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Title: Diagnosis and treatment of eczema in children

Author: Dr Matthew Ridd FRCGP PhD

Address: GP and Reader in Primary Healthcare, Centre for Academic Primary Care Population Health Sciences, Bristol Medical School, University of Bristol, Canynge Hall 39 Whatley Road, Bristol BS8 2PS

T: 0117 331 4557 E: <u>m.ridd@bristol.ac.uk</u> Twitter: @riddmj

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Background

Eczema, the clinical phenotype of atopic eczema/dermatitis, affects around 20% of pre-school age children in the United Kingdom (UK). The disease manifests during the first year of life in 60% but it can develop at any age. It can have a significant psychosocial impact on the child and their family. While eczema improves or resolves in up to 70% of children, markers of persistence are early onset, severe disease, family history, and early allergen sensitisations.

NICE guidance¹ was published in 2007 and is due to be updated soon, as there have been important advances in our understanding of its treatment during this time. The focus of this article is on children with eczema who have disease of mild or moderate severity, in whom diagnosis and management should be possible exclusively within primary care.

Diagnosis

Eczema is diagnosed clinically, the characteristic features being dry, rough and itchy skin. Classically the scalp, cheeks and extensor surfaces are affected in infants; with flexural, especially the cubital and knee folds, involvement later, along with the wrists, ankles and hands (see Figure 2: Eczema Written Action Plan (© University of Bristol)

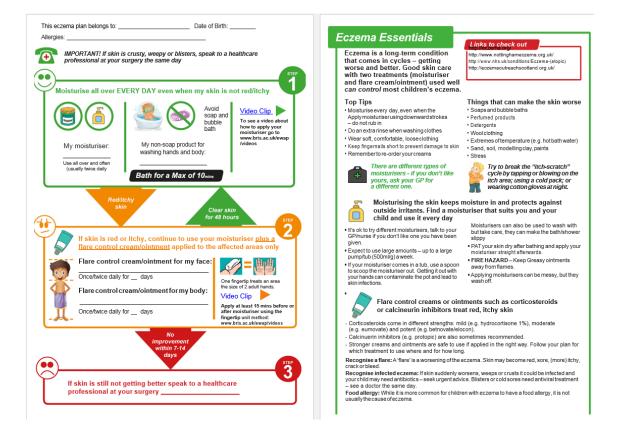


Table 1). Seborrhoeic dermatitis is the most common differential diagnosis in infants, in which the lesions are early onset, greasy rather than dry, involve the scalp (cradle cap) and not itchy.

Management

The main principles of treatment are avoidance of trigger factors, maintenance of the epidermal barrier with emollients, and anti-inflammatory therapy with topical corticosteroids or calcineurin inhibitors. Detergents, wool fabrics, extremes of temperature and humidity and psychological stress are all factors reported to contribute to eczema "flares". Emollients should be used daily and anti-inflammatory treatments in step-up/down manner according to disease severity (Figure 1).

Emollients

Emollients can be used in three main ways: as a "leave on" treatment, soap substitute and/or bath additive.

All patients should use emollients, as a "leave on" treatment – that is, applying them directly to the skin and add or help retain moisture. Used regularly, they improve the skin barrier, comfort and may reduce the number of disease flares. Many different emollients can be prescribed or bought over-the-counter. The main formulations are lotions, creams, gels and ointments, which vary in their consistency from "light" to "heavy". This mainly reflects differences in oil (lipid) to water ratios. Some products also contain humectants which help retain moisture.

There is poor evidence regarding the clinical effectiveness, adverse effects and cost-effectiveness of different products.²³ This is reflected in the guidance issued by Clinical Commissioning Groups and Local Health Boards in England and Wales respectively, who have produced over 100 different emollient formularies that made conflicting recommendations about 109 different emollients.⁴ Recent NHS England guidance (www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-precscribed-in-pc-ccg-guidance.pdf) is clear in that while it discourages the prescribing of emollients for people with "mild dry skin" only, GPs should continue to prescribe them for people with eczema.

Referring to your local formulary, start with emollients without fragrances, urea or antimicrobials, as these ingredients are more likely to cause irritation. Initially, consider prescribing one or more emollients in 100g quantities as "testers", making appropriate amounts (500 grams or millilitres) of the preferred emollient(s) available on repeat prescription thereafter. Make allowance for extra supplies needed for nursery or school, and for different "homes" when the child's parents don't live together. Give clear directions on their use (see Table 2). You may need to prescribe different emollients for different purposes, e.g. an ointment from a tub as a leave-on treatment and a cream in a pump for use as a soap substitute.

Bath additives are distinct from other emollients, as they are designed to poured into the bath and provide "passive" moisturisation. The recently published BATHE trial evaluated their use in 483 children (1-12 years) recruited from primary care.⁵ Participants were allocated to usual care or usual care plus bath additive with the primary outcome measured at 16 weeks. Neither the primary outcomes of patient-reported measure of eczema severity nor any of the secondary outcomes showed any benefit from the use of bath additives. Consequently, mainly emollient guidelines no longer recommend their use, although it is possible that bath additives may still have a role in adults and products that contain antimicrobials may be appropriate for children with recurrently infected eczema.

Topical corticosteroid and calcineurin inhibitors

Topical corticosteroids (TCS) are all classified by their potency from mild through to very potent. Examples are listed in Figure 2: Eczema Written Action Plan (\bigcirc University of Bristol)

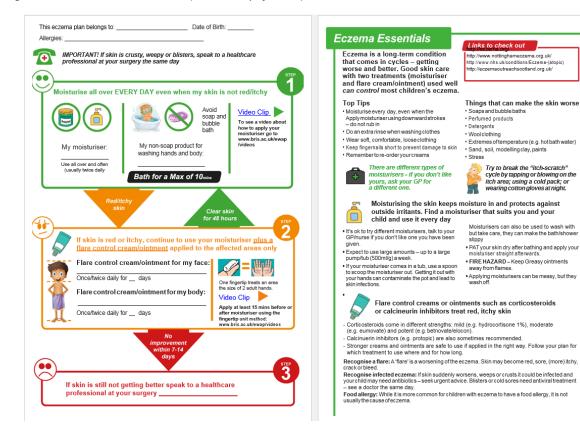


Table 1: Clinical features of eczema

- Pruritus
- Xerosis
- Typical morphology and age specific patterns
 - Facial, neck and extensor involvement in infants or children
 - Current or previous flexural lesions in any age-group
 - Sparing of the groin and axillary regions
- Chronic or relapsing history
- Atopy

Table 2Table 3. The choice of potency should be based on age, body site and severity of eczema. NICE's recommendation of matching potency to severity (mild for mild, moderate for eczema, potent for severe) is easy to remember and apply, but without any evidence, such as how best to assess severity.⁶

For most people with eczema, TCS are the only anti-inflammatory treatment needed, although topical calcineurin inhibitors may have a place for more severe disease and/or eczema in sensitive sites such as the face. Topical pimecrolimus (Elidel) is licensed for mild to moderate eczema, and topical tacrolimus (Protopic) is licensed for moderate to severe eczema. It is recommended that either are only initiated by a specialist/those experienced in managing the condition; and after failure of TCS and/or when there is the risk of TCS side-effects, particularly skin atrophy.

Ointments are generally preferable to creams, unless the eczema is weeping or there is patient preference for creams. TCS and CNI are most commonly used reactively to treat a disease flare, in which case a response to treatment should be expected in 7-14 days, with a view to stepping-down or stopping treatment thereafter. However, some patients may benefit from proactive application of TCS on two consecutive days per week ("weekend therapy") as a maintenance treatment of "hot spots".⁷

Patients and healthcare professionals worry about the risks associated with TCS use, which can be local (skin atrophy, striae and purpura) or systemic (hypothalamic pituitary axis and growth suppression).⁸ In fact, side effects are uncommon in clinical practice and patients may come to more harm from under-use rather than over-use. While the quality and availability of data are limited, a recent review of 36 systematic reviews of TCS safety in people with eczema is reassuring.⁹ It found no significant differences in reports from individual short-term RCTs in the risk of developing skin atrophy with TCS compared to vehicle or between mild and potent TCS, and most trials reported no cases. The largest trial of TCS safety found only one case of skin atrophy in 1213 children followed up for 5 years. A meta-analysis of short-term observational studies in children showed a low overall rate of biochemical signs of adrenal suppression of 3.8% which decreased to 2% with mild potency topical corticosteroids. No clinical symptoms of adrenal insufficiency were observed and the biochemical changes were reversed upon stopping TCS. Skin burning and pruritus are more common with topical calcineurin inhibitors than TCS. However, the use of wet-wraps was found to significantly increased the rate of folliculitis; and there was a higher risk of local site reactions with topical calcineurin inhibitors compared to TCS and with TCS compared to Chinese herbal medicine.

Risks can be minimised by considering the key factors that affect TCS absorption (Table 4). Longterm treatment, higher potencies, vulnerable sites, use of occlusion and/or extremes of age all increase the potential for harm. The finger-tip unit (FTU) is a practical way of guiding the amount to be used: the amount of TCS that is squeezed out from the very end of the finger to the first crease in the finger (from a standard 5mm nozzle tube) is sufficient to treat a skin area about twice that of the flat of the hand with the fingers together. Once daily application of TCS is as effective as twice daily, minimises the risk of adverse effects and simplifies treatment regimes.¹⁰ Appropriate use of TCS minimises the risk of TCS withdrawal, data on which is very limited.

Other treatments

Despite the clear association between eczema and Staphylococcus aureus on the skin, there is uncertainty about what constitutes infection and when antibiotic treatments are likely to confer benefit.¹¹ There is no clear evidence that anti-staphylococcal interventions such as antiseptic bath additive, or the addition of antimicrobial agents to topical therapies, are clinically beneficial in non-infected eczema. The CREAM trial, which randomised 113 children with clinically infected eczema flares, found no meaningful benefit from oral or topical antibiotics over placebo.¹² Instead, stepping-up TCS may be a more helpful approach in this situation.

Specialist clothing manufacturers claim benefits for the management of eczema, by helping regulate humidity and temperature, and possibly through an antimicrobial action. The CLOTHES trial found no evidence of any difference between the 300 children randomised to receive silk garments and standard eczema care alone. While this does not preclude parents from purchasing such garments themselves, the findings argue strongly against them being prescribed on the NHS.

While some guidelines suggest use of sedating, first-generation oral antihistamines when eczema causes sleep disturbance, for most children they have no role. Oral corticosteroids should be avoided in all but the most severe exacerbations, in which case specialist input is warranted.

Overcoming treatment barriers

Treatment should be guided by disease severity and carer and older children's preferences, especially with respect to emollients where acceptability may be influenced by severity, body site, season/climate and cultural beliefs. Recent research has highlighted the importance of identifying and addressing parent's concerns, which can otherwise lead to poor treatment adherence and outcomes.¹³ A common but sometimes unvoiced concern is diet in the affected child and/or the breast-feeding mother. While immediate-type food allergies are more common, evidence that foods such as mild, egg or wheat cause the on-going symptoms of eczema in most children is weak. The role of allergy tests is also controversial and subject to a feasibility trial.¹⁴ There is some evidence that probiotics taken during late pregnancy and breastfeeding (36 to 38 weeks gestation through the first 3 to 6 months of lactation) may reduce risk of eczema in offspring.¹⁵

Evaluating disease severity in psychosocial as well as physical terms; acknowledging the challenges of using topical therapies long-term; and emphasising the "control not cure" message can all help. However, even relatively simple treatment regimens can be difficult to follow, so aiming for "two treatment [emollient and TCS] used well", backed-up by a Written Action Plan (Figure 2, www.bristol.ac.uk/ewap) with links to further information and online videos, may support self-management.¹⁶¹⁷ The ECO programme (https://www.nottingham.ac.uk/eco/about-the-research/about-the-research.aspx) is currently developing and evaluating a website to help people look after children with eczema, but meanwhile there are plenty of sources of reliable information available from eczema support groups (Figure 2: Eczema Written Action Plan (© University of Bristol)

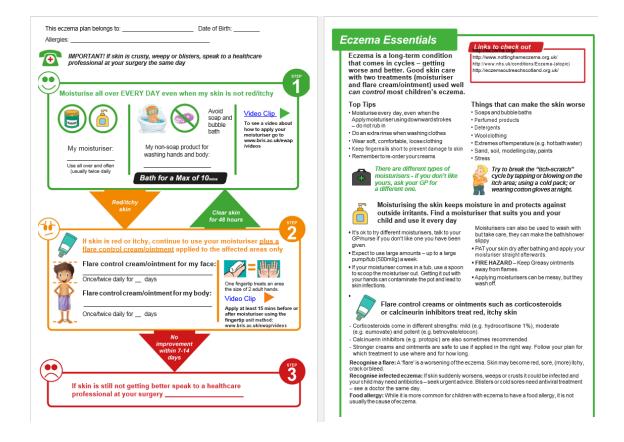


Table 1Table 5).

Conclusions

Although most children with eczema have mild-moderate disease, the impact and challenges of managing the condition should not be underestimated. Two treatments (emollients and topical corticosteroids) used well can control eczema symptoms for the majority. The focus for emollients should be finding one or more "simple" types that parent and child are willing to use daily as "leave on" treatment. For topical corticosteroids, concerns about safety should be addressed and potency matched to site and severity of disease. Supporting information, such as in the form of a written action plan, can help support families in knowing what to use where and when; and well as helping address some of the practical day-to-day issues such as swimming, use of sunscreens and nurse/school attendance. If despite this disease control is poor, then referral to a community or hospital dermatology clinic should be made for further advice and potentially specialist treatment.

Tables and Figures

Figure 1: Eczema treatment escalator

Mild	Moderate	Severe
Emollients	Emollients	Emollients
Mild potency corticosteroids	Moderate potency corticosteroids	Potent topical corticosteroids
	Topical calcineurin inhibitors	Topical calcineurir inhibitors
	Bandages	Bandages
		Phototherapy
		Systemic treatmen

Adapted from NICE (2007)

Figure 2: Eczema Written Action Plan (© University of Bristol)

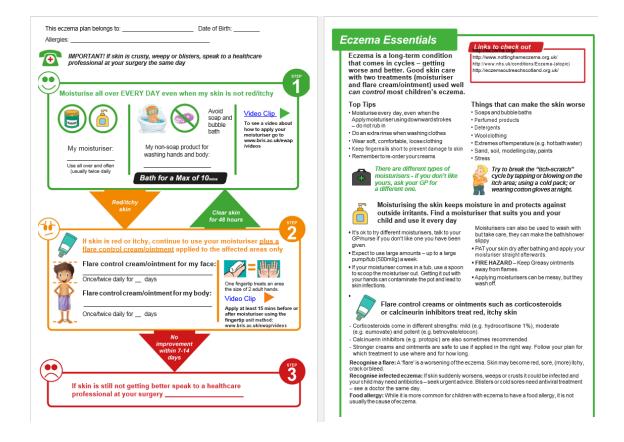


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Table 2: Emollient application

- Wash hands
- With pots, spoon the emollient out and replace the lid (to reduce the risk of infection)
- Apply using downward strokes, allowing it to soak in (rather than rubbing).
- Allow up to 60 minutes between application of emollient and topical corticosteroids or calcineurin inhibitors (to avoid dilution effects)

Table 3: Examples of different potencies of topical corticosteroid

Potency	Examples
Mild	Hydrocortisone 0.1%, 0.5%, 1.0%, and 2.5%
Moderate	Betamethasone valerate 0.025% (Betnovate-RD [®]) and clobetasone butyrate 0.05% (Eumovate [®])
Potent	Betamethasone valerate 0.1% (Betnovate [®]) and mometasone furoate 0.1% (Elocon [®])
Very	Clobetasol propionate 0.05% (Dermovate [®]) and diflucortolone valerate 0.3%
potent	(Nerisone Forte [®])

Table 4: Factors to consider in the safe prescribing of topical corticosteroids

- Age
- Area of the skin being treated
- Duration of treatment
- Potency of the topical corticosteroid
- Occlusion

Table 5: Sources of further information and advice for people with eczema

- National Eczema Society 0800 089 1122 or www.eczema.org
- Eczema Outreach Support 0800 622 6018 or www.eos.org.uk
- Nottingham Support Group for Carers of Children with Eczema www.nottinghameczema.org.uk or @eczemasupport (Twitter)

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