For these patients, a number of new therapeutic approaches have been published over the last years.

Interferon (IFN). In view of the imbalance between decreased IFN- γ and high interleukin (IL)-4 production in patients with atopic eczema, recent research has focused on the effect of IFN- γ in the treatment of severe atopic eczema. Subcutaneous injection of 3×10^6 , i.e., IFN- γ three times a week, resulted in marked clinical improvement of the skin condition (102). In a randomized, placebo-controlled, double-blind study, IFN- γ given by daily subcutaneous injection over a 12-week period was safe, well accepted, and effective in reducing inflammation and clinical symptoms (103), although the overall response was not as dramatic as in the study mentioned before. Data on IFN- γ therapy in atopic eczema are not sufficient to allow a final judgment of its value (104).

Immunophyllins. The efficacy of cyclosporin A (CyA), usually given in a dose of 5 mg/kg per day, in the induction of remission in atopic eczema has been documented in controlled studies (105, 106). However, the use of this drug is still limited to a very few patients because of major concern about its side-effects and the frequent relapse within a few weeks after CyA withdrawal in most treated patients (107). Whereas topical CyA cannot cross the epidermal skin barrier, the immunophyllin tacrolimus (FK506) may act topically and is currently under investigation (108).

Chinese herbal medicine. The trend to natural medicine and natural medical products has increased the popularity of treatment with Chinese herbs. In both adults and children, this therapy has proved to be effective in atopic eczema resistant to conventional

treatment (109, 110). However, the safety of this treatment has been questioned because fatal hepatotoxicity has been reported (111, 112). Therefore, Chinese herbal medicine should be given only under strict medical supervision and restricted to those with severe eczema unresponsive to conventional treatment (113).

Future therapeutic modalities. Reflecting the enormous progress in our understanding of pharmacologic, biochemical, and immunologic mechanisms in atopic eczema during the last decade, a great number of new therapeutic approaches are now under clinical investigation. Among other promising results, those of a polypeptide thymus hormone (114), extracorporeal photophoresis (115), and anti-idiotypic antibodies given as injection of allergen combined with F(ab')₂ fragments of specific antibodies (116) have been published.

References

- Ruzicka T, Ring J, Przybilla B, editors. Handbook of atopic eczema. Berlin: Springer, 1991.
- Ring J. Atopy: condition, disease, or syndrome? In: Ruzicka T, Ring J, Przybilla B, editors. Handbook of atopic eczema. Berlin: Springer, 1991:3-8.
- Ring J, Schäfer T. Epidemiologie allergischer Erkrankungen. Dtsch Derm 1995;43:142-6.
- Schultz Larsen F, Holm NV, Henningsen K. Atopic dermatitis. A genetic-epidemiologic study in a population-based twin sample. J Am Acad Dermatol 1986;15:487-94.
- Schultz Larsen F. A genetic-epidemiologic study in a population-based twin sample. J Am Acad Dermatol 1993;28:719-23.
- Guillet GG, Guillet MH. Natural history of sensitizations in atopic dermatitis. Arch Dermatol 1992;128:187-92.
- Musgrove K, Morgan J. Infantile eczema. A long-term follow-up study. Br J Dermatol 1976;95:365-72.
- Lapidus CS, Schwarz DF, Honig PJ. Atopic dermatitis in children: who cares? who pays? J Am Acad Dermatol 1993;28:699-703.
- Bos JD, Kapsenberg M, Smitt JH. Pathogenesis of atopic eczema. Lancet 1994;343:1338-41.
- Cooper KD. Atopic dermatitis: recent trends in pathogenesis and therapy. J Invest Dermatol 1994;102:128-37.
- Shuster S, Fisher GH, Harris E, Binnel D. The effect of skin disease on self-image. Br J Dermatol 1978;99 Suppl 16:18-19.
- Przybilla B, Eberlein-König B, Rueff F. Practical management of atopic eczema. Lancet 1994;343:1342-6.
- Broberg A, Kalimo K, Lindblad B, Swanbeck B. Parental education in the treatment of childhood atopic eczema. Acta Derm Venereol (Stockh) 1990;70:495-9.
- Sampson HA. The immunopathogenic role of food hypersensitivity in atopic dermatitis. Acta Derm Venereol Suppl (Stockh) 1992;176:34-7.
- Hanifin JM, Raika G. Diagnostic features of atopic dermatitis. Acta Derm Venereol Suppl (Stockh) 1980;92:44-7.
- Przybilla B. Stigmata of atopic condition. In: Ruzicka T, Ring J, Przybilla B, editors. Handbook of atopic eczema. Berlin: Springer, 1991:31-45.
- Ring J, Dorsch W. Altered releasability of vasoactive

- mediator secreting cells in atopic eczema. *Acta Derm Venereol* (Stockh) 1985;114:9-23.
18. Morren MA, Przybilla B, Bamelis M, Heykants B, Reynaers A, Degroef H. Atopic dermatitis: triggering factors. *J Am Acad Dermatol* 1994;31:467-73.
 19. Dahl MV. Antimicrobial agents in the treatment of atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:391-5.
 20. Ring J, Abeck D, Neuber K. Atopic eczema: role of microorganisms on the skin surface. *Allergy* 1992;47:265-9.
 21. Gollhausen R. The phenomenon of irritable skin in atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:306-18.
 22. Nassif A, Chan SC, Storrs FJ, Hanifin JM. Abnormal skin irritancy in atopic dermatitis and in atopy without dermatitis. *Arch Dermatol* 1994;130:1402-7.
 23. Piérard GE. What do you mean by dry skin? *Dermatologica* 1989;179:1-2.
 24. Imokawa G, Abe A, Jin K, Higaki Y, Kawashima M, Hidano A. Decreased level of ceramides in stratum corneum of atopic dermatitis: an etiologic factor in atopic dry skin? *J Invest Dermatol* 1991;96:523-6.
 25. Werner Y, Lindberg M. Transepidermal water loss in dry and clinically normal skin in patients with atopic dermatitis. *Acta Derm Venereol* (Stockh) 1985;65:102-5.
 26. Tupker RA, Pinnagoda J, Coenraads PJ, Nater PJ. Susceptibility to irritants: role of barrier function, skin dryness and history of atopic dermatitis. *Br J Dermatol* 1990;123:199-205.
 27. Abeck D, Ruzicka T. Bacteria and atopic eczema: merely association or etiologic factor? In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:212-20.
 28. Braunstein Wilson B, Deuell B, Platts-Mills TAE. Atopic dermatitis associated with dermatophyte infection and *Trichophyton* hypersensitivity. *Cutis* 1993;51:192-2.
 29. Buslau M, Menzel I, Holzmann H. Fungal flora of human faeces in psoriasis and atopic dermatitis. *Mycoses* 1990;33:90-4.
 30. Savolainen J, Lammintausta K, Kalimo K, Viander M. *Candida albicans* and atopic dermatitis. *Clin Exp Allergy* 1993;23:332-9.
 31. Vieluf D, Ruzicka T. Complications and diseases associated with atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:54-79.
 32. Hünecke P, Bosse K, Finck H. Krankheitsverlauf und psychosoziale Ereignisse während der stationären Behandlung atopischer Ekzematiker – eine Pilotstudie. *Z Hautkr* 1990;65:428-34.
 33. Ginsburg IH, Prystowsky JH, Kornfeld DS, Wolland H. Role of emotional factors in adults with atopic dermatitis. *Int J Dermatol* 1993;32:656-60.
 34. Cotterill JA. Psychosomatic approaches in the treatment of atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:459-65.
 35. Stewart AC, Thomas SE. Hypnotherapy as a treatment for atopic dermatitis in adults and children. *Br J Dermatol* 1995;132:778-83.
 36. Keong CH, Kurumaji Y, Miamoto C, Fukuro S, Kondo S, Nishioka K. Photosensitivity in atopic dermatitis: demonstration of abnormal response to UVB. *J Dermatol* 1992;19:342-7.
 37. Steiger T, Borelli S. Significance of climatic factors in the treatment of atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:415-28.
 38. Kemmett D, Tidman MJ. The influence of the menstrual cycle and pregnancy on atopic dermatitis. *Br J Dermatol* 1991;125:59-61.
 39. Ring J. *Angewandte Allergologie*. 2nd ed. München: MMV Medizin, 1988.
 40. Tuft LA. Importance of inhalant allergens in atopic dermatitis. *J Invest Dermatol* 1949;12:211-19.
 41. Przybilla B, Ring J. Food allergy and atopic eczema. *Semin Dermatol* 1990;9:220-5.
 42. Ring J, Vieluf D. Adverse reactions to food. In: Vermeer BJ, Wuepper KJ, van Vloten WA, Baart de la Faille H, van der Schroeff JG, editors. *Metabolic disorders and nutrition correlated with skin*. *Curr Probl Dermatol* 1991;20:187-202.
 43. Lehmann P, Schmidt K, Goerz G. Nahrungsmittelallergie: Hauttestung mit kommerziellen Nahrungsmittel-extrakten oder mit Naturprodukten? *Z Hautkr* 1990;65:365-70.
 44. Pastorello E, Stoeckli L, Bigli A, et al. Value and limits of diagnostic tests in food hypersensitivity. *Allergy* 1989;44 Suppl 9:151-8.
 45. Fälth-Magnusson K, Kjellman N-IM. Development of atopic disease in babies whose mothers were on exclusion diet during pregnancy – a randomized study. *J Allergy Clin Immunol* 1987;80:868-75.
 46. Lilja G, Dannaeus A, Foucard T, Graff-Lonnevig V, Johansson SGO, Öman H. Effects of maternal diet during late pregnancy and lactation on the development of atopic diseases in infants up to eighteen months of age: *in vivo* results. *Clin Exp Allergy* 1989;19:473-9.
 47. Arshad SH, Mathews S, Grant C, Hide DW. Effect of allergen avoidance on development of allergic disorders in infancy. *Lancet* 1992;339:1493-7.
 48. Chandra RK, Puri S, Hamed A. Influence of maternal diet during lactation and use of formula feeds on the development of atopic eczema in high risk infants. *BMJ* 1989;299:228-30.
 49. Fergusson DM, Horwood LJ, Shannon FT. Early solid feeding and recurrent childhood eczema: a 10-year longitudinal study. *Pediatrics* 1990;86:541-6.
 50. Kojosaari M, Saarinen UM. Prophylaxis of atopic disease by six months' total solid food elimination. *Acta Paediatr Scand* 1983;72:411-14.
 51. Saarinen UM, Kojosaari M. Does dietary elimination in infancy prevent or postpone food allergy? *Lancet* 1980;1:166-7.
 52. Platts-Mills TAE, Chapman D, Mitchell B, Heymann PW, Deuell B. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:192-203.
 53. Clark ADF, Adinoff AD. Aeroallergen contact can exacerbate atopic dermatitis: patch test as a diagnostic tool. *J Am Acad Dermatol* 1989;21:863-9.
 54. Clark RAF, Adinoff AD. The relationship between positive aeroallergen patch test reactions and aeroallergen exacerbations of atopic dermatitis. *Clin Immunol Immunopathol* 1989;53 Suppl:S132-40.
 55. Tanaka M, Aiba S, Matsumura N, et al. IgE-mediated hypersensitivity and contact sensitivity to multiple environmental allergens in atopic dermatitis. *Arch Dermatol* 1994;130:1393-40.
 56. Seidenari S, Manzini BM, Danese P, Gianetti A. Positive patch tests to whole mite culture and purified mite extracts in patients with atopic dermatitis, asthma and rhinitis. *Ann Allergy* 1992;69:201-6.
 57. vanVoort Vader PC, Lier JG, Woest GE, Caenraads PJ, Nater PJ. Patch test with house dust mite antigens in atopic dermatitis patients: methodological problems. *Acta Derm Venereol* (Stockh) 1991;71:301-5.

58. Darsow U, Vieluf D, Ring J. Atopy patch test with different vehicles and allergen concentrations: an approach to standardisation. *J Allergy Clin Immunol* 1995;95:677-84.
59. Kapsenberg ML, Wierenga EA, Bos JD, Jansen HM. Functional subsets of allergen-reactive human T cell clones. *J Immunol* 1990;147:2942-9.
60. Colloff MJ. Exposure to house dust mites in homes of people with atopic dermatitis. *Br J Dermatol* 1992; 127:322-7.
61. Kubota Y, Imai Y, Hori Y. Reduction of environmental mites improved atopic dermatitis patients with positive mite-patch tests. *J Dermatol* 1992;19:177-80.
62. Sada T, Yasue T, Ohashi M, Yasue A. Effectiveness of house dust-mite allergen avoidance through clean room therapy in patients with atopic dermatitis. *J Allergy Clin Immunol* 1992;89:653-7.
63. Leroy BP, Boden G, Lachapelle JM, Jaquemin MG, Saint-Remy JMR. A novel therapy for atopic dermatitis with antigen-allergen complexes: a double blind, placebo-controlled study. *J Am Acad Dermatol* 1993;28:232-9.
64. Rasanen L, Reunala T, Lehto M, Virtanen E, Arvilommi H. Immediate and delayed hypersensitivity reactions to birch pollen in patients with atopic dermatitis. *Acta Derm Venereol (Stockh)* 1992;72:193-6.
65. Reitano S, Visa K, Kahonen K, Kayhko K, Stubb S, Salo OP. Eczematous reactions in atopic patients caused by epicutaneous testing with inhalant allergens. *Br J Dermatol* 1992;144:303.
66. Doms-Gooens A, Morren M. Results of routine patch testing with corticosteroid series in 2073 patients. *Contact Dermatitis* 1992;26:182-91.
67. Niedner R, Schöpf E. Clinical efficacy of topical glucocorticoid preparations and other types of dermatitis in inflammatory diseases, particularly in atopic dermatitis. In: Burg G, editor. *Curr Probl Dermatol* 1993;21:157-69.
68. Coopman S, Doms-Gooens A. Cross-reactions in topical corticosteroid contact dermatitis. *Contact Dermatitis* 1988;19:145-6.
69. Wilkinson SM, Hollis S, Beck MH. Reactions to other corticosteroids in patients with allergic contact dermatitis from hydrocortisone. *Br J Dermatol* 1995;132:766-71.
70. Schöpf E, Mueller JM, Ostermann T. Stellenwert der adjuvanten Basistherapie bei chronisch-rezidivierenden Hauterkrankungen. *Hautarzt* 1995;44:451-4.
71. Braun-Falco O, Plewig G, Wolff HH, editor. *Dermatologie und Venerologie*. Berlin: Springer, 1985:979-1017.
72. Korting HC. *Dermatotherapie*. Berlin: Springer, 1995.
73. Wohlrab W. Neurodermitis und Harnstoff. *Hautarzt* 1992;(Suppl 1):1-4.
74. Wohlrab W. Vehikelabhängigkeit der Harnstoffpenetration in der menschlichen Haut. *Dermatologica* 1984;169:53-9.
75. Gabard B, Bieli E. Measurement of lipid deposition on the skin of the forearm: comparison of different bath oils. *J Soc Cosmet Chem* 1991;42:299-308.
76. Gloor M. Körperpflege bei Neurodermits. *TW Dermatologie* 1991;21:341-8.
77. Gloor M. Wenig waschen und viel cremen! *Therapiewoche* 1992;42:1410-16.
78. White MJ, Batten TL, Ormerod AD. Adverse effects of a daily bathing routine on children with atopic dermatitis. *J Dermatol Treatment* 1994;5:21-4.
79. Stalder JF, Fleury M, Sourisse M, et al. Comparative effects of two topical antiseptics (chlorhexidine vs KMnO₄) on bacterial skin flora in atopic dermatitis. *Acta Derm Venereol (Stockh)* 1992;176 Suppl:132-4.
80. David JJ, Cambridge JC. Bacterial infection and atopic eczema. *Arch Dis Childhood* 1986;61:20-3.
81. Clemmensen O, Hjorth N. Treatment of dermatitis of the head and neck with ketoconazole in patients with type I sensitivity to *Pityrosporum orbiculare*. *Semin Dermatol* 1983;2:26-9.
82. Broberg A, Faergemann J. Topical antimycotic treatment of atopic dermatitis in the head/neck area. *Acta Derm Venereol (Stockh)* 1995;75:46-9.
83. Hornstein OP. Guidelines for topical treatment in atopic eczema. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic eczema*. Berlin: Springer, 1991:345-55.
84. Ippen H, Grimmer G. Carcinogenic hydrocarbons in therapeutic "tars". *Z Hautkr* 1993;68:88-92.
85. Korting HC, Vieluf D, Kerscher M. 0.25% Prednicarbat cream and the corresponding vehicle induce less skin atrophy than 0.1% betamethasone-17-valerate cream and 0.05% clobetasol-17-propionate cream. *Eur J Clin Pharmacol* 1992;42:159-61.
86. Brasch J. The atrophogenic potential of mometasone furoate in a clinical long-term study. *Z Hautkr* 1991;66:785-7.
87. Ortonne JP. Safety aspects of topical methylprednisolone acepnate (MPA) treatment. *J Dermatol Treatment* 1992;3 Suppl 2:21-5.
88. Korting HC, Zienicke H, Braun-Falco O, et al. Modern topical glucocorticoids and anti-infectives for superinfected atopic eczema: do prednicarbate and didedylmethylammonium chloride form a rational combination? *Infection* 1994;22:390-4.
89. Goodyear M, Spowart K, Harper JJ. "Wet-wrap" dressings for the treatment of atopic eczema in children. *Br J Dermatol* 1991;125:604.
90. Mallon E, Powell S, Bridgman A. "Wet-wrap" dressings for the treatment of atopic eczema in the community. *J Dermatol Treatment* 1994;5:97-8.
91. Simons FER, Simons KJ, Becker AB, Haydey RP. Pharmacokinetics and antipruritic effects of hydroxyzine in children with atopic dermatitis. *J Pediatr* 1984;104:123-7.
92. Hanifin JM. Atopic dermatitis: new therapeutic considerations. *J Am Acad Dermatol* 1991;24:1097-1101.
93. Abeck D, Korting HC. Einsatz von Antibiotika bei Hauterkrankungen. *Bayer Internist* 1991;11:45-53.
94. Jekler J. Phototherapy of atopic dermatitis with ultraviolet radiation. *Acta Derm Venereol (Stockh)* 1992; Suppl 171:1-37.
95. Lacoste-Caillet P, Loesche C, Thomas P. Phototherapy of atopic dermatitis: selective UV phototherapy (SUP) versus UVA-UVB. *Nouv Dermatol* 1992;11:353-6.
96. Morrison WL, Parrish JA, Fitzpatrick TB. Oral psoralen photochemotherapy of atopic eczema. *Br J Dermatol* 1978;98:25-30.
97. Sheehan MP, Atherton DJ, Norris P, Hawk J. Oral psoralen photochemotherapy in severe childhood atopic eczema: an update. *Br J Dermatol* 1993;129:431-6.
98. Krutmann J, Czech W, Diepgen T, Niedner R, Kapp A, Schöpf E. High-dose UVA1 therapy in the treatment of patients with atopic dermatitis. *J Am Acad Dermatol* 1992;26:225-30.
99. Kowalick L, Kleinheinz A, Weichenthal M, et al. Low dose versus medium dose UV-A1 treatment in severe atopic eczema. *Acta Derm Venereol (Stockh)* 1995;75:43-5.
100. Berth-Jones J, Graham-Brown RAC. Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993;341:1557-60.
101. Morse PF, Horrobin DF, Manku MS, et al. Meta-analysis of placebo-controlled studies of efficacy of Epogam in the treatment of atopic eczema. Relationship between plasma essential fatty acid changes and clinical response. *Br J Dermatol* 1989;121:75-90.
102. Reinhold U, Kukul S, Brzoska J, Kreyseel H. Systemic

- interferon gamma treatment in severe atopic dermatitis. *J Am Acad Dermatol* 1993;29:58-63.
103. Hanifin JM, Schneider L, Leung D, et al. Recombinant interferon gamma therapy for atopic dermatitis. *J Am Acad Dermatol* 1993;28:189-97.
104. Torrello A, Harto A, Sendagorta E, Czarnetzki BM, Ledop A. Interferon- α therapy in atopic dermatitis. *Acta Derm Venereol (Stockh)* 1992;72:370-2.
105. Sowden JM, Berth-Jones, Ross JS, et al. A multicentre, double-blind, placebo-controlled crossover study to assess the efficacy and safety of cyclosporin in adult patients with severe atopic dermatitis. *Lancet* 1991;338:137-40.
106. Wahlgren CF, Scheynius A, Hägermark Ö. Antipruritic effect of oral cyclosporine A in atopic dermatitis. *Acta Derm Venereol (Stockh)* 1990;70:323-9.
107. Granlund H, Erkkö P, Sinisalo M, Reitamo S. Cyclosporin in atopic dermatitis: time to relapse and effect of intermittent therapy. *Br J Dermatol* 1995;132:106-12.
108. Nakagawa H, Etoh T, Ishibashi Y, et al. Tacrolimus ointment for atopic dermatitis. *Lancet* 1994;334:883.
109. Sheehan MP, Atherton DJ. One-year follow-up of children treated with Chinese medical herbs for atopic eczema. *Br J Dermatol* 1994;130:488-93.
110. Sheehan MP, Rustin MHA, Atherton DJ, et al. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet* 1992;340:13-17.
111. Mostefa-Kara N, Pauwels A, Pinus E, Biour M, Levy VG. Fatal hepatitis after herbal tea. *Lancet* 1992;340:674.
112. Perharic-Walton L, Murray V. Toxicity of Chinese herbal remedies. *Lancet* 1992;340:673.
113. Harper J. Traditional Chinese medicine for eczema. *BMJ* 1995;308:489-90.
114. Hsieh KH, Shaio MF, Liao TN. Thymopentin treatment in severe atopic dermatitis: clinical and immunological evaluations. *Arch Dis Child* 1992;67:1095-1102.
115. Prinz B, Nachbar T, Plewig G. Treatment of severe atopic dermatitis with extracorporeal photophoresis. *Arch Dermatol Res* 1994;287:48-52.
116. Leroy BP, Jacquemin MG, Lachapelle JM, Saint-Remy JMR. Allergen-sensitive atopic dermatitis is improved by injections of allergen combined with F(ab')₂ fragments of specific antibodies. *Br J Dermatol* 1995;132:599-603.

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