

The diagnosis and management of atopic dermatitis

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Abstract

The term “dermatitis” (synonym: eczema) refers to a non-infectious, inflammatory disorder of the skin. There are different forms of dermatitis including seborrhoeic dermatitis (infantile and adult types), primary irritant dermatitis, allergic contact dermatitis, dermatitis associated with venous hypertension, dyshidrotic dermatitis (synonym: idiopathic vesicular dermatitis of the hands and feet), photoallergic dermatitis, HIV-associated dermatitis, nummular dermatitis and atopic dermatitis (AD). Atopic dermatitis is common and is the only form of dermatitis that may affect virtually the entire lifespan of an individual.

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Definitions

The term atopy refers to a complex genetic background, the atopic diathesis, to develop allergic asthma, conjunctivitis, rhinitis and atopic dermatitis. Atopic dermatitis develops in individuals with atopy.

Incidence

The incidence of AD in adults in South Africa is unknown. A study conducted in Cape Town among schoolchildren 13–14 years old found a one-year prevalence rate of 8.3% which increased to 13.3% on follow up. In 3–11-year-old Xhosa children a one-year prevalence rate of 1–2.5% was documented. In Western Europe and Australia up to 20% of children develop AD.

Onset

In 70% of cases AD starts in childhood before the age of five years. About 10% of cases seen in hospital settings start in adults. Asthma develops in 30% of children with AD and allergic rhinitis in 35%.

Cause

Atopic dermatitis is a complex disease relying on the interplay of several factors. The disease is familial with polygenic inheritance. A number of suspected gene loci have been identified. Genetics alone cannot explain the increase of AD in smaller families and in higher social classes. Allergic factors such as house-dust mite (HDM), food allergens and pseudoallergens such as citrus fruit and food additives are implicated in some cases. Non-allergic factors are also involved and include *Staphylococcus aureus* infection, bacterial superantigens, rough clothing, exposure to microbes during infancy, excessive heat and sweating, dry air and irritants that disrupt the barrier function of the skin. Emotional stress is a common flare factor in AD. There appear to be two different types of AD: extrinsic AD (80% of cases, elevated total serum IgE, polyvalent type 1 sensitisation [children against foods and

adults against pollens and HDM], CD4 lymphocytes predominate); and intrinsic AD (20% of cases, total serum IgE normal, polyvalent type 1 sensitisation absent, CD8 lymphocytes predominate). The concept is currently controversial.

Clinical features

Criteria for the diagnosis of AD are listed in Table I and minor diagnostic features in Table II. The experienced clinician always looks for Denne-Morgan lines (infraorbital skin creases), periorbital darkening, circumoral pallor, keratosis pilaris (follicular keratotic papules and papulopustules on the arms and thighs), ichthyosis vulgaris (autosomal dominant, fine scaling most prominent on the lower legs and buttocks), pityriasis alba (whitish, round, dry patches with fine scaling) and other minor features which in children are often pointers to atopy.

The rash is chronic and intensely pruritic. The clinical pattern varies at different stages of life. In infants the entire skin surface with the exception of the nappy area may be involved. In children the face is commonly involved and in adolescents the flexures. In adults the hands and nape are preferential areas.

All forms of dermatitis essentially show similar features and are pruritic. Pruritus induces scratching and rubbing. A video of the typical scratching pattern is available at www.safpj.co.za. Acute dermatitis is characterised by erythema, oedema, vesiculation, oozing and crusting. The main microscopic features are acanthosis and variable intercellular oedema, spongiosis. Chronic dermatitis shows leathery thickening of the skin. The skin is dry, scaly and commonly fissured. Microscopy shows compact orthokeratosis, acanthosis and collagen in vertical streaks in the papillary dermis. Subacute dermatitis is red or brown and scaly. Microscopy displays acanthosis and mild spongiosis. All forms show a lymphocytic infiltrate of variable density.

Clinical findings are depicted in Figures 1–8.



Figure 1: Dermatitis of the face. Note the Dennie-Morgan lines, swelling of the lower lip and nasal discharge



Figure 2: Keratosis pilaris on the lateral aspect of the arm. Lesions are follicular papules and papulopustules



Figure 3: Chronic dermatitis (synonym: lichenification) on the outer aspect of the elbow



Figure 4: Dermatitis of the trunk. Some lesions have a nummular (synonym: round) configuration. Note that the child is scratching the lesions

Table I: Criteria for the diagnosis of atopic dermatitis*

The diagnosis requires evidence of itchy skin (or parental report of scratching or rubbing) plus three or more of the following:

1. History of involvement of the skin creases (e.g. fronts of elbows, backs of knees, fronts of ankles, and areas around the neck or eyes)
2. History of asthma or hay fever (or history of atopic disease in a first-degree relative if the child is under four years of age)
3. History of generally dry skin in the past year
4. Onset in a child under two years of age (criterion not used if the child is under four years of age)
5. Visible flexural dermatitis (including dermatitis affecting the cheeks or forehead and outer aspects of limbs in children under four years of age)

* Adapted from Williams et al

Table II: Minor features of AD

Cradle cap as infant, characterised by yellow crusts on the scalp	Periorbital hyperpigmentation
Dry skin	Facial pallor
Associated ichthyosis vulgaris with hyperlinear palms	Pityriasis alba
Keratosis pilaris	White dermographism
Dry hair	Increased pruritus with sweating
Elevated serum IgE and IgE mediated skin reactions	Disease flares with emotional changes

Dermatitis of the palms and soles (juvenile plantar dermatitis)	Unable to tolerate wool or fat solvents
Nipple dermatitis	Food allergies
Cheilitis. The lips are dry, inflamed and cracked	Recurrent conjunctivitis, keratoconus, anterior and/or posterior subcapsular cataracts
Lateral thinning of the eyebrows (Hertoghe's sign)	Absent or reduced corneal or gag reflex
Double fold of lower eyelid (Dennie-Morgan fold or line)	

Diagnostic approach

1. The diagnosis is based on clinical features, namely typical skin changes varying with the age of the patient.
2. A family history of atopy is important.
3. Skin biopsy is of little value in the diagnosis of AD. Skin biopsy is certainly helpful in the diagnosis of superimposed viral and dermatophyte infections.
4. Serum IgE levels may be of value to distinguish between extrinsic AD and intrinsic AD keeping in mind that the concept is controversial. The serum IgE level has no value in the routine management of patients with AD.
5. Skin prick or radioallergosorbent tests have a high negative predictive value (above 95%). Negative tests for food and



Figure 5: Dermatitis involving the cubital fossa in a child



Figure 6: Dermatitis involving the popliteal fossae in a child



Figure 7: Dermatitis of the lateral neck in a baby. There is some postinflammatory hypopigmentation. It is not always possible to distinguish AD from ISE



Figure 8: Dermatitis of the face. Note the presence of molluscum contagiosum and secondary impetigo

environmental allergens indicate that these allergens are not involved. Positive tests are less useful – the positive predictive value is about 40%. These tests are not indicated in the routine management of patients with AD.

6. Increased cholinergic reactions, namely white dermographism (the production of a white line with surrounding blanching after stroking erythematous skin with a blunt instrument) and paradoxical sweat response to cholinergic agents may be present.
7. The skin is dry related to distorted barrier function.
8. The value of patch testing with airborne allergens (the atopy patch test) is unclear. Routine patch tests may be utilised to diagnose superimposed allergic contact dermatitis.
9. Concomitant food allergy presents with urticaria and gastrointestinal symptoms and may not necessarily exacerbate the AD. Diagnosis with double-blind, placebo-controlled food challenges are the gold standard for diagnosis but are cumbersome.
10. Eye examination is indicated in some cases.

Complications

One of the complications is the so-called **allergic march**. A percentage of patients with AD progress to allergic asthma and eventually rhinitis. There is some evidence to suggest that cetirizine hydrochloride may retard this process.

An extremely common complication of AD is **periodic exacerbation of the disease**. These flares may arise spontaneously or may be precipitated by irritation of the skin, bacterial superinfection, superimposed allergic contact dermatitis and stress.

The dermatitis may become widespread involving more than 90% of the body surface area. This is known as **erythroderma**. Erythroderma impairs quality of life and may cause disturbance of thermoregulation. Electrolytes, protein, water and minerals are lost transepidermally. The risk of superinfection is high. Erythroderma may arise spontaneously or be precipitated by irritation of the skin.

Bacterial superinfection, usually in the form of superficial, or superficial and deep folliculitis, impetigo or ecthyma, is common. Pruritus and subsequent scratching impairs the skin barrier paving the way for infection. *Staphylococcus aureus* is the commonest cause, but group A beta-haemolytic streptococci (GABHS) may also be culprits. Infection with certain serotypes of GABHS may be complicated by glomerulonephritis. Erysipelas and cellulitis are less commonly encountered.

Herpes simplex virus infection is not uncommon. The infection may become widespread on a background of dermatitis associated with constitutional symptoms known as Kaposi's varicelliform eruption (synonym: eczema herpeticum). Acyclovir, intravenously in severe cases, is indicated.

These patients are also more prone to develop **molluscum contagiosum** which is caused by MC viruses. The lesions are pearly white papules and central umbilication is commonly present. The lesions may be few or numerous.

Dermatophyte infections are more common in AD, the so-called AD-dermatophyte syndrome.

In some patients with AD the disease may be exacerbated by exposure to sunlight.

Atopic dermatitis **impairs quality of life** creating social and occupational problems. Sleep disturbance due to itching and scratching is troublesome.

Allergic contact dermatitis may be superimposed on AD. In any patient not responding to appropriate treatment the possibility of underlying allergic contact dermatitis should be contemplated and patch tests done.

Differential diagnosis

Conditions to be considered in the differential diagnosis are listed in Table III. The differential diagnosis will depend on the age of the patient and the location of the dermatitis. The classic features of flexural, facial or nuchal dermatitis are extremely typical and can be diagnosed at a glance. In infants, infantile seborrhoeic dermatitis is in the differential diagnosis. Distinction may be very difficult. Infantile seborrhoeic dermatitis tends to appear before six months of age and AD after six months of age. Infants with seborrhoeic dermatitis appear contented and pruritus and scratching are often absent. The napkin area is commonly involved. In AD this area is often spared. Postinflammatory hypopigmentation is more common than in AD. Infantile seborrhoeic dermatitis has an excellent prognosis and usually resolves spontaneously by two years. Flares are unusual. Sometimes the distinction can only be made as the child grows older. Psoriasiform AD must be distinguished from psoriasis.

Treatment

No disease is more complicated to treat than AD. It is essential to work with the patient and parents and they should be made part of the management team. Listening attentively to their observations is important. Do not decide whether the patient needs an ointment or cream. Ask the patient what he or she prefers – cream or ointment. Adherence to topical treatment is vital in the management of these patients. Adherence can be improved by handing out written instructions, by limiting the prescription, and by scheduling a follow-up visit shortly after initiating topical treatment. Electronic monitoring systems are used in some countries. Delivery of text messages via mobile phones may be helpful. Topical medications can be applied once daily leading to improved adherence. Twice-daily application of topical drugs does not improve outcomes. Steroidophobia should be addressed.

Topical therapy

Frequent applications of emollient creams or ointments are vitally important. The patient should determine, often by trial and error, which of these are most suitable. Although the dry skin of AD usually benefits from an ointment, there are many exceptions to the rule. A soap substitute (such as Epizone A or E) is equally important. There is currently no evidence to doubt that regular emollient use is beneficial for the treatment of the dry skin associated with AD. There is no clear randomly controlled trial (RCT) evidence of their benefit. Whether bath

Table III: Conditions to be considered in the differential diagnosis of AD*

Differential diagnosis of atopic dermatitis	
Diagnosis	Description
Seborrhoeic dermatitis of infancy	Red, shiny relatively well-demarcated areas, typically involving the diaper area, are present in infants four months of age or younger. The lower abdomen and armpits may also be involved and scalp scaling (cradle cap) may be present. The infant appears comfortable. The condition clears within a few months.
Adult-type seborrhoeic dermatitis	Poorly defined erythema due to overgrowth of or sensitivity to <i>Malassezia</i> yeasts is present in seborrhoeic areas (i.e. sides of nose, eyebrows, external ear canal, scalp, front chest, axillae and groin creases.)
Discoid (nummular) eczema	Circular “cracked” areas of erythema one to five cm in diameter are present initially on the limbs, often with secondary infection. In children, discoid eczema is most commonly associated with atopic dermatitis and is often confused with tinea (ringworm). In adults, it may be associated with excessive skin dryness and secondary infection with <i>Staphylococcus aureus</i> .
Irritant contact dermatitis	Cumulative damage to the skin barrier from irritants such as soaps and detergents is present. The clinical appearance can be identical to that of atopic dermatitis, but location at sites of maximal exposure (e.g. fingers) may be helpful in making the diagnosis. Some degree of irritant contact dermatitis is common in persons with atopic dermatitis (e.g. in babies, around the mouth, owing to saliva and wet food, and in the diaper area, owing to urine).
Allergic contact dermatitis	A hypersensitivity reaction exists after sensitisation to specific substances (e.g. the nickel in jewelry, the rubber in gloves, or the glues in some shoes). Localisation may suggest this diagnosis, but patch tests are needed to definitely establish it. This diagnosis may coexist with atopic dermatitis.
Frictional lichenoid dermatitis	Shiny papules occur at elbows, knees and backs of hands probably related to friction. The diagnosis may be common, and may be more so in patients with atopic dermatitis.
Other exogenous skin conditions Scabies	Infestation may produce nonspecific eczematous changes on the entire body. Burrows and pustules on palms, soles, genitalia and between fingers help to establish diagnosis.
Onchocerciasis	The chronic phase may be accompanied by widespread itching and lichenification of the skin similar to that seen in cases of chronic atopic dermatitis.
Insect bites	Secondary eczematous changes may develop in the area of the bites, especially on the limbs, and may be confused with atopic dermatitis.

*Adapted from Williams et al

additives provide additional benefit is particularly unclear. Bubble baths, foaming soap and shampooing while bathing are not recommended. The temperature of the bath should be neither too hot nor too cold. Rough texture towels should not be used and the skin should be dabbed rather than rubbed dry.

Topical anti-inflammatory agents

1. Topical corticosteroids

Topical corticosteroids (CS) are an extremely important treatment modality in patients with AD. Potent steroids are reserved for flares and should be applied for a limited period of time. Once-daily application is adequate. These agents should never be applied

more than twice daily. In the absence of flares less potent products suffice. Steroid no-go areas include the face and flexures. Thinning (atrophy) of the skin is the main side-effect. It is not possible to make recommendations about the "best" topical CS as no RCT has compared all the available preparations of similar potency. In adults and children it has been shown that twice-weekly application of a potent topical CS can prevent flare-ups following stabilisation of the eczema. Such data is not available for infants. Skin thinning is not a major problem if the drug is used correctly.

2. Topical immunomodulators

The calcineurin inhibitors (CNI) are newer agents for the treatment of AD. Pimecrolimus cream 1% (Elidel®) is indicated for mild AD (mild AD: < 5% of BSA involved, no acute changes, no impairment on quality of life [QOL]). Pimecrolimus cream works better than vehicle cream. The cream can be used in steroid sensitive areas such as the face and skin folds. The cream is less effective than betamethasone valerate (Betnovate®) in AD.

Tacrolimus ointment 0.03 and 0.1% (Protopic®) is indicated for moderate (5–30% of BSA involved, acute changes on presentation, significant impairment of QOL) and severe AD (> 30% of BSA involved, acute lesions, severe impairment on QOL), and for maintenance of treatment following induction of remission by topical CS. The 0.03% product can be used in children older than two years and the 0.1% ointment in those older than 15 years. The ointment is applied twice daily until remission occurs and is thereafter tapered. Tacrolimus ointment works better than vehicle cream.

Both preparations are more potent than 1% hydrocortisone. The 0.1% preparation is equivalent in efficacy to potent topical CS such as hydrocortisone butyrate and betamethasone valerate. Transient burning occurs in about half of adults but is seldom of sufficient degree to stop the drug. The risk of skin infection, systemic infection and internal cancers remains to be determined. The cost-effectiveness of the CNI and potent topical CS has not been compared. In children tacrolimus should be used if short bursts of a potent topical CS, emollients and educational support have failed.

Tars are available as creams or mixed-in ointments and may be of some value in lichenified lesions.

Antiseptics (such as triclosan 1–3% cream) may be added to the bath to lessen staphylococcal colonisation. The level of evidence is low. Topical application of these agents is not recommended.

Systemic treatment

1. **Antihistamines** can be used for severe pruritus. Sedating drugs work much better. The nonsedating drugs are rather ineffective. It is postulated that cetirizine hydrochloride is anti-inflammatory and may curtail the atopic march.
2. **Ciclosporin** is indicated for severe refractory AD.
3. **Oral corticosteroids** are indicated for severe refractory AD.
4. **Azathioprine** is indicated for severe refractory AD. Ciclosporin, oral corticosteroids and azathioprine have side-effects and should be used for short-term to medium-term periods during major disease flares, with a return to conventional treatment once control is maintained.
5. Flares of AD may be caused by *S. aureus* and appropriate **antibiotic** treatment is perhaps of benefit.
6. **UVA1** (340–400 nm) is reasonably effective for acute flares and **narrowband UVB** (311 nm) better for chronic disease.

The efficacy of unsaturated fatty acids is unclear. No RCTs have been conducted on methotrexate, mycophenolate mofetil or biologic therapies.

Non-pharmacological measures

It is important to avoid triggers such as wool or nylon clothing, fabric softeners and work that requires frequent hand washing. The roughness of clothing textiles is a more important factor for skin irritation than the type of textile fibre (synthetic or natural). Polyester and cotton of similar textile fineness seem to be equally well tolerated. Dust, unfamiliar pets, sweating and shampoos may play a direct role in worsening AD.

If relevant type 1 allergens are identified, these should be avoided. These include pollens and HDM. HDM can be reduced by allergen-impermeable mattresses and pillow covers and regular vacuuming of the room. Whether these measures contribute to the control of AD is currently controversial. Vacation at high altitude may be beneficial. HDM cannot live above 1 500 m perhaps explaining the effectiveness of high altitude vacation.

An elimination diet is indicated only if type 1 allergy is proven. There is some evidence to support the use of an egg-free diet in those with a specific IgE to eggs. There is no evidence to support the use of an elemental or few-foods diet in AD. A pseudoallergen-free diet may be helpful if clinically suggested. The routine use of restricted diets in infants with AD is strongly discouraged. There is certainly a risk of impaired growth and development.

Three RCTs suggest that psychological interventions such as habit-reversal techniques are useful as adjunct to dermatological treatment of AD.

There is no strong evidence of a protective effect of exclusive breastfeeding for at least three months against the development of AD even amongst children with a positive family history.

Course

Approximately 60% of patients with childhood AD are free of symptoms in early adolescence. Up to 50% of cases may have recurrences in adulthood. A more persistent course is predicted by early-onset disease, severe early disease, concomitant asthma and hay fever and a family history of AD.

Summary

Atopic dermatitis is a common skin disease that has a formidable impact on the QOL of the suffering individual. By correctly diagnosing and treating AD this situation may be ameliorated. Hopefully this manuscript will provide practising clinicians with guidelines to achieve optimisation of the management of patients with AD.

Further reading

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