

ATOPIC ECZEMA: CURRENT THERAPEUTIC ADVANCES

Atopic eczema (AE) is a distressing chronic disease that significantly impairs the quality of life of both patients and their parents. It is the most common chronic skin disorder seen in childhood.



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There is epidemiological evidence of a definite increase in the prevalence of AE in the last few decades. The reasons for this are unclear. AE has been noted to occur more commonly in smaller families, in urban compared with rural children, and in more affluent families. There is also evidence to support the hygiene hypothesis which postulates that lack of exposure to infections early in life may play a role in skewing the immune system to a Th2 cytokine profile, thus predisposing infants to atopic disorders such as asthma, allergic rhinitis and AE.

NOMENCLATURE AND CLASSIFICATION OF ECZEMA

In May 2004 the World Allergy Organisation (WAO) published a new report of its Nomenclature Review Committee. The New WAO Nomenclature is an update of the EAACI document defining terminology for skin allergies.¹

The WAO recommends that the umbrella term for local inflammation of the skin should be dermatitis. The term eczema is a term describing an aggregation of several skin diseases with clinical characteristics in common, involving a genetically determined skin barrier defect.

In children and young adults of atopic constitution, the underlying inflammation is dominated by an IgE antibody-associated reaction, allowing the term AE to be applied. This term should replace the term atopic dermatitis. The diagnosis of AE cannot be reached without an IgE antibody determination or skin test. In other eczema cases where the inflammation is not associated with elevated IgE antibody, these patients are considered to have non-atopic eczema (Fig. 1).

AE is more common in preschool children, with a prevalence of 45 - 64%,² but in adults can be as high as 40%. Children with AE have a greater risk of developing asthma (approximately 30%) than children with non-atopic eczema. They also have associated food allergies and IgE-induced urticaria. Thus the interventional prognostic and co-morbidity implications of a diagnosis of AE are different to those of non-atopic eczema, where the management is largely directed to management of the skin itself.

CLINICAL CRITERIA FOR AE IN CHILDREN

Essential features

- Pruritus
- Eczematous changes
- Chronic or relapsing course
- Typical and age-specific patterns: face, neck, and extensor involvement in infants and children; flexural lesions, especially in older children and adolescents; sparing of the groin and axillae.

Important features

The following features support the diagnosis, but do not occur in all patients:

- early age of onset
- xerosis
- atopy (IgE reactivity).

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Exclusions

The diagnosis of AE depends on the exclusion of conditions such as scabies, allergic contact dermatitis, seborrhoeic dermatitis, psoriasis and ichthyosis.

DISTRIBUTION OF AE IN CHILDREN

In children AE occurs in 2 phases:

- **Infantile phase** (birth - 2 years): these children have mainly erythematous papules and vesicles. The lesions occur on the cheeks, forehead or scalp and are very pruritic. The lesions may extend to the trunk or to the extensor surfaces of the arms and legs. Occasionally involvement of the flexural areas may also occur in this age group.
- **Childhood phase** (2 years - puberty): these children have lichenification in addition to erythematous papules and vesicles. The areas that are involved are the hands, feet, flexural areas of the arms and legs, wrists and ankles. The face may also be involved in the periorbital or perioral area.

QUALITY OF LIFE IN AE

AE significantly affects the quality of life of patients and their families. Infants tend to be irritable, sleep poorly and are often hyperactive because of pruritus. Older children often have low self-esteem, are embarrassed about their skin, lack self-motivation, and are very anxious. They sleep poorly, are often tired and may even perform poorly at school. Studies have shown that 60% of schoolgoing children demonstrated impairment in performance of daily activities, 50% of children with moderate AE and 80% of children with severe

AE perform badly at school and a significant proportion of children show impairment of performance in outdoor sports. Affected children suffer significant psychological impairment and are often tearful in school, worry excessively and often sleep poorly. Studies show a very high percentage of children experience disrupted sleep. This occurs even without the presence of active dermatitis.

A child with AE also significantly influences the family dynamics. A family with a child with AE is significantly psychologically impaired. Mothers of children with AE have been documented to demonstrate significant distress and feel socially isolated. Familial dysfunction has been found to correlate with poor treatment and inadequate control of symptoms.

Atopic march

The atopic march is the process in which children who develop AE and food allergy early in life progress onto developing inhalant allergies and thereafter asthma and allergic rhinitis. Many longitudinal studies have explored this phenomenon. Rhodes *et al.* studied 100 children over a 22-year period in the UK. The prevalence of AE peaked at 20% of children by 1 year of age and fell to about 5% at the end of the study. The prevalence of allergic rhinitis increased slowly over time from 3% to 15% and the percentage of patients with wheezing increased from 5% in the first year to 40% in the last 22 years. Sensitisation to house dust mite peaked at 36% at 22 years of age. The major

risk factor for asthma as an adult was early sensitisation to either foods in the first year or aeroallergens in the first 2 years of life.

In another longitudinal study involving 94 children with AE, 43% of the patients developed AE within 8 years and 45% developed allergic rhinitis. The children with mild AE did not develop asthma or allergic rhinitis. Therefore severity of AE was regarded as a risk factor for the development of asthma.⁴ The German Multicenter Atopic Study (MAS) was a longitudinal study involving 1 314 children over a 7-year period.⁵ In the high-risk infants (with 2 family members with atopy or IgE > 0.9 kU/l), 69% of patients who developed AE by 3 months of age were sensitised to aeroallergens by 5 years of age. At 5 years of age at least 50% of children with early AE and a strong atopic family history had allergic asthma compared with 12% of patients without AE or a family history of atopy.

MANAGEMENT OF ATOPIC DERMATITIS

The management of patients with AE requires a careful and thoughtful approach. The most important aspect of management is patient education. Parents need to be reassured about the AE, and emphasis must be placed on the fact that AE cannot be cured but can be well controlled with proper therapy. Parents may become despondent when doctors neglect to explain the nature of AE, resulting in parents having false expectations. When these expectations are not met, they often consult

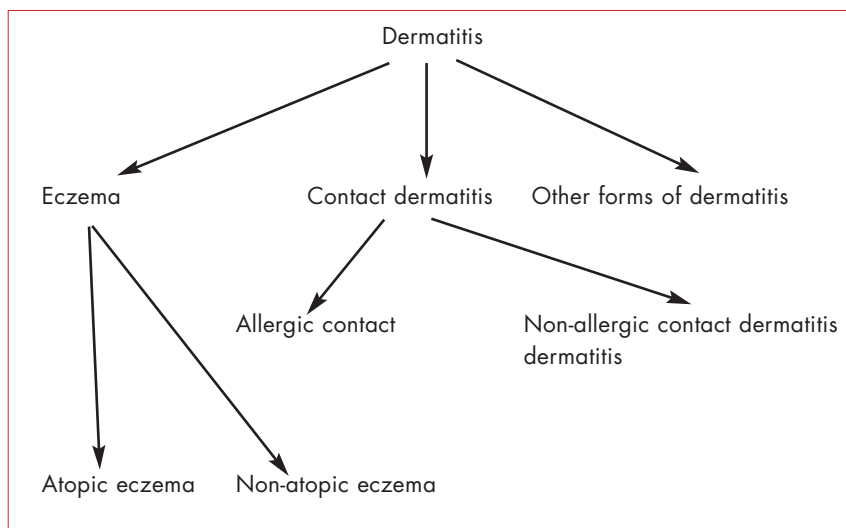


Fig. 1. The new WAO classification of eczema/dermatitis.

alternative health practitioners out of sheer frustration. The management of AE involves use of moisturisers, allergen avoidance, and avoidance of irritants, topical corticosteroids and topical immunomodulators.

Moisturisers

Patients with AE exhibit enhanced transepidermal water loss, and this leads to xerosis of the skin. Hydration can be achieved with soaking baths. To prevent the skin from drying, moisturisers should be applied liberally immediately after the bath. Moisturising the skin has been shown to reduce pruritus, the need for topical steroids and infection by *Staphylococcus aureus*.

Avoidance of allergens

In young infants food allergy has been found to play a role in AE in a subset of patients. Milk, egg, peanut, soy, wheat and fish are responsible for 90% of the foods found to exacerbate AE. Avoidance of these foods in food-allergic patients can significantly improve AE. Avoidance must be based on a proper diagnosis of food allergy. Avoidance of house dust mites has also been shown to benefit patients who have AE and who are sensitive to house dust mite.

Avoidance of irritants

Patients with AE have hyper-reactive skin and react to a variety of irritants. The irritants may be soaps, detergents, moisturisers, and chlorine in swimming pools. These irritants must be avoided in affected patients. Patients should be encouraged to wear cotton clothes, preferably loose fitting. These measures are important in maintaining control of AE.

Topical corticosteroids

Topical corticosteroids have been available for the past 50 years and have been the cornerstone of management of AE.⁷ They are available in varying potencies ranging from very mild to very potent. The mild preparations are generally used on the face and neck areas. Generally treatment is initiated with potent topical steroids for about 7 - 10 days, after which a mild to moderate potency preparation can be used. Topical steroids are very effective in

reducing the inflammation of the skin, thus reducing pruritus as well. When used judiciously they are very effective in controlling AE. The problem with topical corticosteroids is that long-term use may give rise to significant local side-effects such as telangiectasia, skin atrophy and striae formation as well as to systemic side-effects associated with suppression of the hypothalamic-pituitary-adrenal axis. Concern about these side-effects often affects compliance and therefore causes poor control of AE.

Topical calcineurin inhibitors

The availability of calcineurin inhibitors for the management of AE is the most significant advance in the treatment of AE. These drugs are an important class of medication that has selective effects on the T-cell in patients with AE. There are 2 topical calcineurin inhibitors for AE patients, namely pimecrolimus and tacrolimus. Pimecrolimus (Elidel) is the only preparation available in South Africa in this class of medication. Pimecrolimus is an ascomycin derivative with potent calcineurin inhibition that was specifically developed to treat patients with inflammatory skin conditions. It is registered for use in patients over the age of 2 years and clinical trials have shown efficacy and safety in patients from 3 months upwards.

Pimecrolimus is effective topically in patients with AE with little systemic absorption in children and adults with AE. Many large studies have been performed demonstrating the clinical efficacy of pimecrolimus in AE. In one such multicentre, double-blind, randomised study performed in children aged 2 - 18 years, pimecrolimus was found to be more effective than the control vehicle cream over a period of 6 weeks. In a long-term study, pimecrolimus significantly reduced the number of flares compared with vehicle cream over a 1-year period. In trials involving young infants (aged 3 months - 2 years), 67% of patients on pimecrolimus did not require topical steroids compared with 34.8% of patients using the vehicle cream.⁸ In another study of children, 61% of patients in the pimecrolimus group completed 6 months without a flare compared with 34.2% of the control group. A subgroup analysis found that across all severities there was a significant

reduction in the number of flares in the pimecrolimus group.⁹ All the studies in children and adults evaluated safety over 1 year. The safety was consistently equivalent to the vehicle cream. However, burning and stinging of the skin was found in a small proportion of patients in the pimecrolimus group.

CONCLUSIONS

AE significantly affects the quality of life of patients. AE remains a difficult condition to manage. The availability of new classes of drugs such as calcineurin inhibitors is a significant advance in the management of AE. The calcineurin inhibitors can be used as first-line therapy for AE. Patients not responding to calcineurin inhibitors or those experiencing severe exacerbations of AE can use topical steroids for short periods of time. Once control is achieved, calcineurin inhibitors such as pimecrolimus can be used regularly to prevent flares.

References available on request.

IN A NUTSHELL

Atopic eczema significantly affects the quality of life of sufferers.

There are good epidemiological data supporting the view that the prevalence is on the rise. The reasons for this are not clear.

A single treatment modality is not sufficient in controlling the disease.

The availability of new classes of drugs such as calcineurin inhibitors is a significant advance in the management of atopic eczema.

The calcineurin inhibitors can be used as first-line therapy for atopic eczema.

A comprehensive approach is required encompassing allergen avoidance, use of moisturisers, careful application of topical steroids and use of the recently available topical calcineurin inhibitors.

Most patients can be well controlled with a combination of these treatments.