

Management of difficult and severe childhood eczema (syn. 'atopic eczema', 'atopic dermatitis').

McAleer MA ¹

Flohr C ²

Irvine AD ^{1,3,4}

¹Department of Paediatric Dermatology, Our Lady's Children's Hospital Crumlin,
IRELAND

² Department of Paediatric Dermatology, St John's Institute of Dermatology, Guy's and St
Thomas' Hospitals NHS Foundation Trust and King's College London

³Clinical Medicine, Trinity College Dublin, IRELAND

⁴National Children's Research Centre, Dublin IRELAND

Correspondence to:

Alan D. Irvine

Paediatric Dermatology

Our Lady's Children's Hospital, Crumlin

Dublin 12, IRELAND

irvinea@tcd.ie

Phone + 3531 428 2532

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Maeve McAleer and Alan Irvine planned the article; Maeve McAleer did the background reading and prepared the first draft and amended subsequent drafts after input from Carsten Flohr and Alan Irvine. Alan Irvine is the guarantor of the work.

Abbreviations:

AD: atopic dermatitis

CDLQI: children's dermatology life quality index

EASI: eczema area and severity index

EMA : european medicines agency

FDA: Food and drug administration

FLG: filaggrin gene

HHV8: human herpes virus 8

HIV: Human immunodeficiency virus

IgE: immunoglobulin E

UVR: ultraviolet radiation

RCT: randomised control trial

SCORAD: SCORing Atopic Dermatitis

TCIs: topical calcineurin inhibitors

TPMT: thiopurine methyltransferase

POEM: patient orientated eczema measure

UK: United Kingdom

US: United States

VZV: varicella zoster virus

WAO: world allergy organisation

INTRODUCTION:

Childhood eczema is the most common inflammatory skin disease and affects around 20% of children in the UK.[w1] The condition is also referred to as ‘atopic dermatitis’ and ‘atopic eczema’. The correct nomenclature is debated by experts. The World Allergy Organisation recommends ‘eczema’ and this term is widely used in the UK literature. ‘Atopic dermatitis’ is perhaps the more accepted term historically and internationally. For the purposes of this review we will use the term ‘eczema’.

Eczema is associated with a number of co-morbidities, including food and respiratory allergies. It has a significant impact on children’s quality of life and that of their families, for instance through sleep disturbance and a negative impact on schooling (1) (2, 3). This results in a health-related quality of life impairment comparable to other chronic diseases of childhood, including diabetes and asthma. (1)

While mild eczema can often be managed in primary care, around 2% of eczema sufferers have severe disease that does not respond to topical anti-inflammatory treatments or UV light therapy alone. These recalcitrant cases require intensive expert management and an individualised approach, especially when systemic immunomodulatory therapies are used to induce disease control. While these treatments are often life transforming, they have side effect profiles that require close monitoring. At present, there is a distinct lack of evidence to help guide the clinician caring for children with severe eczema. This review summarises the management of difficult eczema in primary care, when to refer to secondary care, and therapeutic options for severe eczema.

Methods Box

We searched PubMed, The Cochrane Collaboration, and the GREAT database (www.greatdatabase.co.uk). The following search terms were used: 'eczema', 'atopic eczema', 'atopic dermatitis', management and treatment. As far as possible, randomised controlled trials and systemic reviews were used to inform the evidence base of this article. Case series have been used where a higher level of evidence does not exist. We also referred to the NICE guidelines on the management of childhood eczema where possible. Expert review articles have also been referenced. In addition, we have included our own clinical views, based on running a specialised service for children with severe eczema for many years.

Main Text

Word count 3260

How common is childhood eczema?

Eczema is the most common chronic inflammatory disease of early childhood and is often the initial step in the 'atopic march', with the subsequent development of food and respiratory allergies (asthma and hay fever).(4)

Eczema affects approximately 10% of children in the US [w2] and around 20% in the UK. [w3, w4] Up to 70% of children with eczema have a spontaneous remission before adolescence. (4) The prevalence of eczema has also shown a significant increase in developing countries, especially in urban areas, where populations have adopted a western lifestyle. [w1, w5]

What causes eczema?

Eczema is a complex disease. Loss-of-function mutations in *FLG*, coding for filaggrin protein, which has a pivotal role in skin barrier function, are strongly linked to eczema risk.[w6] As the vast majority of eczema cases present in early life, and since heritability is more strongly linked to the maternal side, environmental influences that operate *in utero* or in early infancy are very likely to be involved.[w7] For instance, studies have suggested a positive association with water hardness and frequency of washing as well as exposure to antibiotics in early life. [w7] These influences may be partially due to an effect on the skin microflora and further research is needed to understand how environmental and genetic factors interact in the development of eczema.[w7] There are also well characterized systemic and cutaneous immune abnormalities in eczema, including increased total and allergen-specific serum IgE, elevated cutaneous cytokines, T cells, Langerhans cells and inflammatory dendritic epidermal cells, as well as decreased expression of anti-microbial peptides. [w8]

How is eczema diagnosed?

Eczema is a clinical diagnosis, usually made in the primary care setting. It is characterised by itch, skin inflammation, a skin barrier abnormality and susceptibility to skin infection.

The disease can be difficult to define as the clinical features are highly variable and the presentation differs depending on age and ethnicity. (4) (Textbox 1) Whether eczema is one disease or whether there are distinct subphenotypes with different genetic and immunological profiles remains unclear.

With regard to clinical diagnostic criteria, a systematic review concluded that the UK refinement of the Hanifin & Rajka diagnostic criteria (5) is the most extensively validated, both in hospital- and population-based settings as well as a wide range of ethnic groups. [w9](Textbox 2) Many healthcare professionals will not need diagnostic criteria in routine clinical practice, however, although they may prove useful for diagnosing borderline cases.(6)

Approach to Management

Severe eczema is a physically and psychologically demanding disease and requires a comprehensive, holistic, medium- or long-term strategy (Fig. 1). The goals of treatment are to reduce the symptoms, improve quality of life and to decrease the degree and frequency of flares. Furthermore, treatment may modify the overall disease course, and possibly reduce atopic co-morbidities, (7) though more evidence is needed to determine if this is a robust effect. A personalised management plan is essential to ensure adherence to treatment recommendations and treatment success. The management of severe eczema in children often requires a multidisciplinary team approach.

Managing eczema in primary care

Mild eczema can be effectively managed in the primary care setting with effective patient education, regular emollient regimens, and mild or moderate potency topical corticosteroids. There are also NICE guidelines on the treatment of eczema in children. (8)

Patient education

Patient education is essential in the management of eczema and is an important primary intervention. It has been convincingly shown to reduce disease severity and improve quality of life at least over a 1 year period. (9) (10) A RCT concluded that nurses may be better placed to offer educational support, but intervention studies are required to confirm this. [w10]

Bathing and emollients

Regular daily use of emollients is one of the cornerstones of eczema management to counteract skin dryness. Bathing hydrates and cleanses the skin and emollient-based soap substitutes are frequently advised to further moisturise the skin and avoid skin irritation associated with standard soaps. Bathing is usually recommended once daily and emollients are advised once to twice daily or even more frequently, depending on the clinical setting.(11) Ointments contain higher concentrations of lipids and are generally more effective moisturisers than creams. Topical preparations should be dye- and fragrance-free and free of food-derived allergens such as peanut protein. (7)

Despite the universal recommendation of emollient and bath additive use, there is no robust RCT evidence to support this.(12, 13) Of note, the NICE guidelines on the treatment of eczema in children, 2007, recommended that aqueous cream should not be used as an emollient because of its potential to cause irritant reactions.(8) More recently aqueous cream has been shown to increase transepidermal water loss in healthy subjects and those with a history of eczema. [w11, w12] Despite this, aqueous cream is still the most frequently prescribed emollient cream in England. [w12]

Topical corticosteroids

Topical corticosteroids are widely used as first and second line agents in the management of eczema. This class of drugs has anti-inflammatory, antiproliferative, immunosuppressive and vasoconstrictive actions. Topical corticosteroids are grouped by potency, which should be known by prescribers (Textbox 3). The potency of topical corticosteroids should be tailored to the severity of the child's eczema. A proactive rather than reactive approach to treatment is favoured; long term, moisturising treatment to maintain remission with short term 'step-up' treatment for flares.(11) In

mild-to-moderate eczema mild to moderate potency corticosteroids are used for maintenance therapy. Flares are managed with short courses (7 to 14 days) of moderate or potent preparations. Long term potent corticosteroids should not be used in children without specialist advice. Itch is a key symptom for evaluation of response to treatment.(11) Local adverse effects, such as skin atrophy, striae and telangiectasia, can occur with inappropriate topical corticosteroid use, especially on sensitive areas including the face, neck or groin. Systemic adverse effects with use of topical corticosteroids are rare. (7) A systematic review of 10 RCTs showed that there is no evidence that application of topical corticosteroids twice daily is of greater efficacy than a once-daily application. Furthermore, once daily application may increase adherence to treatment recommendations and reduce side-effects and costs. (13, 14)Where eczema is not controlled despite potent topical corticosteroids and full adherence to the prescribe emollient and bathing regimen, or where unsafe quantities of potent topical corticosteroids are necessary for disease management, additional therapeutic approaches are needed.

Antimicrobial therapies

Eczema flares are often attributable to infection, most commonly with *Staph aureus*. These infections can be clinically subtle.(4) Signs of bacterial infection include weeping, crusts, pustules, failure to respond to therapy, and rapidly worsening eczema. However, although there is no doubt about the role of skin infection in eczema flares, two Cochrane reviews of 26 RCTs of anti-staphylococcal measures (prophylactic and treatment) in routine eczema care concluded that there was no clear evidence of an additional clinical benefit. (15) (16) Nevertheless, it is still accepted clinical practice to use antimicrobial measures in patients with frequent skin infections. Combination corticosteroid and antimicrobial ointments can be used for short periods in infected eczema, but a course of oral antibiotics may be equally effective and associated with less resistance development in bacterial strains. A small, investigator-blinded RCT of 31 patients (aged 6 months to 17 years) with moderate-to-severe, clinically infected eczema reported that bleach baths (dilute sodium hypochlorite baths, concentration 0.005%), used in conjunction with intermittent nasal mupirocin, decreased the clinical severity of eczema over a 3 month period. (17) However, the results could be explained

by regression to the mean and more evidence is needed to determine the exact role of such antiseptic measures in routine clinical practice.

Children with severe eczema are also at increased risk of eczema herpeticum, (Fig. 2) which can be recurrent. (18) Early diagnosis and prompt treatment are essential and parents should be educated about the clinical signs and the need to seek medical advice. Chickenpox and viral warts can be more severe in children with eczema. Molluscum contagiosum are frequently encountered in children with eczema and can flare the disease when infected.

Colonisation with the yeast *Malassezia furfur* has also been reported to complicate eczema, particularly in the head and neck areas. Clues are a sharp cut off line between affected and unaffected skin and only partial response to topical anti-inflammatory therapy. In such cases, the addition of a topical antifungal agent can result in significant improvement.[w13]

Antihistamines

Systemic antihistamines are widely prescribed in eczema in the belief that they will reduce itch. The role of histamine in the itch of eczema is unclear, and it may only play a small part. (11) There is no good quality evidence for the usefulness of antihistamines in the management of eczema, and they are not routinely recommended. In an acute flare of eczema with significant sleep disturbance, a 7-14 day trial of an appropriate sedating antihistamine can be offered to children over 6 months.(8)

When should a child with eczema be referred for specialist care?

A child with eczema should be referred for specialist care if the diagnosis is uncertain, if the disease is not controlled satisfactorily with appropriate first line therapies, if there are severe and/or recurrent skin infections, or if there are significant disease-associated social or psychological problems for the child and/or parent.(8)

What is 'severe' eczema?

While there is no universally agreed definition of severe eczema, from a clinical point of view, severe disease can be thought of as eczema that is resistant to first line topical

therapies and associated with a considerable impact on quality of life. The EADV European Taskforce on Atopic Dermatitis defined severe AD as having an eczema severity score (SCORAD) >40 or 'persistent' disease, while the NICE eczema guidelines refer to 'widespread areas of dry skin, incessant itching, and skin redness', but there is no universal consensus on what constitutes a severe case or 'persistent' disease. (11)

The use of validated and reliable severity scores in AD/eczema is important in documenting the treatment response to systemic therapies. Balancing safety concerns with efficacious treatment is of particular importance in children, and objective outcome scores can facilitate this. Of 20 named severity scales, only 3, viz: the SCORing Atopic Dermatitis (SCORAD), the Eczema Area and Severity Index (EASI), and the Patient Oriented Eczema Measure (POEM) scores, have been adequately tested. (3, 6) The Infants Dermatitis Quality of Life index (IDQOL) and Children's Dermatology Life Quality Index (CDLQI) are useful and validated quality of life metrics in children with skin disease. (1)

How common is severe childhood eczema?

Most cases of childhood eczema are mild. Severe eczema is less common, but presents a management challenge. A UK study of 1760 children with eczema found that 84% had mild disease, 14% were classified as moderate and 2% were in the severe category. [w14] A Norwegian population survey reported similar findings. [w15]

How is severe eczema managed?

Topical Calcineurin Inhibitors (TCIs)

Topical calcineurin inhibitors (tacrolimus ointment 0.03% and 0.1% and pimecrolimus ointment 1%) block the production and release of pro-inflammatory cytokines. (7) They are approved by the FDA and EMEA as second-line agents for the short-term and pulsed, long-term treatment of moderate to severe eczema in immunocompetent patients, aged over 2 years. The NICE guidelines for childhood eczema recommend the use of TCIs where first-line treatment of moderate to severe eczema with potent TCS is contraindicated or has failed in children aged 2 years and older. They are also beneficial in areas of delicate skin, such as around the eyes, the face, the neck and the nappy area

where the potential risk of skin atrophy due to potent corticosteroid use is of concern. NICE recommends that TCIs are only used by physicians (including GPs) with a special interest and experience in dermatology.

As for potent corticosteroids, a systematic review and meta-analysis showed that twice weekly application of 0.1% tacrolimus ointment ('weekend therapy') in patients with stable eczema, compared with vehicle (excipient) alone, significantly increased the time between disease exacerbations and the total number of disease free days was increased. (19)The safety profiles of TCIs are reassuring to date and no causal link with respect to carcinogenicity has been demonstrated. (12, 20) There is, however, early but unconfirmed epidemiological evidence of cutaneous lymphoma risk, although longer-term data are needed to fully address these concerns. [w16]

Occlusive treatments (wet wraps).

Occlusion of the skin is widely used in the management of severe eczema. Occlusive dressings increase skin hydration, act as a barrier to scratching, and promote restful sleep. The occlusion also promotes penetration of topical corticosteroids. However, wet wraps can exacerbate infections and increase dryness if not used appropriately and therefore need patient and parent education. (7) The wraps themselves consist of a bottom (wet) and top (dry) layer. They are generally left in place over night and applied for 5 to 7 days in a row. In a critical review of 11 studies, only 2 of which were RCTs, wet wraps were reported as a useful short-term treatment to induce disease remission. (20)

Ultraviolet Light Treatment

A systematic review of 9 RCTs of ultraviolet light therapy (UVR) (21) found it to be effective for eczema compared with placebo and it can be an approach to delay or prevent the need for systemic immunomodulatory drugs, especially in children with dark (type V and VI) skin. A child's inability to comply with safe UVR therapy may, however, preclude treatment in younger children and the practical aspect of three times a week treatment for several months may prove too difficult for some families. In addition, the long-term risk of skin cancer is unknown and of particular concern in white children. When considering UVR as a potential therapy for severe eczema, the

physician should also be cognizant of the possibility of the subsequent need for systemic immunomodulatory drugs, which would further increase the patients' skin cancer risk.

Systemic immunomodulatory therapies

Children with severe eczema may require systemic immunosuppression to achieve disease control. Prior to considering systemic immunomodulatory therapy, possible causes for the failure of first and second line therapies should be explored (Textboxes 4 & 5). Topical therapies require some expertise and can be labour intensive for families. Patients with disease refractory to standard therapies can be admitted to hospital or day care for observation of treatment application and response, before such therapies are deemed failures.

Systemic immunomodulatory therapies utilised in the management of severe eczema are not licensed for use in children and adolescents, apart from Ciclosporin A, which is licensed in Germany for the management of eczema in patients over 16 years of age. The evidence base for usage and safety of these drugs in childhood eczema is not well established; practice has to be guided by experience in adult patients and the use of these drugs in other severe childhood inflammatory disorders; neither of which is ideal. Differences in prescribing practice across geographic regions are largely due to established custom and practice and individual prescriber familiarity with agents rather than based on best evidence, and this is an area that urgently requires more intervention studies. All immunomodulatory medications need pre-treatment screening investigations, as well as close monitoring for side effects throughout the duration of therapy. (Textbox 6)

Ciclosporin A

Ciclosporin is a potent inhibitor of T-lymphocyte-dependent immune responses and interleukin 2 production. It is fast acting, allowing prompt induction of remission in severe eczema. The most notable side effects of nephrotoxicity and hypertension limit long-term therapy. As a result, ciclosporin A may be used as a short term treatment or as a bridge between therapies.

A systematic review of 10 RCTs investigating ciclosporin for eczema concluded that it is an effective therapy for eczema compared with placebo but that relapse is rapid once therapy is discontinued, with clinical scores often returning to baseline values within 8 weeks.(13) Schmitt and colleagues systematically reviewed 11 prospective clinical studies investigating ciclosporin A, and all demonstrated decreased disease activity.(22) The effectiveness of ciclosporin A was similar in children and adult patients,(22) with better tolerability seen in younger patients. (23)

Azathioprine

Azathioprine is an inhibitor of purine synthesis that reduces the proliferation of leucocytes. The target cells and mechanism of action in eczema are not fully elucidated. (24) Azathioprine has a complex metabolism with several immunosuppressant metabolites. The balance between thiopurine metabolites is governed by thiopurine methyltransferase (TPMT) activity. (24) The pre-treatment determination of TPMT genotype or activity level allows informed drug dosing to minimise myelotoxicity. Other side effects include headache and gastrointestinal upset, hepatotoxicity and drug hypersensitivity. Azathioprine has a slow onset of action, with a notable clinical improvement at 2-8 weeks into therapy. [w17] One double-blind, placebo controlled, cross-over RCT of eczema in adults reported that azathioprine was significantly associated with improvement in quality of life measures. There was a mean reduction in disease activity of 27% after 12 weeks of treatment.(25) In a series of 28 children with severe eczema treated with azathioprine, 61% reported significant improvement, 21% some improvement, and 18% no improvement. Seven patients (25%) experienced laboratory abnormalities necessitating a dose adjustment. (26) Personal experience is that patients treated with azathioprine take longer to respond and do not rebound as often or as rapidly as those treated with ciclosporin on discontinuation of therapy.

Methotrexate

Methotrexate is a commonly used treatment for other chronic inflammatory diseases including adult psoriasis and childhood arthritis. Its mode of action is not fully understood, but it has anti-inflammatory effects and also reduces allergen-specific T cell activity. [w18] It is thought to augment concentrations of adenosine which acts as an

endogenous anti-inflammatory agent by mediating cytokine release and adhesion molecule expression, as well as by binding to adenosine cell surface receptors. (27) Gastrointestinal disturbance, liver function abnormalities and bone-marrow suppression are potential side effects, although the medication is generally well tolerated.(27) There is a paucity of evidence for the use of methotrexate in eczema with a single RCT of methotrexate use in eczema in adults. (28) This was a single-blind, parallel group RCT in 42 patients with severe eczema. Patients were randomly assigned to receive either methotrexate or azathioprine for 12 weeks. This study suggests that methotrexate and azathioprine may be equally effective in treating eczema in the short term, but larger adequately powered studies with longer follow up periods are required. [w19] One case series of 25 paediatric patients with refractory discoid eczema treated with methotrexate reported 16 patients 'cleared' and a further 3 patients 'almost cleared'. The medication was well tolerated and no adverse events were observed. (29)

Mycophenylate mofetil

Mycophenylate mofetil selectively and reversibly inhibits inosine monophosphate dehydrogenase, which suppresses the de novo pathway of purine synthesis, resulting in selective suppression of lymphocyte function. Unwanted effects on other cell types are minimised. The most frequent side effects are gastrointestinal disturbance. Mild increases in serum levels of liver enzymes are also reported. Significant bone marrow suppression is uncommon.(30) Mycophenylate mofetil is used in recalcitrant eczema, although there has been no controlled study investigating its efficacy. A retrospective case series of 14 children with severe eczema treated with mycophenylate mofetil reported 4 children cleared completely, 4 had an 'excellent', 5 a 'good' and one an 'inadequate' response. Mycophenylate was well tolerated in all patients. (30) Another paediatric case series reported 12 patients who transitioned from azathioprine to mycophenylate for management of their eczema. Eight reported 'significant' and 4 'no improvement'. (26)

Are there any novel therapeutic targets for severe eczema?

It is hoped that new insights into the complex pathophysiology of eczema will allow more targeted treatments aimed at dysregulated structural or immune functions and

that a better understanding of eczema endophenotypes will facilitate a more individualised therapeutic approach. Furthermore, insights into filaggrin synthesis and function will facilitate strategies aimed at the reversion of low filaggrin expression. [w20] The increased risk of skin infection could be addressed by agents that induce antimicrobial peptides, [w20] and biologics that influence the early development of specific B- and T- cell clones may aid to reduce the inflammatory cascade in AE. [w21] All this requires more basic research and, eventually, well designed randomised controlled trials with clearly defined diagnostic criteria and outcome domains related to disease severity, long-term control of flares, and patient's quality of life. [w22]

Methods box

We searched Medline, The Cochrane Collaboration, and the GREAT database (www.greatdatabase.co.uk). The following search terms were used: 'eczema', 'atopic eczema', 'atopic dermatitis', 'management' and 'treatment'. As far as possible, evidence from randomised control trials and systemic reviews were used. Some case series have been used in the absence of a higher level of evidence. Expert review articles have been referenced. In addition, expert opinion based on clinical experience is included.

Textbox 1 – Clinical features of eczema

- Clinical manifestations vary with age.
- Typically starts in early infancy - eczematous, erythematous papules and vesicles lesions on the cheeks and the scalp. Scratching causes crusted erosions.
- Childhood phase (approximately 2 years old to puberty) - primarily involves the flexures, the nape of the neck, and the dorsal limbs with lichenified papules and plaques.
- In adolescence and adulthood - dry, scaly, erythematous, lichenified plaques affect the flexures, head, and neck and dorsa of the hands and feet.
- Eczema presents differently in Asian, African and Afro-Caribbean children
- Skin can appear darkened rather than erythematous.
- There can be extensive lichenification and prurigo lesions.
- Extensor limbs and buttocks are predominantly involved rather than the flexures.
- Follicular and discoid patterns of atopic eczema are more common in darker skin children.

Textbox 2 – UK refinement of the Hanifin and Rajka diagnostic criteria for AD

In order to qualify as a case of AD with the UK diagnostic criteria, the child:

Must have:

An itchy skin condition in the last 12 months

Plus three or more of:

- i. Onset below age 2*
- ii. History of flexural involvement
- iii. History of a generally dry skin
- iv. Personal history of other atopic disease**
- v. Visible flexural dermatitis

* not used in children under 4 years

** in children aged under 4 years, history of atopic disease in a first degree relative may be included

Textbook 3: Topical Corticosteroid potency classes and examples

1. Mild – 1% hydrocortisone
2. Moderate – Betamethasone valerate 0.025% (Betnovate-RD®) and Clobetasol butyrate 0.05% (Eumovate®)
3. Potent – Betamethasone valerate 0.1% (Betnovate®), Hydrocortisone butyrate 0.1% (Locoid®), Mometasone furoate 0.1%(Elocon®)
4. Suprapotent – Clobetasol propionate 0.05% (Dermovate®)
5. Combination antimicrobials and corticosteroid – Hydrocortisone acetate 1% (mild) + fusidic acid 2% (Fucidin H®), Clobetasone butyrate 0.05% (moderate) + oxytetracycline 3% + nystatin (Trimovate®), Betamethasone valerate 0.1% (potent) + neomycin sulphate 0.5% (FuciBET®), Hydrocortisone butyrate 0.1% (potent) + chlorquinadol 3% (Locoid C®)

Textbox 4

Approach to non-response to first line therapies

1. Assess adherence to treatment recommendations and technique including quantities of topical agents applied and directly observed application
2. Assess for role of infection including *Staphylococcus aureus* and herpes simplex infection.
3. Consider the role of allergens exacerbating the disease – immediate type allergy to foods and aeroallergens as well as delayed type hypersensitivity to a contact allergen, including topically applied medicaments.

Textbox 5

Potential triggers for eczema

Irritants – hard soaps, detergents, fragrances

Infections – *Staph aureus*, herpes simplex, molluscum contagiosum

Overheating

Psychological stress

Aeroallergens – pollens, grasses, animal dander, house dust mite

Food allergens – in particular egg, peanut, and cow's milk

Textbox 6

Suggestions for pre-treatment screening and other general considerations for systemic immunosuppressant treatment in eczema (depending on the population being treated).

Pre-treatment infections screening includes VZV immune status, viral hepatitis screen, Mantoux/ImmunoSpot tuberculosis screening, HIV status, depending on the population being treated. This requires local interpretation.

Pregnancy prevention should be considered when appropriate. FDA pregnancy categories are as follows: ciclosporin C, azathioprine D, mycophenylate mofetil D and methotrexate X.

Live vaccines (e.g. MMR, Yellow fever, Typhoid) are contraindicated while taking ciclosporin, methotrexate and azathioprine.

Killed vaccines (e.g. influenza, hepatitis A, polio, rabies) may be less likely to induce immunisation in immunosuppressed individuals. Immunosuppressed patients may have more severe forms of infections such as influenza, and these are therefore advised in patients on systemic immunosuppressants.

Annual pneumococcal and influenza vaccines are recommended.

Patients and parents should be educated on sun behaviours while on immunosuppressants due to an increased risk of skin cancer.

Vitamin D levels should be checked before and during immunosuppressant treatments and supplemented as necessary. (Careful sun avoidance is recommended in immunosuppressed patients. Vitamin D deficiency is common in Northern climates and will be exacerbated by active sun avoidance.)

Each treatment has individual screening protocols for renal, hepatic and bone marrow impairment, and prescribers need to be familiar with these.

Full and frank discussion and disclosure with children and parents about risk benefit balance before initiating therapy.

Textbox 7

Summary points

- Eczema is associated with significant morbidity for the patient and family.
- Patient education is essential for the treatment of this complex, chronic disorder.
- Topical anti-inflammatory therapy together with regular use of emollients can effectively manage the majority of children with eczema.
- Patients with eczema are particularly susceptible to infection with *Staph aureus*, herpes simplex virus and molluscum contagiosum. These infections can cause disease flares and treatment resistance.
- Patients with severe eczema may require systemic immune-modulatory therapies. These are prescribed off-label and require close monitoring by a physician experienced in their use.

Textbox 8

Questions for future research

Does the regular use of emollients directly after birth in high risk children reduce the risk of eczema development?

Does treating eczema early prevent severe disease?

Does early intervention prevent respiratory allergies in later life?

Are there eczema endophenotypes, and do these allow the development of personalised therapy?

Textbox 9

Tips for non-specialists

- Explore the effect of the condition on the child's sleep, schooling, sports, social activities and family life. Acknowledging and, if possible, addressing these stressors can improve management success.
- Ensure that topical treatments, including emollients and topical corticosteroids, are being applied correctly. Patient and parent education is vital. Directly observed treatment is useful in determining patient/parental concordance with treatment.
- Topical corticosteroid phobia is a common cause of non-adherence and needs to be addressed.
- Consider skin infection, which can be clinically subtle, in patients unresponsive to first line therapy.
- Patients on systemic therapies need frequent expert assessments for treatment response, changes in disease status and potential side effects.

ADDITIONAL EDUCATIONAL RESOURCES

The American Academy of Allergy, Asthma & Immunology – www.aaaai.org
(Information for professionals on eczema and food allergies, including latest research summaries)

Centre of Evidence Based Dermatology, University of Nottingham -
<http://www.nottingham.ac.uk/scs/divisions/evidencebaseddermatology/index.aspx>
(Evidence based dermatology site including information from the Cochrane Skin Group, the UK Clinical Trials Dermatology Network, and the NHS Evidence website)

Cochrane Skin Group - <http://skin.cochrane.org>
(Evidence based dermatology with systematic reviews)

Health Technology Assessment for Atopic Dermatitis (UK, 2001):
<http://www.hta.ac.uk/fullmono/mon437.pdf>
(A systematic review of treatments for atopic dermatitis)

NICE Guidelines: <http://guidance.nice.org.uk/CG57>
(NICE guidelines on the management of atopic eczema in children)

All these resources are free to access.

INFORMATION RESOURCES FOR PATIENTS

National Eczema Association (UK) <http://www.eczema.org>
(Parent information website on eczema and general management principles)

National Eczema Association (USA) www.nationaleczema.org
(Patient/parent website on eczema including information for schools and teachers)

Eczemanet – www.skincarephysicians.com/eczemanet/index.html

(Patient/parent information on eczema, types and treatment)

Under My Skin: A kid's guide to Atopic Dermatitis – www.undermyskin.com

(Online books for children with eczema)

DermNet NZ <http://www.dermnetnz.org/dermatitis/treatment.html>

(Patient/parent information on treatments for eczema)

Nottingham Support Group for Carers of Eczema -

<http://www.nottinghameczema.org.uk>

(Patient/parent information on the disease, including latest research and media coverage of eczema)

The Eczema Centre – www.eczemacentre.org

(Patient/parent resources on disease and treatment, including factsheets on bleach baths and wet wraps)

Ciclosporin:

<http://www.bad.org.uk/Portals/Bad/Patient%20Information%20Leaflets%20%28PILs%29/Ciclosporin%20Update%20Jan%202010%20-%20lay%20reviewed%20Nov%202010.pdf>

Azathioprine:

<http://www.bad.org.uk/Portals/Bad/Patient%20Information%20Leaflets%20%28PILs%29/Azathioprine%20Update%20May%202010%20-%20lay%20reviewed%20Dec%202010.pdf>

Methotrexate:

<http://www.bad.org.uk/Portals/Bad/Patient%20Information%20Leaflets%20%28PILs%29/Methotrexate%20Update%20Mar%202010%20-%20lay%20reviewed%20Dec%202010.pdf>

Mycophenylate mofetil:

http://www.bad.org.uk/Portals/_Bad/Patient%20Information%20Leaflets%20%28PILs%29/Mycophenolate%20Mofetil%20Update%202010%20-%20lay%20reviewed%20Jan%202011.pdf

(Patient information from the British Association of Dermatologists on ciclosporin, azathioprine, methotrexate and mycophenylate mofetil.)

All these resources are free to access.

Image Legends

Figure 1: This child had severe eczema despite maximal topical therapy and inpatient management.

Figure 2: This baby had eczema herpeticum. After an incubation period of 5 to 12 days, eczema herpeticum presents as multiple, disseminated, vesiculopustular lesions and painful punched out erosions.

Aoife's story (aged 8)

Life with eczema before treatment:

When I had eczema it was hard for me not to scratch.

I hated getting blood on my clothes all the time.

I felt sad at times not being able to do stuff, not being able to swim, and not being able to walk properly.

I never liked people saying things about my skin when they saw it.

I wished I could have done stuff like everybody else.

I hated getting in trouble for scratching.

If I would sit and think about my skin, scary question would come to my head.....Would eczema go away? Would my body ever look normal? Would people laugh at me?

Life now after treatment:

I feel so much happier now.

I'm able to do stuff like everybody else :)

Life is so much easier for me now.

Now my skin is better I don't have to worry about people laughing about me.

I don't have to wear gloves at night to stop me scratching during the night.

Now I feel just like everybody else:)

Aoife's mother's story

One of the hardest things was the sleep deprivation. One night seemed to roll into another. As parents we felt very out of our depth. The other children in our family felt very neglected as all of our time was consumed by her skin and creams, baths and bandages as well as washing clothes and sheets because they were so badly soiled with blood. We always needed to watch her in case she scratched and made things worse. It was very stressful watching Aoife scratch herself to pieces and nothing we did or said would stop her. It is a condition that can get very out of control, not only medically but also in the way it can affect your state of mind. It was the worst thing we have been

through as a family. I now feel very blessed to have come out the other side. It may not be a terminal illness but it was very hard to cope with. We now have found such peace and feel we have control of Aoife's condition with the help of her medications. We have learned so much along the way and now just look ahead to good times.

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