

# Evidence-based treatment of atopic eczema in general practice

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Atopic eczema is a common chronic condition characterised by dry, itchy skin associated with flares and remissions.

The prevalence of atopic eczema (AE) in Western societies is estimated at 10 - 20% in children under 14 years of age. South African rural, peri-urban and urban figures are 0.7%, 1.1% and 3.7%, respectively (Professor G Todd — personal communication). Although there may be individual variations, patients with AE generally have a higher incidence of asthma and hay fever, as well as a history of similarly affected family members. The exact cause is unknown but a combination of genetic and environmental factors probably interacts. The importance of environmental factors is emphasised by the observation of a higher incidence of AE in relatives who have moved from rural to more urban communities.

## CLINICAL FEATURES

Acute eczema is characterised by red, itchy skin and often by vesicles that ooze serum, resulting in crust formation. Scratching may result in secondary infection and associated complications.

In chronic eczema recurrent scratching results in thickening of the skin, prominence of skin marking and colour change (hyperpigmentation or hypopigmenta-

tion); this combination of signs is sometimes referred to as lichenification.

The clinical presentation of AE differs somewhat according to the age of the patient.

### Infantile AE

The onset may be as early as within the first few weeks of life. There is a predilection for involvement of the head and neck, especially the face (Fig. 1). Distinction from infantile seborrhoeic dermatitis may be difficult, but the latter is characterised by the presence of a greasy scale (so-called 'cradle cap') and the absence of

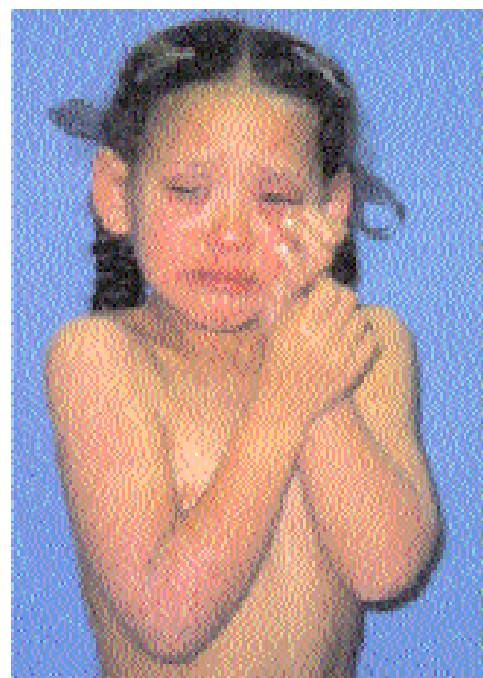


Fig. 1. Child with moderately severe atopic eczema.

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itch, which may be difficult to assess in the very young.

### Childhood AE

After the age of 2 years the skin lesions tend to have a predilection for the folds, especially the antecubital and popliteal fossae of the arms and legs, respectively (Fig. 2).



Fig. 2. Typical flexural involvement.

### Adult AE

In the older patient skin involvement may be similar to childhood eczema or localised to one area, e.g. hand dermatitis.

In more severe disease, involvement in all age groups may be more extensive and in some cases may encompass more than 90% of the integument (if acute and red, sometimes referred to as erythrodermic eczema).

## EVIDENCE-BASED MANAGEMENT

There are many remedies in use, and consequently many claims of usefulness are made by both patients and doctors. This article only looks at evidence from double-blind, randomised controlled trials (RCTs), which are largely regarded as the best evidence for the effectiveness of interventions.

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### UP TO THE YEAR 2000

RCTs of interventions for AE are comprehensively summarised in a systematic review by Hoare and co-workers.<sup>1</sup> This review is extensive and summarises data from 272 RCTs covering 47 different interventions. The authors state that 'there was reasonable RCT evidence to support the use of oral cyclosporin, topical corticosteroids, psychological approaches and UV therapy' (as quoted by Bigby).<sup>2</sup>

There was either insufficient or no RCT evidence for many other interventions, such as maternal allergy avoidance for disease prevention, oral antihistamines, evening primrose oil, emollients, avoidance of enzymatic washing powders, cotton as opposed to synthetic fibres for clothing, and the use of twice-daily as opposed to once-daily topical corticosteroids. It is important, however, always to remember that the absence of evidence does not necessarily mean that the intervention is not successful.

An RCT which we think may be of particular value for general practitioners, is one which examined the effect of antihistamines in relieving pruritus. This study<sup>3</sup> concluded the following: 'Although antihistamines are often used in the treatment of atopic dermatitis, little objective evidence exists to demonstrate relief of pruritus. The majority of

trials are flawed in terms of the sample size or study design. Based on the literature alone, the efficacy of antihistamines remains to be adequately investigated.

Anecdotally, sedating antihistamines have sometimes been useful by virtue of their soporific effect and bedtime use may be warranted. There is no evidence to support the effectiveness of expensive non-sedating agents.'

### AFTER THE YEAR 2000

The following abstracts of a number of RCTs published after the abovementioned review<sup>1</sup> may be useful to the general practitioner:

- 'Moisturizers are widely used in AE. The use of 20% glycerin cream was compared with the urea-saline cream. No differences were found regarding skin reactions such as stinging, itching and dryness/irritation.' The study concluded that a 'glycerin containing cream appears to be a suitable alternative to urea/sodium chloride in the treatment of atopic dry skin'.<sup>4</sup>
- Short bursts of a potent corticosteroid (0.1% betamethasone valerate applied for 3 days followed by the base ointment for 4 days) were compared with a mild steroid (1% hydrocortisone applied for 7 days) in mild or moderate AE in patients recruited from general practices and from a hospital outpatient clinic. The study<sup>5</sup> concluded that: 'A short burst of a potent topical corticosteroid is just as effective as prolonged use of a milder preparation for controlling mild or moderate AE in children.' The study duration was 18 weeks.
- House dust mite allergy is common in AE and, although closely associated with hay fever (allergic rhinitis), it has also been suspected of increasing the severity of AE. Oosting *et al.*<sup>6</sup> investigat-

ed this association and concluded that: 'Use of house dust mite-impermeable encasings resulted in a significant decrease in allergen concentrations. However, this reduction in allergen load did not result in significant changes in clinical parameters between the groups.'

## The wet-wrap dressing technique has proved to be beneficial in cases of exacerbated atopic dermatitis (AD) skin lesions.

- The wet-wrap dressing technique has proved to be beneficial in cases of exacerbated atopic dermatitis (AD) skin lesions. The aim was to investigate the effect of wet-wrap dressings in a controlled trial comparing a steroid-containing (mometasone furoate 0.1%) and a steroid-free (vehicle) preparation in an inpatient comparison study. Twenty children aged 2 - 17 years with exacerbated AD were treated twice daily with wet-wrap dressings over a 5-day period. The study concluded that 'Application of the wet-wrap dressing technique for exacerbated AD lesions is effective, combination with a topical steroid being superior to a steroid-free application without bearing the risk of a bacterial superinfection.'<sup>7</sup>
- A systematic review of the benefit of breast-feeding in preventing AE concluded that: 'Exclusive breast-feeding during the first 3 months of life is associated with lower incidence rates of AD during childhood in children with a family history of

atopy. This effect is lessened in the general population and negligible in children without first-order atopic relatives. Breast-feeding should be strongly recommended to mothers of infants with a family history of atopy, as a possible means of preventing AE.'<sup>8</sup>

- The effect of early supplementation with gamma-linoleic acid (GLA) (i.e. oil of evening primrose) given as borage oil supplement (containing 100 mg GLA) or sunflower oil supplement as a placebo daily for the first 6 months of life was investigated by Van Gool and co-authors.<sup>9</sup> The main outcome measures were the following: the incidence of AD in the first year of life (by UK Working Party criteria), the severity of AD (SCORing Atopic Dermatitis; SCORAD), and the total serum immunoglobulin E (IgE) concentration at the age of 1 year. The results showed a favourable trend for severity of AD associated with GLA supplementation (SCORAD  $\pm$  SD: 6.32  $\pm$  5.32) in the GLA-supplemented group compared with 8.28  $\pm$  6.54 in the placebo group ( $p = 0.09$ ;  $p = 0.06$  after adjustment for total serum IgE at baseline, age 1 week). However, there were no significant effects on the other atopic outcomes. The authors' conclusion was that 'Early supplementation with gamma linoleic acid in children at high familial risk does not prevent the expression of atopy as reflected by total serum IgE, but it tends to alleviate the severity of atopic dermatitis in later infancy in these children.'
- Two recent RCTs examined the effectiveness of tacrolimus (a synthetic immune modulator with cyclosporin-like effects) in AE. The study by Reitamo and co-workers<sup>10</sup> concluded that: 'The efficacy of 0.1% tacrolimus

ointment was similar to that of 0.1% hydrocortisone butyrate ointment and was lower for 0.03% tacrolimus ointment. No serious safety concerns were identified.' (Please note that 0.1% hydrocortisone butyrate ointment is a potent corticosteroid with similar strength to betamethasone valerate.) In another study<sup>11</sup> the same group compared tacrolimus to 1% hydrocortisone acetate (a mild corticosteroid) and concluded that: 'Tacrolimus, 0.03% and 0.1%, was significantly more effective than 1% hydrocortisone acetate and 0.1% tacrolimus was more effective than 0.03% tacrolimus in the treatment of moderate-to-severe AD in children. No safety concerns were identified.'

- A recent study<sup>12</sup> on the effectiveness of pimecrolimus compared with placebo showed impressive results: 'First flare was 144 days in the pimecrolimus group and 26 days in the control group ( $p < 0.001$ ). Pimecrolimus treatment was also associated with improvement in signs and symptoms of AD, pruritus, patients' self-assessment and quality of life.' The authors concluded that: 'Pimecrolimus cream 1% bid is an effective, well-tolerated, long-term treatment for AD in adults, substantially reducing the number of flares compared to a conventional therapy and consequently reducing or eliminating the need for corticosteroid.'
- Azathioprine has been used anecdotally and has now been proved in an RCT to be 'an effective and useful drug in severe AD although it is not always well-tolerated. Monitoring of the full blood count and liver enzymes is advisable during treatment.'<sup>13</sup>

### SUGGESTED PRACTICAL MANAGEMENT OF AE

• **Diagnosis.** Making the correct diagnosis is largely dependent on the history (personal and family history of atopy, i.e. asthma, hay fever) and examination (acute versus chronic eczema and areas of predilection).

• **Moisturisers.** Although there are no RCTs on the effect of soap, we have found the substitution of soap with aqueous cream very helpful (less drying and therefore less likely to induce itch and scratching). We recommend petroleum jelly or emulsifying base as a moisturiser. These are oily and may not be acceptable to all patients, in which case water-based moisturisers such as aqueous, cetomacrogol, liquid paraffin and other creams containing glycerin or urea<sup>4</sup> may be more acceptable. Generally, lotions are not very useful. To reduce the risk of added irritants we warn our patients to avoid antiseptic, topical antihistamine and perfume-containing creams and ointments.

• **Topical steroids.** For acute flares, we recommend the use of 1% hydrocortisone acetate to the face and neck and topical betamethasone to the body as well as wet wraps<sup>7</sup> (we use two layers of cotton tubular bandage as a dressing, a wet (damp — warm water) layer underneath and a dry layer on top) for up to a maximum of 5 days (see Figs 3 and 4). It is important to continue with the liberal use of moisturiser. The use of wet wraps may be continued even without topical corticosteroids (i.e. with moisturiser alone). The advantages of wet wraps include increased contact with the skin during treatment (topical steroid is not rubbed off onto bed linen), and reduction of the skin temperature — thus reducing warmth, sweating and itch and indirectly improving sleep.



Fig. 3. Wet-wrap treatment of a baby.

The quantity of topical steroid is measured according to the 'finger tip' method.<sup>14</sup>

• **Antihistamines.** The effect of antihistamines on itch has not been proved beyond doubt, but sedating antihistamines are useful by virtue of their soporific effect. There is no evidence to support the effectiveness of expensive non-sedating agents.

• **Oil of evening primrose** may be helpful, but more RCTs are needed to confirm the beneficial effects, particularly in view of the cost involved. Therefore oil of evening primrose is not routinely recommended in our centre but neither is it discouraged in the individual patient who inquires about its usefulness (discuss the insufficient evidence with the patient or parent).



Fig. 4. Wet wraps in an older child. Note relative sparing of the face.

• **Newer macrolide treatments.**

There is an excellent chapter by Williams *et al.*<sup>15</sup> on the evidence-based treatment of AE. It summarises data from 7 RCTs on tacrolimus as follows: 'About a third of study participants with moderate-to-severe AE achieve excellent results, defined as at least 90% improvement in the physician's global assessment. A transient burning sensation is a common side-effect that occurs in about half of adults investigated, but is seldom severe enough to necessitate stopping treatment.'

Tacrolimus is recommended for moderate to severe disease, whereas pimecrolimus is effective in mild to moderate disease. In the USA, pimecrolimus is approved for 'short-term intermittent therapy in the treatment of mild-to-moderate AD in non-immunocompromised patients 2 years or older, in whom

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the use of alternative, conventional therapies is deemed inadvisable . . . or in patients who are not adequately responsive or are intolerant to conventional therapies.<sup>16</sup>

Note that the effect of these treatments is equivalent to moderately potent topical steroids. Topical steroids are safe and effective, provided they are used for short, intermittent periods as recommended above. The use of the newer biological treatments is limited by the cost and availability.

What about patients who do not respond? They should be referred to a dermatologist for consideration of other treatment which may include ultraviolet light (with or without topical or oral psoralens), azathioprine, and cyclosporin. Oral steroids are best avoided for the treatment of AE.

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## IN A NUTSHELL

Atopic eczema (AE) is a common chronic condition characterised by a dry, itchy skin, associated with flares and remissions.

The exact cause of AE is unknown, but a combination of genetic and environmental factors probably interact. The importance of the latter is emphasised by the observation of an increased incidence in relatives who have moved from a rural to an urban environment.

The clinical presentation varies according to the age of the patient.

Many remedies are usually tried by both the patient and the doctor, but we only consider treatments based

on evidence from randomised controlled trials (RCTs).

Practical management consists of the correct diagnosis, moisturising the skin with aqueous cream or petroleum jelly, topical steroids and wet wraps in acute flare-ups, and the use of the newer macrolide treatments in patients with moderate to severe AE. However, use of the latter is limited by cost and availability.

Breast-feeding by a mother with a history of atopy may go some way towards preventing a child from developing eczema later in life.

The usefulness of antihistamines to prevent itch has not been proved beyond doubt, nor has that of evening primrose oil.

## SINGLE SUTURE

### Using household possessions to identify the poor

Information on income and expenditure are difficult and time-consuming to obtain, but those working on child-health interventions need information on household economic status. An alternative is to use information on household possessions and characteristics of a family's house. For example, households owning a car can be judged to be wealthier than those owning a motorcycle, which in turn are deemed wealthier than those owning only a bicycle. Electricity implies wealth, as does ownership of a television rather than just a radio. Such information, which is available in demographic, health and other surveys, can be combined into one index of wealth by various means.

(Victoria CG, *et al. Lancet* 2003; **362**: 233-241.)