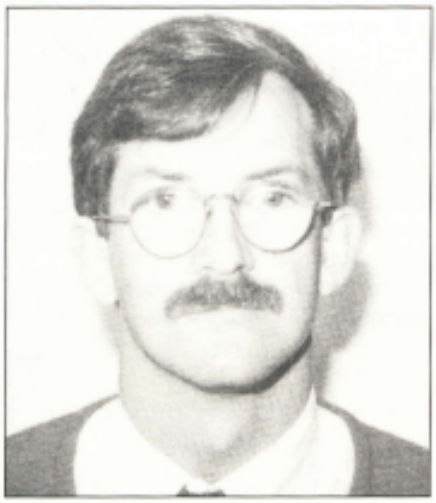
# Atopic dermatitis. An Approach to an Allergic Enigma — AJ Morris



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## Curriculum vitae

Adrian Morris graduated from UCT Medical School in 1983. After his housemanship at Groote Schuur Hospital, his SHO posts included paediatrics at Red Cross Childrens' Hospital and emergency medicine at Groote Schuur Hospital. He then completed GP Vocational training in Surrey, (England) before returning to Cape Town in 1988, to join a group family practice in Newlands. He obtained the DCH (SA) in 1989 and the MFGP (SA) in 1990. Allergy and clinical immunology are his special interests. He is a member of the British Society for Allergy and Clinical Immunology, and was a delegate at their 1991 and 1992 annual conferences. While in England, he attended the BSACI GP training course in Allergy. He was elected onto the executive committee of the Allergy Society of South Africa in 1992.

*Summary*

*Atopic Dermatitis or Infantile Eczema is one of the most common relapsing skin disorders of childhood and one of the most difficult to treat. Despite an ever increasing incidence, the exact aetiology and diagnostic features of Atopic Dermatitis remain unclear. The dry hyper-irritable skin and the misery associated with this condition, disrupts the life of both the affected child and his or her family. Treatment is aimed at controlling the symptoms until natural resolution occurs.*

*S Afr Fam Pract 1993; 14: 255-62*

KEYWORDS:
Dermatitis, Atopic; Physicians, Family; Infant; Allergy and Immunology.

*"It's not the eruption that itches, but the itch that erupts."*

This condition was originally described by Besnier in 1892, but the term "Atopic Dermatitis" was only introduced by Wise and Sulzberger in 1933.

The incidence of Atopic Dermatitis (AD) or Infantile Eczema (synonyms: Prurigo Besnier, Neurodermatitis Constitutionalis) varies from 3 to 10% of the population, with an ever-increasing incidence over the past 30 years .[1] This has been ascribed to progressive urbanisation and increased levels of irritants and pollutants in the home. It commonly appears after about 3 months of age and begins to clear by 3 to 5 years of age. By puberty 40% of cases have completely resolved.

Atopic Dermatitis appears to be inherited as an autosomal dominant trait with poor penetrance.[2]

Patients with atopic dermatitis have a greater predisposition to associated pityriasis alba, forefoot dermatitis, perioral eczema, icthyosis vulgaris, anterior subcapsular cataracts and often later develop occupational irritant dermatoses.[3] Only allergic contact dermatitis seems to be less common in the atopic dermatitis sufferer (with the exception of nickel allergy).

10% of children with severe atopic dermatitis are growth retarded on account of, either the debilitating nature of the disease itself, chronic steroid administration or even restrictive diets which may have been instituted.

## Pathophysiology

An underlying immune abnormality or dysregulation will predispose certain individuals to develop atopic dermatitis.[4] Although serum IgE and peripheral eosinophil counts are raised, indicating an immediate type 1 immune reaction, the histologic appearance seems more indicative of a delayed cell mediated type 4 reaction with no obvious tissue eosinophilia.

In atopic dermatitis, a consistent defect occurs in T lymphocyte suppressor function (CD8+). This results in less efficient IgE synthesis suppression due to inadequate T cell interferon gamma production and associated excess Interleukin-4 production.[4] Moreover, there is hyper-releasibility of histamine by blood basophils with associated

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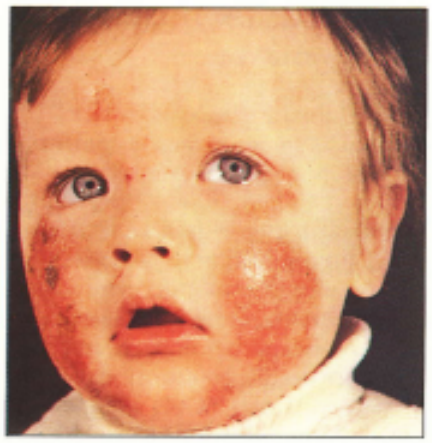


*Infantile distribution with exudative facial lesions – Courtesy Schering – Plough International.*

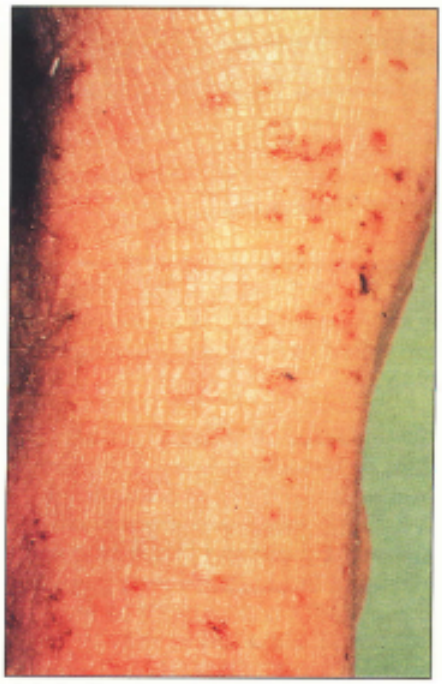
elevation of cyclic AMP phosphodiesterase activity. Neutrophil and monocyte chemotaxis is also abnormally impaired, while IgA levels seem to be temporarily reduced in infants with atopic dermatitis. These factors lead to an increased susceptibility to viral infections such as herpes simplex (which may be generalised as Eczema Herpeticum), and molluscum

White Dermatographism is pathognomonic of atopic dermatitis.

contagiosum. There is also a higher incidence of cutaneous fungal and bacterial infections as well as decreased reactivity to intradermal testing with Tuberculin and Candida antigens. Smallpox vaccination was contra-indicated as it could lead to a generalised vaccinia infection.

It has been suggested that the raised IgE and IgG4 levels noted in 80% of atopic dermatitis sufferers may be an epiphenomenon more relevant to respiratory symptoms than the actual skin lesions themselves. Skin prick allergy testing in individuals with atopic dermatitis may result in initial urticarial and, after 48 hours, frank eczematous lesions. Thus casting doubt on the role of IgE.[5,6]

Histologically the picture initially shows epidermal microvesiculation (spongiosis), with lymphocyte and macrophage infiltration resulting in wet weepy eczema. Later, thickening of the epidermis (acanthosis) occurs with lichenification, fissuring and post inflammatory hypo- or hyper-pigmentation. The epidermal and dermal macrophages or so called Langerhans cells have increased cell bound IgE which may potentiate the binding of irritants and allergens from the skin surface and augment



*Adult distribution with dry flexural lichenified lession. Courtesy Schering - Plough International.*

their presentation to T lymphocytes in the regional lymph nodes. Mast cells and Langerhans cells are significantly increased in chronic lesions, while few eosinophils or basophils are noted. However, immunohistologic techniques have shown dermal deposits of pro-inflammatory eosinophil cationic protein in the lesions of atopic dermatitis.[6] Capillary walls may be

An ever-increasing incidence over the past 30 years.

thickened and increased capillary numbers are seen. Demyelination and fibrosis of cutaneous nerves can also be observed at all levels of the dermis.

The dryness of the skin (Xerosis) may be related to abnormal control of sweat production and decreased sebaceous secretions. As a result, on the positive side, these individuals are less likely to develop acne vulgaris at puberty! White Dermatographism is a paradoxical cutaneous vasoconstrictive reaction to firm stroking of the erythematous skin and is pathognomonic of atopic dermatitis.[5,6]

### Clinical Manifestations

The main symptoms of atopic dermatitis are a chronic relapsing course with intense itching and dry hyper-irritable skin which is initially exudative and later due to scratching, thick lichenified lesions develop in a typical age-related distribution. A family history of atopy can usually be elicited in these children. The lesions get worse in winter due to dryness of the skin and aggravation from woollen clothing.

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### *Infantile distribution:*
(3 months to 2 years)

The lesions occur on the cheeks (milk crusts), neck folds (monks cowl), and groin but relatively spare the napkin area. The limb extensor surfaces may be involved. Lesions are usually oedematous with erythematous papulo-vesicles and marked excoriation and crusting.

### *Childhood distribution:*
(2 to 12 years)

In this age group, drier lichenified plaques are more predominant than exudative lesions. The dermatitis now appears in the flexures, especially the antecubital and the popliteal fossae, neck, wrists and ankles. In the Afro-Asian population the extensor pattern may persist with more prominent icthyosis.

### *Adult distribution*
(12 years onward)

The flexures, feet and hands are involved with pigmentary lesions also occurring on the neck.[7]

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The role of food hypersensitivity is still controversial.

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### *Associated dermatological features include:*

*Keratosis pilaris* is a common autosomal dominant trait associated with atopy and due to hyper-keratosis of hair follicles which become filled with horny plugs. This occurs in childhood and presents as rough skin on the outer aspect of the arms and the thighs.

*Hyperlinear palms, plantar forefoot*

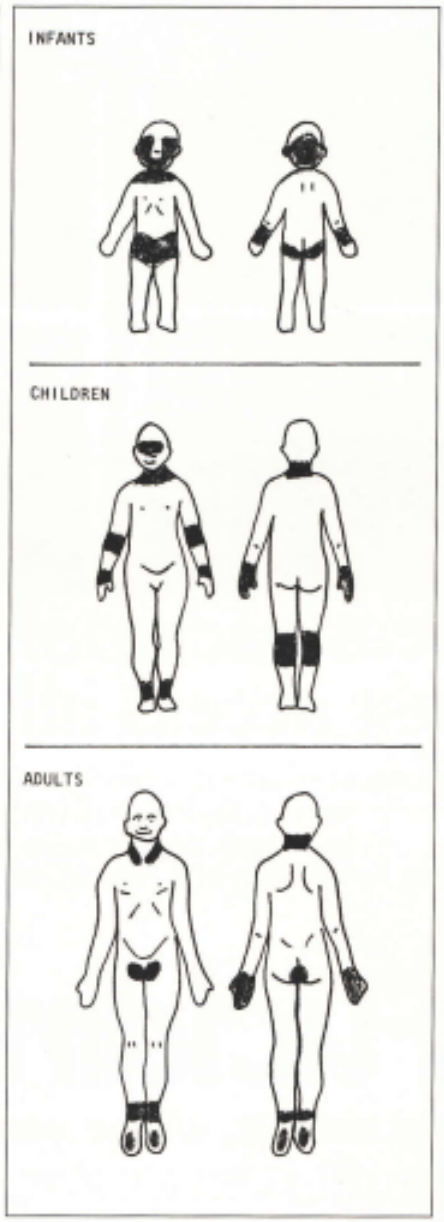


*Figure 1: Distribution of Atopic Dermatitis.*

*dermatitis* and *ichthyosis vulgaris* (especially on the anterior tibial area) are all secondary to the lichenification process.

*Pityriasis alba* is an asymptomatic fine, raised hypopigmented plaque which is seen on the face and the upper arms.

*Circumoral contact urticaria* is commonly due to the irritant effect of tomatoes, citrus fruit and marmite.

*Cutaneous infections* with viruses such as *herpes simplex* may lead to eczema herpeticum. *Staphylococcal* colonisation of atopic skin often leads to impetigo and exacerbates the atopic dermatitis.

Other features associated with atopic dermatitis are *cheilitis, keratoconus, white dermatographism, nipple eczema, eyelid dermatosis* and *periauricular fissures.*

As recently as 1980, Hanifin and Rajka[8] proposed a list of major and minor diagnostic criteria for atopic dermatitis which are now universally accepted.

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Begins to clear by 5 years and often settles by puberty.

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The role of IgE mediated food hypersensitivity in atopic dermatitis is still controversial but up to 10% of cases can be exacerbated by foods such as cows milk, eggs, wheat, peanuts, fish and soya protein. Positive skin prick tests for food allergens are inconsistent whereas a negative skin prick test virtually excludes that food as a source of hypersensitivity. Strict avoidance of the offending food allergen is the only proven therapy. Oral cromolyn is of no benefit. If food allergy is

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Table 1: Guidelines for the Diagnosis of Atopic Dermatitis.
(Hanifin & Rajka, 1980)

**Must have 3 or more major features:**

Pruritis
Typical morphology and distribution
  a) Flexural lichenification or linearity in adults
  b) Facial and extensor involvement in infants and children
Chronic or chronically relapsing dermatitis
Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

**Plus 3 or more minor features:**

Xerosis
Ichthyosis/palmar hyperlinearity/keratosis pilaris
Immediate (type 1) skin test reactivity
Elevated serum IgE
Early age of onset
Tendency toward cutaneous infections (esp Staph aureus and herpes simplex)/impaired cell-mediated immunity
Tendency toward nonspecific hand or foot dermatitis
Nipple eczema
Cheilitis
Recurrent conjunctivitis
Dennie-Morgan infraorbital fold
Keratoconus
Anterior subcapsular cataracts
Orbital darkening
Facial pallor/facial erythema
Pityriasis alba
Anterior neck folds
Itch when sweating
Intolerance to wool and lipid solvents
Perifollicular accentuation
Food intolerance
Course influenced by environmental/emotional factors
White dermatographism/delayed blanch

strongly suspected, an elimination diet may be necessary but should be supervised by a qualified dietician.[9]

Stress also undoubtedly plays a role in an exacerbation, this may be due to an abnormal neurovascular response and release of neuropeptides, resulting in hyperaemia, erythema and pruritis.[5]

### Differential Diagnosis of Atopic Dermatitis

The following dermatoses of infancy are often confused with atopic dermatitis.[7]

*Seborrhoeic dermatitis* is commonly seen in infants under 3 months of age. It is a non-itchy, greasy scaling dermatosis which involves the axilla, scalp (cradle cap), flexures, napkin area, eyebrows, back of ears, trunk and shoulders.

Up to 10% of patients can be exacerbated by foods such as milk, eggs, wheat, etc.

*Napkin dermatitis* is due to the ammoniacal irritant in urine and is restricted to the napkin area, it spares the skin folds and is exacerbated by the occlusive effect of plastic waterproofs.

*Candida dermatitis* occurs in the napkin area, involves the skin folds and extends via satellite lesions down the legs and up the trunk. Candida albicans may secondarily infect atopic and napkin dermatitis.

*Scabies* consists of a very itchy moth-eaten dermatitis and extends to the wrists and interdigital spaces with visible mite burrows. In infants facial lesions may occur as well as bullous lesions on the feet.

*Psoriasis* may affect infants. The lesions consist of slightly raised plaques which may spread up the trunk and usually involve the flexures.

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*Hyper-Immunoglobulin E syndrome* (Staphylococcal abscess syndrome).

This rare condition is associated with extreme elevations of serum IgE levels and increased susceptibility to staphylococcal and candidal infections resulting in deep infections of the skin, lungs, sinuses and other organs.[10]

### Investigations

Laboratory findings in general including skin prick testing are disappointing.[11] IgE and eosinophil counts are usually elevated but of little diagnostic value as they may be an epiphenomenon. Positive food and inhalant RAST tests are inconsistent and non-specific and can be due to respiratory allergy. Skin prick tests tend to be accentuated due to the underlying immune abnormalities. The characteristic delayed blanch reaction to methacholine injection may help in diagnosing atypical atopic dermatitis. Skin biopsy is rarely indicated.

Stress undoubtedly plays a role.

### Treatment:

#### *Preventative measures:*

Breast feeding of infants to at least 6 months of age should be encouraged because of the general benefits. However maternal diet during lactation should be carefully monitored as infants can react to food allergens transmitted via the mother's breast milk. It has been suggested that breast feeding may simply postpone the development of food allergy.[9]

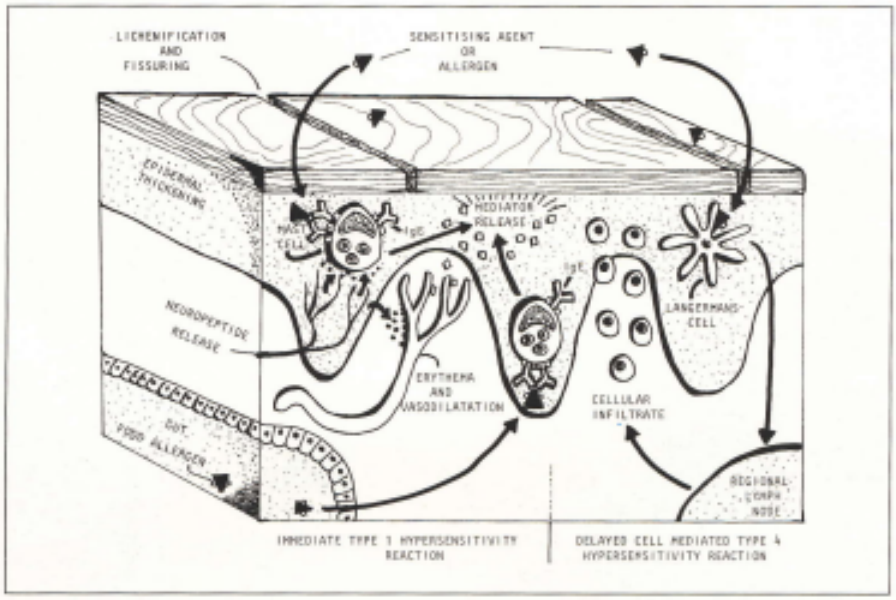


*Figure 2: Pathophysiology of Atopic Dermatitis.*

Infants should avoid hot humid or cold dry weather, excessive sweating, woollen and synthetic clothing and perfumed soaps. The role of diet is debatable, but one should probably try to avoid the 6 common sensitising foods in the first year of life. A stepwise trial of elimination of cows milk, egg, fish, peanuts, wheat and soya may be implemented in older children.[9] Non-biological washing powders (Lux, Sunlight, Fab, Radion and Skip) are preferable. Punch, Biotex, Surf and Omo should be avoided. Bubble baths, household antiseptics and medicated soaps must not be used. Bath water should be luke warm and moisturising emollients must be applied within 3 minutes of patting the skin dry - no rubbing.[8] Often soap has to be avoided altogether, in which case aqueous cream or Cetaphil lotion can be used as cleansers. Local household skin irritants such as wool, mohair, nylon and feathers should be removed. Housedust mite and animal dander avoidance measures may need to be implemented.[12] Recent data has suggested that natural latex, an allergen present in latex dummies, might occasionally exacerbate atopic dermatitis.

Oral cromolyn is of no benefit.

As much skin as possible should be covered with non-allergenic lightweight clothing, taking care not to overdress or overheat the child. Cotton night gloves or mittens can be used to prevent nocturnal scratching, and by cutting fingernails short excoriation and secondary infection will be limited.

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Elbow splints occasionally need to be applied at night to stop scratching in more severe cases. Swimming pool chlorine will irritate the skin, and emollients should be applied after bathing or swimming. There is no contra-indication to routine vaccinations except in the case of smallpox vaccination which could lead to a generalised vaccinia eruption, and BCG vaccination which

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Avoid woollen and synthetic clothing.

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may also exacerbate severe atopic eczema. Young adults should decide on a career that is less likely to expose them to irritant chemicals and should probably avoid nursing, hairdressing, catering, motor mechanics or cleaning. Protective gloves with cotton inner linings will help prevent irritant contact dermatitis. Finally, these children should be given plenty of affection and attention, with liberal handling and play.

### Medical Management

Medical management treads the narrow path between satisfactory symptom control and unwanted side-effects.

### First Line Treatment

*Emollients* are the mainstay of treatment in mild cases and are often all that is needed to settle irritation and prevent dryness of the skin. They may be used in the bath and always after bathing to maintain and improve the barrier effect as well as rehydrate and soothe the skin. Water-miscible creams are suitable for moist or weeping lesions whereas ointments are generally chosen for dry, lichenified or scaly lesions or where a more occlusive effect is required.

Although *Petroleum jelly* (Vaseline) is an ideal moisturiser for dry skin, many patients find it too greasy and cosmetically unacceptable.

*Emulsifying ointment* consists of emulsifying wax 30%, white soft paraffin 50%, and liquid paraffin 30% by weight. Another paraffin-based preparation is *HEB* (Haldens Emulsifying Base) which forms an excellent vehicle for diluting steroids for application to large skin surface areas.

*Aqueous cream BP* or Ung Emulsificans Aqueosum (UEA) consists basically of emulsifying ointment 30 g, phenoxyethanol 1 g in purified water 69 g. Other similarly based creams include *E 45, Cetomacrogol* and *Ultrabase.*

*Oilatum cream,* a 21% protein free polyunsaturated vegetable oil, is excellent as a skin application and the emollient form can be added to bath water.[12]

*Zinc Oxide* (Fissan paste) forms a good protective barrier and in combination with *Calamine* is weakly anti-eczematous and sometimes a useful option. Localised excoriated lesions may improve if bandaged with zinc oxide impregnated cotton bandages.

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Non-biological washing powders (Lux, Skip, Sunlight) are preferable.

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In the more chronic lesions with marked thickening of the skin and scaling, keratolytics such as *Salicylic acid 2%, Ichthammol* or *Coal tar* may be useful. Eulactol, a combination of lactic acid and 10% urea, hydrates the skin and enhances steroid penetration.

Table 2: Relative strengths of various steroid preparations.

| | |
|---|---|
| Low potency | 1% hydrocortisone (safest)<br>Mylocort, Procutan |
| Medium potency | Eumovate, Aclosone. |
| High potency | Betnovate, Synalar, Nerisone, Diprosone, Propaderm, Elocon, Advantan. |
| Very high potency | Dermovate, Diprolene, Synalar forte, Nerisone forte |

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*Topical Steroids:*

These remain the most effective method of treating inflamed skin lesions. Steroid creams or ointments should be applied twice daily. *1% hydrocortisone* is safest to apply in infants and on the face, it is unlikely to cause any skin atrophy. Stronger fluorinated steroids may be used in areas other than the face for acute exacerbations and for short term periods. Tachyphylaxis, the rapid onset of tolerance to the action of a drug after too-frequent application may be overcome by applying potent steroids twice daily for 2 days, alternating with 2 days of no treatment.

Severely thickened and lichenified areas especially in older children and adults may require *clobetasol proprionate 0,05%* (Dermovate) which is 1 000 times more potent than 1% hydrocortisone,[14] or *betamethosone dipropionate, salicylic acid 30 mg* (Diprosalic). *Clobetasone butyrate 0,05%* (Eumovate) should probably not be exceeded in strength when treating infants and young children. *Clioquinol* (Vioform), an antiseptic, may be added to steroid preparations.

Unwanted local side-effects of the stronger fluorinated steroids include:

- Epidermal thinning with atrophy, telangiectasia, striae, facial rosacea and steroid purpura.
- Altered pigmentation, hypertrichosis, perioral dermatitis and folliculitis.
- Secondary skin infections with staphylococci and candida albicans.[13]

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Newer non-fluorinated corticosteroid creams such as *methylprednisolone aceponate 1,0 mg* (Advantan) or *mometasone furoate* 1 mg (Elocon) may provide greater potency with a relatively wider range of safety.

Systemic steroids are only indicated for short term treatment of severe and extensive lesions.

Acute weeping lesions may require treatment with soaks and solutions.

*Aluminium acetate* (Burrows solution), *Potassium permangonate 1:8 000, Zinc sulphate, Glycerine in ichthammol* and *Physiological saline* have all been used in the past but tend to be messy and time consuming forms of treatment.[14]

### *Antibiotics:*

Flucloxacillin or Erythromycin provide effective anti-staphylococcal cover in secondarily infected exacerbations of atopic dermatitis. Topical preparations such as mupirocin (Bactroban) and fucidate (Fucidin) can be applied to localised septic lesions.

### *Antihistamines:*

The efficacy of antihistamines in the management of atopic dermatitis remains uncertain. At best, they provide only a 50% reduction in pruritis.[6] Much of their therapeutic effect is due to sedation and thus *Promethazine* and *Hydroxyzine* are most suited for nocturnal scratching.

*Ketotifen* may play a role in prophylaxis. The role of the newer non-sedating antihistamines is open to debate.

### Second Line Therapy:

Severe cases may benefit from a spell in hospital when systemic treatments can be implemented in a controlled and allergen free environment.

*Gamolenic acid* capsules (Epogam) or Evening Primrose Oil supplements may reduce symptoms in a small proportion of patients by replacing gamma linoleic acid (GLA), a deficiency of which may result in dry itchy skin.[3,15]

Ultraviolet light therapy (UVA and UVB) or psoralens plus UVA *(PUVA)* seem to help the skin lesions by selectively destroying Langerhans cells and hence antigen presentation to lymphocytes is reduced.[9,15]

Immunosuppressant therapy such as *Prednisolone, Azathioprine, Interferon gamma* and *Cyclosporin A* have all been successful in adult patients but carry a significant risk of toxicity.[15]

*Chinese herbal tea therapy.*
Recent placebo-controlled double-blind clinical trials in the UK by Atherton et al[16] have shown that decoctions of chinese herbal tea have led to marked improvement in severe chronic atopic dermatitis that failed to respond to conventional therapy. Although not particularly palatable, this therapy should be considered in refractory cases once it becomes commercially available. The exact nature of the active ingredient in the tea is unclear, but it seems to have both anti-inflammatory and anti-microbial properties. This form of treatment is an exciting discovery and should prove to become quite popular, if ongoing clinical trials continue to demonstrate its efficacy.

For further patient orientated information regarding the various treatment modalities, the British National Eczema Society can be contacted at 4 Tavistock Place, London WC1H 9RA, UK.

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