



Scottish Intercollegiate Guidelines Network



## **Management of atopic eczema in primary care**

A national clinical guideline

**National Meeting Draft  
16<sup>th</sup> September 2009**



## KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

### LEVELS OF EVIDENCE

1 <sup>++</sup>	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1 <sup>+</sup>	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 <sup>-</sup>	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 <sup>++</sup>	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 <sup>+</sup>	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 <sup>-</sup>	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

### GRADES OF RECOMMENDATION

*Note: The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.*

- A** At least one meta-analysis, systematic review, or RCT rated as 1<sup>++</sup>, and directly applicable to the target population; *or*  
A body of evidence consisting principally of studies rated as 1<sup>+</sup>, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2<sup>++</sup>, directly applicable to the target population, and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>
- C** A body of evidence including studies rated as 2<sup>+</sup>, directly applicable to the target population and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 2<sup>++</sup>
- D** Evidence level 3 or 4; *or*  
Extrapolated evidence from studies rated as 2<sup>+</sup>

### GOOD PRACTICE POINTS

- Recommended best practice based on the clinical experience of the guideline development group.

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# 1 Introduction

## 1.1 THE NEED FOR A GUIDELINE

Atopic eczema is a very common chronic inflammatory disorder affecting the skin. It affects both sexes equally and usually starts in the first months of life. A study of atopic eczema in the Scottish population found an overall one-year period prevalence of 2.3%.<sup>1</sup> Prevalence was highest in children less than two years of age (9.8%), and diminished with increasing age. Thirty eight percent of all patients with atopic eczema were adults. The normal progression of atopic eczema is for it to resolve during childhood, but it may persist into adult life or recur in the teenage or early adult years. Occasionally, it may develop for the first time in mature adulthood.

The causation of atopic eczema is complex and not fully understood. It has a genetic basis, but a variety of environmental factors have been implicated, including air pollution, low humidity, heat, excessive use of soaps, house dust mite, food allergens, bacteria and stressful life events. It may relate to mutations in the gene coding for filaggrin, a normal constituent of cells in the epidermis that contributes to the epidermal permeability barrier.<sup>2</sup> Defects in this protein may allow irritant and allergy-inducing substances to enter the skin, and initiate inflammation.

Depending on disease severity, atopic eczema may have a considerable adverse effect on the quality of life of affected individuals and their families, and may result in significant physical, psychological, social and occupational impediment. Sleep disturbance is common, and may lead to tiredness, irritability and lack of concentration during the day. The time required caring for the skin and the effect on everyday activities, including possible restrictions of sporting and leisure activities, can have lifestyle implications for sufferer and carer. Embarrassment about appearance may result in lack of self confidence and poor self image. Atopic eczema may adversely influence a child's emotional and social development<sup>3</sup> and may predispose to psychological difficulties.<sup>4</sup>

Atopic eczema also has a major economic impact for the National Health Service and for individuals. The Scottish study estimated the annual cost to the NHS of treating atopic eczema (in the mid nineties) was £125 million, and the annual personal cost to the UK population £297 million.<sup>5</sup> The annual cost to society of lost working days was estimated at £43 million, making the total expenditure on atopic eczema in the UK £465 million. An estimate of the cost in 2002 of community dispensed prescriptions for topical corticosteroids for atopic eczema is £11.6 million.<sup>6</sup>

The majority of the treatment for atopic eczema is delivered by the primary healthcare team, with only a minority of sufferers referred to secondary care.<sup>7</sup> Atopic eczema is a multifaceted condition that can be a therapeutic challenge, especially in primary care, and there appears to be a real potential for improving the outcome of its treatment in the community (Kerr et al, in press), and perhaps the cost effectiveness of treatment.

## 1.2 REMIT OF THE GUIDELINE

### 1.2.1 OVERALL OBJECTIVES

This guideline provides recommendations for the management of atopic eczema in children and adults in primary care, based on current evidence for best practice. It includes advice on the various topical treatments for atopic eczema (including moisturisers, topical corticosteroids, topical calcineurin inhibitors and dressings), anti-infective treatments (such as antibiotics and antiseptics), antihistamines, complementary therapies, and the roles of food allergy and environmental factors. It excludes treatments that are usually carried out in secondary care, such as phototherapy and systemic immunosuppressant drugs.

### 1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to all community based healthcare professionals who manage patients with atopic eczema, particularly general practitioners, health visitors, practice and community based nurses, dietitians and pharmacists, as well as patients with atopic eczema and their carers.

### **1.3 DEFINITIONS**

The words *eczema* and *dermatitis* mean the same thing and are interchangeable: thus *atopic eczema* is the same as *atopic dermatitis*. The papers cited use both terms, but, for consistency, the condition is referred to as *atopic eczema* throughout the guideline. The term *eczema* describes a skin disorder that is usually itchy and which is characterized by observable changes that include redness, blistering, oozing, crusting, scaling, thickening and sometimes colour change (although not all of these changes will necessarily occur together).

The term *atopic* is used to describe conditions such as eczema, asthma, seasonal rhinitis and hay fever, which often have a genetic basis and may be associated with a tendency to allergy.

### **1.4 STATEMENT OF INTENT**

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

#### **1.4.1 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM**

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in the section on implementation.

## 2 Key recommendations

The following recommendations were highlighted by the guideline development group as being clinically very important. They are the key clinical recommendations that should be prioritised for implementation. The clinical importance of these recommendations is not dependent on the strength of the supporting evidence.

Not available in this draft.

## 3 Diagnosis and severity assessment

### 3.1 DIAGNOSTIC CRITERIA

A systematic review showed that the UK diagnostic criteria are the most extensively validated for assessing patients with suspected atopic eczema.<sup>8, 9</sup> There is no evidence for any form of atopic testing.<sup>10</sup> | 2 + +

Criteria must include:<sup>8</sup>

- an itchy skin condition (or parental report of scratching or rubbing in a child)

Plus three or more of the following:

- history of involvement of the skin creases (including cheeks in children under 10)
- a personal history of other atopic disease (or history of any atopic disease in a first degree relative in a child under four years)
- a history of a generally dry skin over the previous year
- visible flexural eczema (or eczema involving the cheeks, forehead and outer limbs in children under four years)
- onset under the age of two years (not used if child is under four years).

**B** The UK diagnostic criteria should be used to diagnose atopic eczema.

### 3.2 MEASURES OF CLINICAL SEVERITY

There are numerous objective scoring systems for assessment of the severity of atopic eczema. In a systematic review, only three were considered sufficiently tested and validated; SCORAD, EASI and POEM. These are most useful in clinical trials rather than daily clinical practice.<sup>11</sup> | 2 + +

### 3.3 COMORBIDITIES

Atopic eczema may predispose to and coexist with other dermatological disorders that may complicate diagnosis, such as scabies, herpes simplex infection, staphylococcal and streptococcal infection, superficial fungal infection and contact dermatitis (irritant and allergic). In particular, widespread herpes simplex (eczema herpeticum) should be considered in any patient with rapidly deteriorating atopic eczema.<sup>12</sup> | 4

### 3.4 SYNDROMIC ASSOCIATIONS

Some genetic disorders are associated with a pattern of cutaneous inflammation that resembles atopic eczema: these include Wiskott-Aldrich syndrome, anhidrotic ectodermal dysplasia, phenylketonuria, Netherton's syndrome, ataxia-telangiectasia and agammaglobulinaemia.<sup>12</sup> | 4

### 3.5 QUALITY OF LIFE ASSESSMENT

A number of quality of life measures examining atopic dermatitis or generic skin disease, have been developed and validated for different patient groups. These are used mainly in research rather than in clinical practice:

- for infants (up to 4 years): IDQoLI (infants dermatitis quality of life index); DFI (dermatitis family impact);
- for children: CDLQI (children's dermatology life quality index), CADIS (childhood atopic dermatitis impact scale)
- for adults: QoLIAD (quality of life index for atopic dermatitis); Skindex-16; DLQI (dermatology life quality index)

At present there is no validated measure of QoL for older children and adolescents with atopic eczema.

There is a correlation between severity of eczema and quality of life in children and adults.<sup>13, 14</sup> In children one study has shown that the correlation is not dependent on age or gender.<sup>15</sup> More severe eczema has a greater impact on the family.<sup>16</sup>

2+

**B** GPs should be aware of the adverse effects of atopic eczema on patients and on family life.

## 4 Emollient therapy

Emollients are skin-softening agents and are the mainstay of treating uncomplicated atopic eczema as they help restore the impaired barrier function of the epidermis. (Cork1997; Cork 1999; Lewis-Jones, 2007) [Reference to be added](#)

Annex 2 describes guidance around the selection and application of emollients.

Creams, lotions and ointments are all beneficial <sup>17-20</sup>, although greasier preparations (ointments) are most effective. No contemporary comparative trials were identified, but cream and lotion formulations tend to be cosmetically more acceptable to patients than ointments <sup>18, 20</sup>.

Emollient therapy has been demonstrated to significantly increase the efficacy of topical corticosteroids <sup>21</sup> and to have a steroid-sparing action.<sup>19</sup>

**A** Patients with atopic eczema should be treated with emollients. Creams, lotions, ointments, or a combination can be used, depending on patient choice.

The more dry the skin the greasier the emollient should be. Ideally, very dry skin should be treated with ointments, moderately dry skin with a cream or gel, and mildly dry skin with a lotion.

Studies have shown that soaps, bubble bath and shower products may leave barrier-impairing residues on the skin after rinsing with water, and some can cause skin irritation.<sup>22-24</sup>

**A** Patients or parents of children with atopic eczema should be advised that soaps, bubble bath and shower products may further irritate the skin or cause emollients to be less effective if applied immediately after the use of these products.

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## 5 Topical corticosteroids

Topical corticosteroids (TCS) have been in clinical use as anti-inflammatory agents for more than five decades. Notwithstanding, or perhaps because of, their longevity as an effective treatment for cutaneous inflammatory disorders, there is a relative paucity of evidence to support their use in the management of atopic eczema compared with more recently developed products. Studies that have been conducted show a large benefit from the use of TCS.<sup>25</sup>

1 + +

### 5.1 POTENCY

The potency (ie the effectiveness in reducing inflammation) of an individual TCS has historically been determined by its ability to cause vasoconstriction, and TCS are categorised into four groups; 'mild', 'moderately potent', 'potent' and 'very potent'.<sup>26</sup>TCS potency is dependent on a number of factors, which include the unique properties of the corticosteroid moiety, its modification, concentration, formulation and its penetration into the skin. It is generally accepted that there is a direct relationship between the potency of a TCS and its potential to cause local and systemic side effects.

Clinical decisions relating to choice of TCS potency should be tailored to the age of the patient, the body region being treated, and the degree to which the skin is inflamed. No contemporary good quality evidence was identified to assist in the choice of the potency of TCS in the treatment of the inflammatory element of atopic eczema.

The potency of a traditional corticosteroid preparation applied to 'delicate' areas of skin, such as the face and flexures of an adult and to all areas of a child's skin, should be limited to mild and moderately potent. The safety profiles of the more novel potent corticosteroids (fluticasone propionate and mometasone furoate) suggest that these preparations can be safely used for atopic eczema in both adults and children.

Very potent TCS, such as clobetasol propionate, are useful in the treatment of chronic lichenified atopic eczema.

### 5.2 POTENTIAL SIDE EFFECTS

TCS have the potential for systemic (in particular, hypothalamic-pituitary-adrenal (HPA) axis suppression and iatrogenic Cushing's syndrome) and local adverse effects. TCS are absorbed through the skin and may expose the user to possible systemic effects. A variety of factors can determine the degree to which a TCS is absorbed into the circulation, including the molecular structure of the steroid, the vehicle, the amount applied to the skin and the surface area over which it is used, its duration of application, the use of occlusion, the age and size of the patient, the intensity of cutaneous inflammation and inherent metabolic differences between individuals.<sup>27</sup> Once absorbed, there may be differences in the mechanism by which different corticosteroids are metabolised.

2 + +

Of the local adverse effects, the most concerning is cutaneous atrophy (skin thinning) which may lead to prominently visible small blood vessels and striae (stretch marks). Other local adverse effects include perioral dermatitis, rosacea-like facial changes, folliculitis, pruritus, hypopigmentation, allergic contact dermatitis and the spread of fungal infection (tinea incognita). The systemic adverse effects and the atrophogenic consequences of TCS are presumed to be more likely in children than adults, and to be dependant on the potency of the TCS. Facial and flexural skin is considered to be more susceptible than other areas to TCS-induced thinning. [Reference to be added](#)

The daily application of a very potent TCS (0.1% fluocinonide cream) to at least 20% of the body surface area of children as young as three months for two weeks did not suppress the

HPA axis in any child. The twice daily application of 0.1% fluocinonide cream did cause HPA axis suppression in 10%, although the risk was no greater for infants and young children than for adolescents.<sup>28</sup> A potent TCS (0.1% hydrocortisone butyrate) applied thrice daily to at least 25% of the body surface of children aged 5-12 years with atopic eczema for up to four weeks caused no adrenal suppression in any of the 20 children in the study.<sup>29</sup> The twice daily application of a potent TCS (0.05% fluticasone propionate cream) for three to four weeks to at least 35% of the body surface area (mean 64%) of 43 children aged three months to six years with moderate to severe atopic eczema caused HPA axis suppression in just two, both of whom received higher than average amounts of TCS; recovery of HPA axis function was rapid after discontinuation of TCS.<sup>30</sup>

2 +  
3

An RCT of the effect of a two week course of a potent TCS (mometasone furoate) on bone growth in children with mild to moderate atopic eczema showed no statistically significant effect.<sup>31</sup> A two week treatment period may be insufficient to detect a detrimental effect. Some observational studies have reported an apparent delay in childhood growth as the result of TCS treatment.<sup>27</sup>

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2 + +

Although the local adverse effects of TCS are well described, there are insufficient vehicle-controlled studies of adequate duration to accurately determine their incidence in patients with atopic eczema. The potential for cutaneous side effects has not been adequately evaluated for the majority of the traditional TCS. There are much better data for the relatively novel TCS (fluticasone propionate and mometasone furoate).

There are few data as to how long TCS can be used without causing skin thinning. 0.1% hydrocortisone butyrate applied three times daily for up to four weeks caused no local side effects in children aged five to 12 years with atopic eczema.<sup>29</sup> Fluticasone propionate cream 0.05% has a low potential for causing cutaneous atrophy, even when used twice daily for three to four weeks in children with moderate to severe eczema as young as three months of age.<sup>30</sup> The application of 0.05% fluticasone propionate in an average amount of 26.6 g/week in children less than three years of age and 53.9 g/week in children from three to six years of age for three or four weeks caused no signs of either cutaneous atrophy or HPA axis suppression. No definite signs of skin thinning occurred in any of the children and the two children who showed evidence of HPA axis suppression received considerably more than the average, suggesting that short term (three to four weeks) weekly exposure to 30 g of 0.05% fluticasone propionate cream in children less than three years old and 60 g in three to six year olds is not likely to induce significant adverse effects.

2 + +

The twice weekly application of 0.005% fluticasone propionate ointment to adults with atopic eczema for 16 weeks caused no skin atrophy (nor HPA axis suppression as measured by serum cortisol levels).<sup>32</sup> The use of 0.005% fluticasone propionate ointment to the face and intertriginous regions of adults with atopic eczema as a two-week acute treatment followed by a maintenance regime of twice weekly application on consecutive days for eight weeks caused no cutaneous atrophy, although the numbers in the study were low.<sup>33</sup> Mometasone furoate used to stabilise atopic eczema of at least moderate severity in adults, followed by a prophylactic maintenance regime (twice weekly for six months) caused possible treatment-related skin atrophy in only one of 68 patients.<sup>34</sup> The intermittent twice weekly application of 0.05% fluticasone propionate cream to children and adults (aged three months to 65 years) with moderate to severe atopic eczema for up to 48 weeks caused no skin thinning in either the adult or paediatric subjects.<sup>35</sup>

1 +

Four RCTs of TCS usage in healthy volunteers demonstrated that skin showing early atrophy can return to normal on stopping the TCS.<sup>25</sup>

1 + +

The treatment of children with atopic eczema for four weeks with a mild (1% hydrocortisone) or potent (0.05% betamethasone dipropionate) TCS resulted in no evidence for the "rebound phenomenon" (reactivation of inflamed areas, on stopping TCS application, with, compared to their pre-treatment state, a resultant worsening). (Sanabria-Silva et al, 1991)

1 + +

Glaucoma is known to be associated with TCS usage around the eyes, although the degree of

risk has not been established.<sup>27</sup> The twice daily application of clobetasone butyrate 0.05% ointment for three weeks to treat eyelid eczema in 20 patients with atopic keratoconjunctivitis did not affect intraocular pressure and did not cause any adverse effects (Nivenius et al, 2007). In contrast to the well documented side effect of systemic corticosteroid therapy causing posterior subcapsular cataracts, the few cases of cataracts that have been associated with the periocular application of TCS suggests only a possible, but as yet unsubstantiated, risk.<sup>27</sup>

2 + +  
1 -

The local immunosuppressive properties of TCS have called into question the possibility that TCS might induce skin malignancies by inhibiting immuno-surveillance mechanisms, but this concern is not substantiated by the available clinical data.<sup>27</sup> Similarly, there is no documented association with TCS usage and systemic malignancy or systemic infection.<sup>27</sup>

2 + +

Although long term uninterrupted use of TCS may result in systemic side effects and local skin atrophy, especially in children, the evidence suggests that when TCS are used in short courses of up to one to three weeks, with continued emollient therapy in-between such courses, significant side effects are unlikely to occur. There are no data to guide the clinician regarding how frequently TCS courses can be safely given. Although the evidence base suggests that the relatively novel TCS, fluticasone propionate and mometasone furoate, are both effective and safe, there are few data to indicate that the more traditional TCS are any less so. **Reference to be added.**

1 +

**D Prescriptions for topical corticosteroids should indicate the maximum duration of the course.**

**D Repeat prescriptions for topical corticosteroids should not be given without clinical monitoring of the patient.**

**D Patients receiving topical corticosteroids should be reviewed regularly to ascertain response to therapy, and to assess the skin for development of atrophic change at a stage when it might be reversible.**

**D Worsening of inflammation in a patient receiving topical corticosteroids should prompt consideration of the possibility of allergic contact dermatitis to the topical corticosteroids.**

**C Periodic monitoring of hypothalamic-pituitary-adrenal axis function is appropriate for patients at high risk of suppression (those receiving large amounts of topical corticosteroids).**

**B Particular caution is required when topical corticosteroids are used in the periocular region.**

### 5.3 APPLICATION TECHNIQUE

There is little evidence to guide practitioners and patients in the method of application of TCS and the quantities to be used. Traditional advice has been to suggest that TCS are applied intermittently, sparingly and thinly to minimise the risk of adverse effects, but this convention has caused concern that, by implication, it may engender unnecessary anxiety in patients and health professionals alike, and result in under-treatment of patients with atopic eczema.<sup>36</sup> The good safety profile of TCS suggests that they should be applied in a manner and in amounts that ensures that patients reap their full benefit.

4

An attempt to rationalize advice concerning the amount of TCS to apply to different body areas employs the "fingertip unit" (FTU), defined as the volume of a ribbon of cream or ointment the length of the distal phalanx of an adult's index finger expressed from a tube with a 5 mm

diameter nozzle.<sup>37</sup> The aim of this measure is to assist patient understanding of the dosage of topical preparations, by using a simple chart that can be personalised to the individual, explaining how many FTUs should be applied to each body region.

4

With regard to intermittent usage of TCS, an RCT has demonstrated that a short course of a potent TCS (0.1% betamethasone valerate) is as effective as the prolonged use of a mildly-potent TCS (1% hydrocortisone) for controlling mild to moderate atopic eczema in children.<sup>38</sup>

1 +

There does not appear to be any evidence that applying a TCS immediately followed by an emollient is any different from vice versa, or that effectively mixing a TCS with emollient reduces the efficacy of the TCS. A pragmatic approach is that at least 30 minutes should separate TCS and emollient applications.

It is generally considered sound advice to suggest that TCS are applied in the direction of the body hair in order to prevent accumulation of TCS at the hair bases which may predispose to folliculitis.

Patients with atopic eczema or carers should receive detailed education and instruction on the application of TCS, ideally by an appropriately trained nurse.

**D** Topical corticosteroids should be used in short courses of up to one to three weeks, with continuous emollient therapy.

**D** Patients should be advised to apply topical corticosteroids in an amount that is sufficient to adequately cover the areas of inflamed skin.

**D** Patients may benefit from being introduced to the concept of the fingertip unit as a means of ensuring adequate usage of topical corticosteroids.

Allow 30 minutes between the application of topical corticosteroids and emollients.

Topical corticosteroids should be applied in the direction of body hair.

#### 5.4 FREQUENCY OF APPLICATION

A meta-analysis and economic analysis concluded that both once daily and twice daily application of TCS are both effective, without clear evidence that the twice daily application confers any significant clinical advantage over once daily. No cost-effectiveness studies were found, and cost minimisation analysis proved complex due to wide variations in product price.<sup>6</sup>

1 + +

**A** Patients with atopic eczema should be advised to apply topical corticosteroids once daily initially. If there is an inadequate response the frequency should be increased to twice daily.

## 5.5 STEP DOWN AND MAINTENANCE REGIMENS

The constant usage of TCS is undesirable because of the risk of local and systemic side effects. It is common clinical practice to use TCS, of appropriate potency, in short bursts of perhaps one to three weeks, interrupted by periods of emollient therapy. An alternative regime is to commence treatment with a potent or very potent TCS, and then to “step down” to a weaker preparation as the inflammation settles, although there is no RCT evidence to support this practice in the management of atopic eczema.<sup>25</sup> 1 + +

A large multicentre trial of topical fluticasone propionate applied on two consecutive evenings each week to areas of skin normally affected by eczema for 16 weeks demonstrated a significant reduction in relapse rate.<sup>39</sup> Patients applying the cream formulation of fluticasone propionate (0.05%) were 5.8 times less likely to relapse than those applying a placebo cream, and those applying the ointment formulation (0.005%) were 1.9 times less likely to relapse. 1 +

Another large RCT study showed that atopic eczema patients (children and adults) receiving long term intermittent 0.05% fluticasone propionate cream, applied just twice weekly for up to 48 weeks, in addition to regular daily emollients, were 7.7 times less likely to have a relapse than those receiving the intermittent vehicle and emollients.<sup>35</sup> This regime was considered to be both efficacious and safe. 1 +

An open study of twice weekly mometasone furoate (0.1%) cream in adults with moderate to severe atopic eczema, following a stabilising course of daily mometasone furoate, resulted in 90% remaining free or virtually free of eczema after six months of prophylactic treatment.<sup>34</sup> 2 +

A large RCT in adolescent and adult patients with moderate to severe atopic eczema has demonstrated that patients receiving maintenance therapy with methyl-prednisolone aceponate 0.1% cream, applied twice weekly, with daily emollient therapy, for 16 weeks had a 3.5 fold lower risk of suffering a relapse of their eczema than those treated with emollient alone.<sup>40</sup> 1 +

**A** Maintenance therapy (after a period of stabilisation) should be considered in patients with moderate to severe atopic eczema experiencing frequent relapses. Topical fluticasone propionate or mometasone furoate, applied twice weekly for at least 16 weeks to areas previously affected is indicated.

## 5.6 SYSTEMIC CORTICOSTEROIDS

A small number of RCTs which have assessed systemic corticosteroid therapy with placebo in the management of patients with moderate to severe atopic eczema have demonstrated a large beneficial treatment effect on short term response.<sup>41, 42</sup> No longer term studies have been identified.<sup>25</sup> 1- 1 + +

A short course of oral prednisolone should be considered in patients when a flare of moderate to severe atopic eczema has not responded to intensive topical therapy and is having a significant detrimental impact on quality of life, and provided there are no contraindications.

## 6 Calcineurin inhibitors

### 6.1 TACROLIMUS AND PIMECROLIMUS

Topical calcineurin inhibitors (TCIs) are novel non-steroidal agents used in the treatment of atopic eczema. Currently two TCIs are available, which are tacrolimus as 0.1% and 0.03% ointments and 1% pimecrolimus cream.

Tacrolimus is a TCI with immunomodulating properties in the skin. It is a macrolide produced by *Streptomyces tsukubaensis*, a fungus found in the soil of Mount Tsukuba in Japan. It acts directly on the T-lymphocytes and, through a cascade of actions, inhibits immune responses in the skin that are postulated to play a role in atopic eczema.

The ascomycin derivative pimecrolimus is the other topical immunomodulator that is currently used in atopic eczema.

Pimecrolimus by topical application is licensed for mild to moderate eczema. Tacrolimus is licensed for topical use in moderate to severe atopic eczema. Both are drugs whose long term safety and place in therapy is still being evaluated and it is currently recommended that they should not be used as first line treatments ( By BNF and NICE 2007) unless there is a specific reason to avoid or reduce the use of topical corticosteroids , which are traditionally the first line treatment of choice ( BNF 2009).

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### 6.2 EFFECTIVENESS

#### 6.2.1 CALCINEURIN INHIBITORS VERSUS PLACEBO

Both tacrolimus and pimecrolimus are more effective than placebo.<sup>43, 44</sup> Tacrolimus 0.1% is more effective than 0.03%.<sup>45</sup>

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The effectiveness of tacrolimus in treating moderate to severe atopic eczema in children and adults has been reported in various studies, in which the majority of patients had moderate to severe disease. The efficacy and safety of topical pimecrolimus has been reported in different populations, with the majority of the study populations having mild to moderate atopic eczema.<sup>44</sup>

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#### 6.2.2 CALCINEURIN INHIBITORS VERSUS TOPICAL STEROIDS

The advantage of calcineurin inhibitors over topical steroids is unclear. There is little evidence comparing tacrolimus with appropriate strengths of topical corticosteroids but it appears to be more effective than mild potency steroids in control of moderate to severe atopic eczema. There were no statistically different outcomes looking at tacrolimus versus potent topical corticosteroids but the studies identified were of poor quality and low power.<sup>43, 44</sup>

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Tacrolimus 0.1% is as effective as potent topical steroids and more effective than mild topical steroids.<sup>43, 44</sup> It may have a place in treatment at resistant sites where side effects of topical steroids develop adverse effects quickly, eg the face and neck.<sup>43</sup> In adults with moderate to severe atopic eczema treated for six months, 0.1% tacrolimus ointment is more effective than TCS ointment (1% hydrocortisone acetate on face and hydrocortisone butyrate on trunk and limbs)..<sup>46</sup> Combination treatment with desoximetasone and tacrolimus offers efficacy and tolerability over tacrolimus alone in patients with atopic eczema.<sup>47</sup>

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Pimecrolimus is less effective than potent topical steroids.<sup>43, 44</sup> Pimecrolimus is more effective than a basic cream at controlling mild to moderate atopic eczema. It is likely to be cost effective compared to topical corticosteroids in the treatment of adults and children with mild

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	to moderate eczema of the face and body. <sup>45</sup> There is no evidence to suggest that pimecrolimus is effective in people who fail to respond to topical steroids. <sup>48</sup>	1 +
6.2.3	USE IN INFANTS AND CHILDREN	
	In infants and young children treatment with pimecrolimus 1% for up to two years was well tolerated and resulted in a marked and sustained improvement in their atopic eczema. <sup>49</sup> One large cohort study concluded that tacrolimus monotherapy in paediatric and adult patients for up to eighteen months led to continuous improvement without any change in safety profile. <sup>50</sup> Use for 12 months is not atrophogenic and reverses TCS induced skin atrophy. <sup>51</sup>	2 + 2 +
	TClS are used in the treatment of children with atopic eczema, especially where there is a risk of topical corticosteroid adverse effects, perhaps due to their prolonged use in stubborn areas, or their use in sensitive areas such as the face.	2 -
	Tacrolimus ointment (0.03% and 0.1%) may be an effective and safe alternative to other therapies in children under two years with atopic eczema. <sup>52</sup> Two studies in children have shown that 0.03% tacrolimus and 0.1% tacrolimus are more effective than 1% hydrocortisone acetate (HA) and (individually) 1% pimecrolimus. <sup>53, 54</sup> Children with moderately severe atopic eczema may benefit in the short term from a change to topical tacrolimus, particularly if they are currently being treated with mildly potent topical steroids. <sup>55</sup> In a study on infants pimecrolimus 1% lead to a rapid improvement of all morphological signs of eczema. <sup>56</sup>	1 + 1 + 2 - 1 +
6.2.4	LONG TERM OUTCOMES	
	TClS are relatively new treatments for atopic dermatitis and there is little research into long term efficacy or continuous dosing regimes .One cohort study showed that over four years of intermittent or continuous prolonged use 0.1% tacrolimus ointment patients expressed a high degree of satisfaction with the treatment, although only half the patients completed the full study period. <sup>57</sup> .	2 +
	In long term management of patients with atopic eczema, pimecrolimus used by adults for 26 weeks provided more (p<0.001) TCS free days than the placebo, reducing the number of flares requiring TCS application from 1.39 to 0.97 (p=0.0014). <sup>58</sup> Another RCT study of adults with moderate to severe atopic eczema using pimecrolimus for up to a year showed a significant number of patients (276 out of 658 in study) could be maintained without TCS for up to a year in the pimecrolimus group. (Luger et al 2004) In adults with moderate to severe atopic eczema treated for six months, 0.1% tacrolimus ointment is more effective than TCS ointment (1% hydrocortisone acetate on face and hydrocortisone butyrate on trunk and limbs). <sup>46</sup>	1 + + 1 +
6.2.5	APPLICATION FREQUENCY AND TREATMENT REGIMENS	
	Current recommendations for pimecrolimus are a twice daily dose regimen, with treatment being discontinued after 6 weeks if there is no response. With tacrolimus again twice daily treatment is advocated with a reduction to once daily, or in the case of 0.1% ointment a switch to 0.03% ointment , as the skin improves.(BNF 2009)	1 +
	Pimecrolimus applied once daily is as effective as twice or four times daily. <sup>48</sup> Increasing application from twice daily to four times daily to treat moderate or severe atopic eczema for up to three weeks does not alter the efficacy of treatment or the safety profile. <sup>59</sup>	1 -
	0.03% tacrolimus ointment applied once or twice daily is significantly more efficacious than 1% HA in treating moderate to severe atopic eczema in children. Twice daily application of tacrolimus 0.03% ointment results in the greatest improvement in patients with severe atopic eczema at baseline, compared to 0.03% tacrolimus cream applied once daily or 1% hydrocortisone acetate. <sup>60</sup>	1 +
	In adults, 12 month twice weekly proactive tacrolimus ointment application was effective in preventing, delaying and reducing the occurrence of atopic eczema exacerbations. <sup>61</sup>	1 -

- B** Topical pimecrolimus and tacrolimus are not recommended for the treatment of patients with mild atopic eczema.
- B** Topical tacrolimus or pimecrolimus can be used as treatments of moderate to severe atopic eczema in patients aged two years and older that has not been controlled by topical steroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin damage.
- B** Pimecrolimus is recommended as a treatment option for patients over two years old with moderate atopic eczema on the face and neck, that has not been controlled by topical corticosteroid, where there may be a serious risk of important adverse effects from further topical corticosteroid use, especially irreversible skin atrophy.
- B** For facial atopic eczema in children aged two years and over that requires regular long term or frequent use of mild topical steroids, clinicians should consider changing to topical calcineurin inhibitors.

### 6.3 ADVERSE EFFECTS

Adverse drug reactions associated with TCIs are primarily skin application site reactions that tend to be of mild and short duration.<sup>44</sup>

TCIs, to date, have little in the way of long-term safety data, especially when compared with the more traditional topical treatments of emollients and topical steroids. However research available so far suggests there is no current evidence of any increased risk of cutaneous or systemic malignancy.

The local side effect profile with TCI is predominantly local (burn, sting, itch) with a non-statistically significant trend that favours an increase in infections especially viral mediated disease versus vehicle controls. Results from vehicle controlled trials show no increased malignancy risk, although the studies are not of sufficient duration or exposure to give a definitive answer grading whether patients with atopic eczema treated with a TCI are at an increased risk of cutaneous neoplasms. Systemic exposure to topical TCI use has not been shown to result in any significant systemic physiological effects or toxicity. TCIs are not mutagenic or genotoxic. The major theoretical consideration for their role in carcinogenesis is with respect to inhibition of immunosurveillance through systemic absorption or local effects. There is some evidence that TCIs may even inhibit cutaneous carcinogenesis through an anti-inflammatory effect on tumour promoting T-cells. Some reports of spontaneous lymphoma have occurred outside of the clinical trials but there is no direct evidence to link these to any TCI treatment.<sup>27</sup>

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Side effects experienced by users of tacrolimus and pimecrolimus were more burning of the skin and a stinging sensation compared with use of topical corticosteroids.<sup>43, 48</sup> Transient burning of the skin was also higher in users of tacrolimus 0.03% and 0.1% compared to users of hydrocortisone acetate.<sup>53, 54</sup> Other trials reported that the creams were well tolerated<sup>44</sup> or the burning and stinging side effects were mild and transient.<sup>45, 46, 62</sup>

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Pruritis was reported in some studies but the itching abated with use.<sup>50, 63</sup> It may be that by breaking the scratch/itch cycle, pimecrolimus cream facilitates faster control of atopic eczema.<sup>63</sup>

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There was no statistically significant difference in risk of adverse events between tacrolimus and pimecrolimus in the treatment of children with atopic eczema.<sup>54</sup> Few side effects were reported in a trial of children using pimecrolimus, other than skin burning. It concluded that children respond well to pimecrolimus.<sup>64</sup> Pimecrolimus 1% cream was also reported as effective and well tolerated in the long term (26 weeks) in children with mild to moderate

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atopic eczema.<sup>65</sup>

In a systematic review no evidence was identified to show use of pimecrolimus was associated with less skin thinning than corticosteroids.<sup>48</sup>

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Long term use (up to four years) of tacrolimus 1 % did not indicate an increased risk of adverse events in children and adults.<sup>57</sup>

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Systemic exposure to topical calcineurin inhibitors has not been shown to result in any significant systemic physiological effects or toxicity.<sup>27</sup>

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**A Patients should be warned of the potential side effects of topical calcineurin inhibitors.**

**B Topical calcineurin inhibitors should not be applied to skin which appears actively infected (*bacterial or viral infection*).**

## 7 Dressings

Occlusive dressings are a traditional way to stabilise acute flares of atopic eczema and historically they have been used in conjunction with ichthammol. No RCTs or trials from the past five years were identified relating to the efficacy of medicated dressings, consisting of ichthammol-containing ointment or cream or ichthammol-impregnated cotton bandages over a TCS of appropriate potency and a greasy emollient. It is the expert opinion of the group that they can be a very effective treatment for the acute management of chronic atopic eczema.

Other dressings are available, such as tubular bandages, suits and gloves. No good quality evidence was identified comparing the efficacy of different dressings.

Patients with chronic or moderate to severe eczema should be advised to cover up affected areas.

Medicated dressings, consisting of ichthammol-containing ointment or cream or ichthammol-impregnated cotton bandages over a TCS of appropriate potency and a greasy emollient, should be used for the acute management of patients with chronic atopic eczema.

A systematic review of 24 studies suggests that wet wrap treatment (WWT) is an effective short-term measure in children with severe or refractory atopic eczema, particularly when used with a TCS rather than an emollient only.<sup>66</sup> One publication comparing the use of daily WWT over hydrocortisone acetate cream with the use of hydrocortisone acetate cream twice daily without WWT in a cohort of children with atopic eczema of moderate degree showed no difference between the two groups.<sup>67</sup>

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Wet wrap dressings over diluted potent TCS for up to 14 days appeared to be safe, with only transient suppression of early morning cortisol measurements and no reports of prolonged suppression of the hypothalamic-pituitary-adrenal axis after short term intervention treatment.<sup>66</sup> Short term growth and bone turnover during WWT with diluted TCS in eight children were not significantly affected.<sup>66</sup>

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Most of the publications in the systematic review were observational, with only two RCTs relating to the efficacy of WWT.<sup>66</sup> The majority of these data relate to children rather than adults, and patient numbers were generally small. There were wide methodological differences between the studies, and additionally they used different TCS, in varying dilutions (5-50%): fluticasone propionate and mometasone furoate were the most commonly used, and have the advantage of having a potent local effect with relatively low systemic absorption, but which TCS is best to use and to what extent it should be diluted is not clear. Good clinical efficacy and safety were evident using a 10% dilution of fluticasone propionate cream under the wet-wrap.<sup>66</sup>

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The optimum methodology for WWT remains to be determined, and large prospective studies are required.

WWT can frequently be uncomfortably chilling and may be poorly tolerated, especially by older children; folliculitis is common. It should also be borne in mind, especially when being undertaken by carers or members of the primary care team, that it is a labour intensive and time-consuming treatment, requiring adequate training.

# 8 Anti-infective measures

## 8.1 INTRODUCTION

Staphylococcus aureus is recognised as an important provocation factor for atopic eczema and is consistently isolated from eczematous skin lesions. The degree of colonisation has been found to be associated with disease severity. Staphylococcal antigens have been shown to act as superantigens in patients with atopic eczema and they may also function as allergens as the level of toxic specific IgE correlates with the severity of atopic eczema in children and adults.<sup>68, 69 70</sup> Microbial superantigens have been shown to induce corticosteroid insensitivity, therefore eradication of staphylococcus may have a steroid sparing effect.<sup>71</sup>

Patients with atopic eczema appear to have a predisposition to colonisation with Staphylococcus aureus. The skin lesions of 80-100% of patients with atopic dermatitis are colonised with S. Aureus compared to 5-30% of individuals without the condition.<sup>72</sup>

No studies were identified examining the role of streptococcus in atopic eczema, although it is a pathogen found in skin swabs in a small proportion of patients.

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## 8.2 EFFECTIVENESS OF ANTIMICROBIAL MEASURES

### 8.2.1 CLINICAL PRACTICE

Antimicrobial measures, particularly oral antibiotics, are widely and routinely used in clinical practice despite a small and inconclusive evidence base.<sup>73</sup>

### 8.2.2 SKIN SWABS

There is no evidence that swabbing affected skin or potential sites influences outcome.

**D** Routine swabbing of skin is not indicated. Swabs should be considered in patients with recurrent infection, or if the clinical picture is atypical or suggestive of streptococcal infection.

### 8.2.3 ORAL ANTIBIOTICS

In a study of ten patients treated with oral antimicrobials there was a significant improvement in SCORAD. Recolonisation occurred quickly and was not associated with a corresponding deterioration in SCORAD.<sup>72</sup> In a Cochrane review oral antibiotics were not associated with benefit in non-infected (2 trials, 66 participants) or infected eczema (1 trial, 33 participants).<sup>73</sup>

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Oral antibiotic treatment may be useful in patients with recurrent infection but long term use of antibiotics is not recommended. Treatment of bacterial infections should be based on local and regional antibiotic sensitivities.

### 8.2.4 TOPICAL ANTIBIOTICS COMBINED WITH CORTICOSTEROIDS

There is conflicting evidence for the addition of antibiotics to topical corticosteroids, which were shown to reduce the staphylococcal numbers in some studies, but showed no clinical benefit in others.<sup>73</sup> There is weak evidence that use of a combination therapy in moderate to severe atopic eczema may be useful in the early phase of treatment of lesions particularly when severe.

**D** Short term use of topical antibiotics should be considered where patients have localised clinically infected severe eczema.

#### 8.2.5 BATHING AND CLEANSING

A Cochrane review identified only a small number of studies and found no benefit for antibacterial soaps, bath additives or topical antibiotics/antiseptics.<sup>73</sup>

- Daily bathing is recommended to cleanse and hydrate the skin.

## 9 Antihistamines

Results from trials on the efficacy of antihistamines in patients with atopic eczema are inconclusive.<sup>74-76</sup> Safety of the use of antihistamines has been demonstrated,<sup>74, 77</sup> and can be used in comorbidities associated with atopic eczema.

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In a study of 60 mg fexofenadine twice daily plus 0.1% hydrocortisone butyrate twice daily versus placebo plus 0.1% hydrocortisone butyrate twice daily patients were asked to score the severity of pruritus during the day and at night. Patients treated with fexofenadine reported a 16% reduction in daytime score and 15% at night, compared with those on placebo who reported a 10% reduction for both day and night.<sup>76</sup>

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A small trial of 48 patients, mean age 73 months, using mometasone 0.1% cream once daily plus a placebo of syrup at night after a bath, or loratadine 5 mg/5 ml, showed the placebo was more effective than loratadine using SCORAD, pruritus and drowsiness the following day as outcome measures.<sup>74</sup>

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- Antihistamines should be offered to patients with atopic eczema on a trial basis if topical treatments are showing little or no benefit.
- Sedating antihistamines should generally only be used at bedtime.

## 10 Environmental factors

### 10.1 HOUSE DUST MITE

The link between house dust mite and atopic eczema is not clear. Studies conducted have addressed different variables and have small study populations. Allergy to mites may be an aggravating feature for some people and for others it may only be one of many factors. As a general rule there may be merit in trying to reduce house dust mite levels but the exact means of achieving this is unclear.<sup>25, 78-83</sup>

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### 10.2 CONTACT WITH PETS

A systematic review on keeping pets around the time of birth concluded that there is no evidence to suggest that early pet exposure is associated with increased risks of subsequent eczema.<sup>84</sup> A further systematic review confirmed that there is no reason to recommend restrictions in pet keeping for persons without an increased risk of allergies.<sup>83</sup>

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No good quality studies were found as to whether having a cat or dog in the home is responsible for disease flares in those with pre-existing eczema.

### 10.3 HUMIDITY

Insufficient evidence was identified to evaluate the effectiveness of the avoidance of extremes of temperature or humidity in the management of patients with established atopic eczema. A systematic review commented that an indoor climate which supports mould growth (high humidity, low ventilation) should be avoided.<sup>83</sup> A cross-sectional study demonstrated that dampness and mould was associated with a higher prevalence of eczema symptoms.<sup>82</sup>

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### 10.4 CONTACT WITH IRRITANTS

No good quality trials were identified addressing the avoidance of irritant contacts in washing powders, fabric softeners and fragranced products.

A systematic review found two RCTs which evaluated clothing material in atopic eczema.<sup>25</sup> Both studies suggested that there was nothing special about cotton for patients with atopic eczema apart from smooth fibres. Other synthetic fibres can be constructed with similar smooth fibres using yarns and fabric construction that is just as comfortable.

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Three small RCTs showed that the use of silver coated textiles can reduce the severity of atopic eczema due to an antibacterial effect.<sup>85-87</sup>

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A lack of robust evidence was identified on the avoidance of irritants in the workplace. Expert opinion would suggest that workers with atopic eczema may have exacerbations if they have to frequently wash hands ("wet work") or if they are exposed to known irritants.

# 11 Dietary modification

## 11.1 FOOD ALLERGY

Clinical history and physical examination should play a key role in identifying potential food trigger factors. Food allergy plays a role in triggering of immediate and delayed skin reactions in children with moderate or severe atopic eczema. The main foods triggering immediate reactions are cow's milk, egg and nuts. Immediate reactions to wheat, soya, fish and shellfish occur less frequently.<sup>88</sup>

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The children's age should be considered during history taking. Parents should be questioned about the pattern of atopic eczema in the child from birth. Allergy to cow's milk, egg and soya is less likely if the atopic eczema developed after two years of age. History taking should include consideration of foods eaten, quantities, and foods not eaten in order to direct which foods to test for. The following are signs of immediate allergic reactions:<sup>88</sup>

- widespread redness of rash
- urticaria
- increased itch
- facial swelling
- rhinitis
- wheeze
- cough
- difficulty breathing
- vomiting and abdominal pain
- voice change
- profound drowsiness, floppiness or loss of consciousness.

4

Children who are suspected of having food allergy should be referred for specialist investigation and management of allergy. It is difficult to recommend any specific test to rule out allergy due to the heterogeneity of published diagnostic accuracy studies and relative lack of information in test costs or effectiveness. The double-blind placebo-controlled food challenge (DBPCFC) tests remain the gold standard for diagnosing food allergy.<sup>88</sup>

4

The atopy patch test (APT) could not predict hypersensitivity to hen's egg or cow's milk not identified by skin prick test, specific IgE or histamine release in children aged 3 yrs with or without a diagnosis of atopic eczema (sensitivity of test for cow's milk 0%, hen's egg 40%, specificity of test for cow's milk 99% and hen's egg 99%, positive predictive value (PPV) cow milk 0%, hen's egg PPV 39%, negative predictive value (NPV) cows milk 99% hen's egg 99%).<sup>89</sup> Often APT results showed false positive with low PPV of 45%.<sup>90</sup>

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APT's had high sensitivity (81-96% for any reaction immediate, delayed or delayed combined) for cow's milk egg and soya. Specificity for any reaction to wheat was more variable. Compared to DBPCFC sensitivity results for any reaction to cow's milk, egg, wheat and soya were all much more variable.<sup>88</sup>

4

The accuracy of skin prick tests (SPT) using crude allergen extracts from foods versus those from commercial allergen extracts was significantly higher. In the case of soybeans the results of the SPT using commercial allergen extract was clinically insignificant for a prediction of soybean allergy.<sup>91</sup> The relative risk of an infant with atopic eczema having a food allergy is 5.9 for the most severely affected groups studied and there is a strong association between IgE mediated food allergy as tested by skin prick testing and severity of atopic eczema in the age group studied, birth to 12 months old.<sup>92</sup>

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Compared to DBPCFC testing the SPT had high sensitivity (90-95%) for diagnosing immediate response to fish and peanut or to several foods together. Specificity for these foods was more variable. Compared with an open food challenge, sensitivity and specificity results for any reaction (immediate, delayed or combined) to all allergens were also more variable.<sup>88</sup>

4

IgE in serum does not predict whether an individual child will show a clinical reaction to cow's milk or hen's egg after a time of avoidance. Specific IgE in serum and skin prick tests are not useful predictors of loss of symptomatic food hypersensitivity. Children with higher total IgE levels and those with higher specific IgE levels to cow's milk, hen's egg and wheat have a higher risk of persistent food allergy after a 16 month exclusion diet. Results indicate that children with higher IgE levels and those with specific IgE levels to cow's milk, hen's egg and wheat may have a risk of persistent food allergy after sixteen months of exclusion diet. Due to a large overlap in parameters IgE is not reliable in individual patients so retesting by food challenge remains mandatory.<sup>93</sup> Sensitivity of IgE was 76% and specific IgE were often false positives with low predictive value of 64%.<sup>90</sup>

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The sensitivity of specific IgE for detecting any reaction (immediate, late and combined) to cows milk and egg was high (83-100%) compared to DBPCFC. Sensitivity for detecting immediate reaction to wheat, soya and fish and peanut compared to DBPCFC was also high (but only in one study). Compared with open food challenge, results were less consistent across all foods tested.<sup>88</sup>

4

A systematic review of poorly conducted studies concluded that there is no evidence of benefit in the use of an elemental or few foods diet in patients with atopic eczema.<sup>94</sup> There appears to be no benefit of an egg and milk free diet in patients with atopic eczema, with the exception of infants who have positive IgE to eggs.<sup>94, 95</sup> One study found 51% of the children had a significant improvement in body surface area with the exclusion diet compared to normal diet (RR 1.51, 95% CI 1.07 to 2.11). Change in surface area and severity score was significantly improved in the exclusion diet compared to the normal diet at the end of six weeks (Mean difference (MD) 6.10, 95% CI 0.06 to 12.14) and end of treatment (MD 6.10, 95% CI 0.06 to 12.14).<sup>94</sup>

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**D**

**A diagnosis of food allergy should be considered in patients with atopic eczema who have previously reacted to food with immediate symptoms, or in infants and young children with moderate to severe eczema which has not been controlled by appropriate management, especially if associated with colic, vomiting, altered bowel habit or failure to thrive.**

**D**

**Children with atopic eczema who are suspected of having a food allergy (after taking a thorough history and carrying out a physical examination) should be referred to an appropriate local specialist for further investigation and management.**

Parents and carers of children with atopic eczema should be advised that there is no evidence to support the use of high street or internet allergy testing.

## 11.2 MATERNAL DIET

A Cochrane review concluded that there is no strong protective effect of maternal antigen avoidance during pregnancy on the incidence of atopic eczema or asthma during the first 18 months of life (RR 1.01, 95% CI 0.57 to 1.79).<sup>96</sup> Such a diet may have an adverse effect on maternal or fetal nutritional status or both. The trials suggest a lower incidence of positive skin prick tests to egg antigen at six months but the effect was not evident at 18 months. There was no benefit at either age to skin prick tests to milk antigen.

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In one trial cord IgE levels were higher in the experimental (antigen avoidance) group. Longer term atopic outcomes were not reported.<sup>96</sup>

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Another study showed a significant lower mean gestational weight gain (weight mean difference (WMD) -3.0, 95% CI -5.21 to 0.79) percentage of pregnancy weight. The pooled results of two trials suggest that maternal antigen avoidance may be associated with a higher risk of pre-term birth (RR 10.66, 95% CI 0.53 to 192.26) and a possible adverse effect on mean birth weight (WMD -83.45, 95% CI -221.87 to 54.97).<sup>96</sup>

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Antigen avoidance in lactation found no protective effect of maternal antigen avoidance during the child's first 18 months of life (RR 0.73, 95% CI 0.32 to 1.64). Dietary avoidance by mothers breast-feeding infants with established atopic eczema was associated with a nonsignificant reduction in eczema severity. The Cochrane review concluded that the evidence is insufficient to infer that antigen avoidance during lactation is beneficial or harmful.<sup>96</sup>

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Reviews state there is no evidence for a protective effect of a maternal exclusion diet during pregnancy or lactation.<sup>97-99</sup>

4

**A** **Pregnant women at high risk of giving birth to a child with atopy, and women who are breastfeeding, should not be advised to follow an antigen avoidance diet.**

If a mother reports changes in the severity of their breastfed infant's eczema following ingestion of certain foods, a trial of an allergen-specific exclusion diet should be considered.

## 11.3 INFANT FEEDING

### 11.3.1 BREAST FEEDING

A Cochrane review concluded that, while exclusive breast feeding for six months results in reduced morbidity in infants and benefits to the mother<sup>96</sup> breast feeding is not statistically significantly associated with the prevalence of atopic eczema in the first year of life.<sup>100, 101</sup>

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Exclusive breast feeding for less than four months does not increase the risk of infants developing atopic eczema at one year of age, with or without a family history of atopic eczema (AOR 1.16, 95% CI 0.90 to 1.48, p=0.254).<sup>102</sup> At 18 months of age, those breast fed for four months had an increased risk of developing atopic eczema if they had parents without atopy (IRR = 1.29, 95% CI 1.06 to 1.55) compared to children with one atopic parent (IRR = 1.11 95% CI 0.94 to 1.31) or two parents with allergy (IRR = 0.88 95% CI 0.69 to 1.13).<sup>103</sup>

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Exclusive breast feeding for four months or more reduced the risk of eczema at four years by

20%. Partial breastfeeding after exclusive breast feeding ended did not add any additional effect to the risk reduction.<sup>104</sup> At the age of three years breast feeding was found to be protective for atopic eczema compared with conventional cow's milk formula.<sup>105</sup>

2+

Longer duration of breast feeding is associated with a lower risk of eczema in two-year old infants of mothers without allergy or asthma ( $p=0.01$ ) and a slightly lower risk in those mothers with allergy but no asthma ( $p=0.14$ ).<sup>101</sup>

2+

Breast feeding exclusively for longer than nine months does not confer any advantages and could be a factor for a greater risk of atopic eczema at five years, especially in children with a family history of allergy. This risk does not extend to eleven years.<sup>106</sup>

2+

### 11.3.2 FORMULA FEEDING

A Cochrane review showed no evidence to support feeding using hydrolysed formulas compared to exclusive breast feeding for the prevention of allergy or food intolerance up to childhood. There was no evidence of benefit from the use of a hydrolysed formula in preference to human milk for early short term feeding in low-risk infants. In high-risk infants who are unable to be completely breast fed, there is limited evidence that long term supplementation with hydrolysed formulas compared to cow's milk formula reduces the risk of infant and childhood allergy.<sup>107</sup>

1+

One systematic review found that there was some evidence to support the use of extensively hydrolysed cow's milk formulae over regular cow's milk formulae in the prevention of atopic eczema in high risk families. There is no evidence to support the use of soy milk as opposed to cow's milk supplementation.<sup>25</sup> This is supported by a Cochrane review which showed that in high-risk infants receiving prolonged formula feeding no benefit was found for the use of soy formula compared to cow's milk formula for the prevention of allergy or food intolerance.<sup>108</sup>

1+ +

Limited evidence was shown in one RCT that use of an extensively hydrolysed casein formula may prevent allergy, predominantly eczema, at six years of age ( $p=0.002$ ).<sup>109</sup>

2+

Expert opinion suggests that in infants at high risk who are not breastfed exclusively for four to six months atopic dermatitis may be delayed or prevented by the use of extensively or partially hydrolyzed formulae compared to cow's milk formula. Not all formulae have the same protective effect and extensively hydrolysed may be more protective than partially hydrolyzed in the prevention of atopic disease.<sup>97, 98</sup>

4

Soya-based formulae contain phyto-oestrogens and are not recommended in the UK as the primary protein source in infants under ten months.<sup>88</sup> Goat's milk should not be offered to bottle fed babies because it is nutritionally inadequate and shares 95% of cross-reacting allergens with cow's milk. Both diets based on unmodified proteins of other species milk (eg goat's milk, sheep's milk) or partially hydrolysed formulae should not be used in children with atopic eczema for the management of suspected cow's milk allergy. Diets including soya protein can be offered to children aged six months or over with specialist dietary advice.<sup>88</sup>

4

- Mothers should be advised that there is no conclusive evidence that breastfeeding improves or exacerbates the risk of their child developing eczema. Advice from national guidelines that infants should be exclusively breast fed for the first six months should be followed.
- A** **Hydrolysed formulas should not be routinely offered to infants for the prevention of atopic eczema in preference to breast milk.**
- D** **Soya-milk or other species milk (*goat's, sheep's milk*) should not be offered to bottle fed babies.**
- D** **Children, who are not breast fed and have a cow's milk free diet for longer than eight weeks should be referred for specialist dietary advice.**
- D** **Children over six months who include soy protein as an alternative to cow's milk or infant formula should be referred for specialist dietary advice.**

#### 11.4 INTRODUCTION OF FOOD

Evidence that the introduction of solid food to infants before four months of age increases the risk of allergic disease is conflicting and inconsistent. There is a consistent association between the persistence of eczema and the introduction of solid food before the age of four months that is supported by long term follow-up studies and the dose-dependent nature of the association.<sup>110</sup>

1+

A cohort study which reviewed children at two years of age did not find evidence to support a delayed introduction of solids in months five to six (OR 1.14 95% CI 0.86-1.5) or beyond six months of life (OR 1.31 95% CI 0.93-1.86) for the prevention of atopic eczema and atopic sensitization. This also applied to the introduction of single foods, any solids and solid diversity at ages four-to-six months. Introduction of a high number of different solids food groups by six months of age reduced the odds of atopic eczema within all children (AOR: 0.66; 95% CI 0.46-0.94) and within children with early skin or allergic symptoms (AOR: 0.47; 95%CI 0.28-0.77) Within all children there was no evidence for a protective effect at two years of a delayed introduction of solids on symptomatic atopic eczema. A more diverse diet at four months of age increases the odds of symptomatic atopic eczema and the introduction of various solids beyond four months of age decreases the odds of symptomatic atopic eczema in children without early skin or allergic symptoms. If the introduction of solids is postponed to later than six months there is no additional protective effect on children with symptomatic atopic eczema. In those children who have an early skin reaction or allergic symptoms the late introduction of dairy products was associated with an increased risk of symptomatic atopic eczema. This most likely indicates reverse causality.<sup>111</sup>

2+

At six years of age the prevalence of eczema did not differ between children who were introduced to solids in the first four months of life, four-to-six months or after six months. There was an increased risk of eczema in children without early skin or allergic symptoms when a greater diversity of food was introduced before four months of age. In children whose parents had allergy there was no difference in results with any protective effect on atopic outcome. Delayed introduction of solids only significantly increased sensitization to food at six years.<sup>112</sup>

2+

A delay in introduction of cow's milk products (p=0.01) and other food products (p=0.02) is associated with a higher risk of eczema.<sup>113</sup>

2+

In pre-term infants early introduction to a diverse range of solid foods by 17 weeks post term may predispose them to eczema development by 12 months post-term (OD 3.49, 95% CI 1.51 to 8.05). Children who have non-atopic parents who introduced them to solid food before 10 weeks post-term were also at increased risk of eczema (OR 2.94, 95% CI 1.57 to 5.52).<sup>114</sup>

2+

**B**

**Parents should be advised not to introduce solids to their child’s diet before four-to-six months of age.**

**B**

**Parents should be advised that there is no evidence to delay introduction of solids, including potentially allergic food, after six months of age to prevent the development of atopic eczema.**

## 11.5 FOOD SUPPLEMENTS

### 11.5.1 PRO- AND PREBIOTICS

A meta-analysis concluded that If pregnant women and/or newborns are supplemented with probiotics the child may be protected against atopic eczema at the age of two years but the evidence for the treatment of eczema with probiotics is not shown. It recommended that further studies are required to confirm the recommendations of this meta-analysis.<sup>115</sup>

1+ +

In another meta-analysis treatment with probiotics for one-to-two months was found to reduce the severity of atopic eczema in half the RCTs evaluated with children with high total or allergen specific IgE especially those with food allergy, being most likely to benefit. Use of probiotics, however, did not significantly change most of the inflammatory markers measured.<sup>116</sup>

1-  
1+

Dietary supplementation with *L rhamnosus* but not *B animalis* subsp. *lactis*, substantially reduced the cumulative prevalence of eczema at two years (Hazard ratio (HR) 0.51 95% CI 0.30 to 0.85 and 0.90 95% CI 0.58 to 1.41. respectively).<sup>117</sup> One placebo-controlled trial showed no therapeutic effect of *L rhamnosus* GG against mild-to-moderate atopic dermatitis in infancy.<sup>118</sup>

1+  
1-  
1+

A Cochrane review concluded there is insufficient evidence to determine the role of prebiotic supplementation of infant formula for prevention of allergic diseases. On small trial reported a reduction in eczema in high risk infants who are formula fed.<sup>119</sup>

1+ +

### 11.5.2 VITAMIN SUPPLEMENTS

Children treated with zinc versus placebo showed no significant difference in outcome at eight weeks, other than higher itch scores in the zinc group. Vitamin E treatment appears to prevent worsening of atopic eczema versus placebo (8% vs 78%) but showed little improvement in the condition.<sup>88</sup>

4

### 11.5.3 ORAL ESSENTIAL FATTY ACID SUPPLEMENTATION

Supplementation of essential fatty acid had no clinically relevant effect on severity of atopic eczema.<sup>120</sup>

1-

### 11.5.4 DIETARY GAMMA-LINOLENIC ACID SUPPLEMENTATION

In infants with atopic eczema gamma-linolenic acid supplementation seemed to reduce total IgE in the first year of life. The number of infants developing atopic eczema was lowest in the

1-

cohort of infants who had never been breastfed.<sup>121</sup>

#### 11.5.5 FISH

The introduction of fish to infants before nine months of age can have a protective effect on eczema. It has been suggested that the high ratio of omega 6 to omega 3 fatty acids could contribute to the pathogenesis of allergic disease. Fish is high in omega 3 fatty acid.<sup>122</sup>

2-

Regular fish consumption before the age of one appears to be associated with a reduced risk of allergic disease and sensitisation to food. A risk reduction was also seen for severity of allergic disease such as persistent disease or multiple allergic diseases at the age of four years. Sensitisation to fish is rare, even among those with early introduction of fish.<sup>123</sup>

2+

#### 11.5.6 ORGANIC FOOD

Consumption of organic dairy products is associated with lower eczema risk (OR 0.64, 95% CI 0.44 to 0.93) but there was no association with organic meat, fruit, vegetables or eggs or the proportion of organic foods within the diet with the development of eczema.<sup>124</sup> Further studies are needed to substantiate these findings.

2-

## 12 Complementary and alternative therapies

### 12.1 HERBAL REMEDIES

A Cochrane review and an RCT found no conclusive results or significant improvement from the use of traditional Chinese herbs in the treatment of patients with atopic eczema.<sup>125, 126</sup> One RCT reported an improvement in symptoms in patients treated with oral konjac ceramide, a Japanese herbal preparation, for two weeks. Numbers in this trial were small (25 in each arm).<sup>127</sup> Only one methodologically robust RCT was identified comparing herbal ointment with a placebo ointment. There was no significant difference between the groups in terms of benefit of either treatment.<sup>128</sup>

1+  
1-

### 12.2 DEAD SEA TREATMENT

A small RCT (30 participants) trialled bathing one arm in a Dead Sea salt solution and one in tap water for 15 minutes per day for six weeks.<sup>129</sup> There was an improvement in transepidermal water loss, a 40% decrease in skin roughness ( $p < 0.05$ ), 14% increase in stratum corneum hydration ( $p < 0.05$ ) and an improvement in redness after bathing the arm in a solution of Dead Sea salts regularly for 6 weeks. In the sub group which was found at baseline to have elevated transepidermal water loss there was a large improvement (approx 30%) in trans epidermal water loss.

1-

### 12.3 PSYCHOLOGICAL AND RELAXATION THERAPIES

A systematic review concluded that there is insufficient evidence to show efficacy of psychological interventions as an adjunct to conventional therapy. There is some evidence that educational interventions can improve the severity of a child's eczema and their parents' quality of life.

1+

### 12.4 OTHER THERAPIES

No robust evidence was identified for the use of acupuncture, homeopathy, hypnotherapy or reflexology in the treatment of patients with atopic eczema.

# 13 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing atopic eczema with patients, parents and carers and in guiding the production of locally produced information materials.

## 13.1 SOURCES OF FURTHER INFORMATION

### National Eczema Society

Hill House  
Highgate Hill  
London  
N19 5NA  
Tel: 020 7281 3553  
Helpline: 0800 089 1122 (8am to 8pm Monday to Friday)  
Email: [info@eczema.org](mailto:info@eczema.org)  
Website: <http://www.eczema.org>

Patient support organisation, offering help and information to everyone affected by eczema.

### Eczema Scotland

114 Hanover Court  
North Street  
Glenrothes  
Fife  
KY7 5SB  
Tel: number  
Email: [emailaddress@emailaddress.co.uk](mailto:emailaddress@emailaddress.co.uk)  
Website: [www.website.org.uk](http://www.website.org.uk)

### British Skin Foundation

4 Fitzroy Square  
London  
W1T 5HQ  
Tel: 020 7391 6341  
Website: [www.britishskinfoundation.org.uk/](http://www.britishskinfoundation.org.uk/)

The British Skin Foundation is a registered charity which raises funds for skin disease research. The website provides patient information leaflets.

## 13.2 CHECKLIST FOR PROVISION OF INFORMATION

This section explains what information patients/carers can reasonably expect to be provided with at the key stages of the patient journey. No trials were identified from the last five years on the efficacy of different formats for delivering patient treatment information. The following checklist was designed by members of the guideline development group based on their clinical experience and their understanding of the evidence base.

Diagnosis
<ul style="list-style-type: none"><li>▪ Provide patients and parents or carers of children with eczema with an explanation of what the skin condition is, including: why it has happened, and, if applicable, why other siblings do not have the condition</li><li>▪ Explain the causes of eczema, emphasising that it is not infectious</li><li>▪ Provide reassurance that the condition can be improved through a variety of treatment options and avoidance of irritants.</li></ul>
Treatment

Patients should receive a full explanation of how to use treatments and a demonstration of how to apply dressings. It is essential that the patient understands the instructions for each type of treatment prescribed to them and has the opportunity to discuss concerns regarding potential side effects. Advice should be given by the prescriber and the pharmacist at every opportunity.

- Explain:
  - the importance of emollients
  - how, when and why topical treatments are applied, for how long they can be used and the safety of using steroid.
- Explain how to identify infection and what to do about it
- Discuss the effectiveness of other therapies, eg alternative and complementary therapies, use of sunbeds.

Many patients will consider using complementary and alternative therapies. Healthcare professionals should discuss this with patients, encouraging them to:

- tell their doctor/nurse what they have been using, so their conventional treatment can be adjusted accordingly
- ask their doctor/nurse's opinion before commencing a complementary or alternative therapies, and especially before spending money on them
- ask the provider of complementary or alternative therapies for published evidence of the efficacy of the treatment. Discuss what evidence a prescriber would look for when considering a new treatment.

#### Secondary prevention

Dietary factors – foods to avoid, introducing solids

Advice on vaccinations

#### Psychosocial factors

Provide advice on:

- careers that should be avoided due to exposure to irritants and environmental factors
- environmental factors that could exacerbate eczema, eg swimming
- provide contacts details of organisations that provide support and financial assistance for carers of people with eczema (*see section 13.1*)

# 14 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

## 14.1 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

Not available in this draft.

Key recommendation	section	Likely resource implication
<b>R Recommendation</b>	2.1	
<b>R Recommendation</b>		
<b>R Recommendation</b>		

## 14.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

Not available in this draft

### 14.2.1

- R Recommendation.**
- R Recommendation.**

### 14.2.2

- R Recommendation.**
- R Recommendation.**

### 14.2.3

- R Recommendation.**
- R Recommendation.**

# 15 The evidence base

## 15.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Databases searched included Medline, Embase, Cinahl, PsychInfo and the Cochrane Library. The year range was 2004-2009. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

### 15.1.1 PATIENT ISSUES

At the start of the guideline development process, a SIGN Information Officer conducted a standard SIGN literature search for qualitative and quantitative studies that addressed patient issues of relevance regarding atopic eczema, with a date range 2002-2008. A further search was conducted on patient and social aspects. The results of the two searches were summarised and presented to the guideline development group to inform them of key patient issues for consideration when devising the key questions. Databases searched include Medline, Embase, Cinahl and PsychInfo.

## 15.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline. The following areas for further research have been identified:

- RCTs on the use of prebiotics or probiotics as dietary supplements either in antenatal mothers of high risk babies, newborn formula fed infants or infants up to two years old to reduce severity or treat atopic eczema.
- Comparisons between dressings with ichthammol and wet wrap dressings.
- Studies on the efficacy of different formats and delivery of patient information in improving management, self care and concordance with treatment in patients with atopic eczema.

## 15.3 REVIEW AND UPDATING

This guideline was issued in 2010 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk).

# 16 Development of the guideline

## 16.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. *The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations.* Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline Developer's Handbook", available at [www.sign.ac.uk](http://www.sign.ac.uk)

## 16.2 THE GUIDELINE DEVELOPMENT GROUP

<i>Dr Michael Tidman (Chair)</i>	<i>Consultant Dermatologist, Royal Infirmary of Edinburgh</i>
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<i>Dr David Haldane</i>	<i>Consultant in Occupational Health, Dykebar Hospital, Paisley</i>
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<i>Dr Mary Mealyea</i>	<i>Associate Specialist in Dermatology, Royal Hospital for Sick Children, Glasgow</i>
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<i>Dr Tracey Secrett</i>	<i>General Practitioner, Bearsden</i>
<i>Dr Doug Smith</i>	<i>General Practitioner, Banchory</i>
<i>Sister Anne Smith</i>	<i>Chair, Eczema Scotland, and Clinical Nurse Specialist in Dermatology, Royal Infirmary of Edinburgh</i>
<i>Ms Ailsa Stein</i>	<i>Programme Manager, SIGN</i>
<i>Mrs Eileen Wallace</i>	<i>Patient representative, Stirling</i>
<i>Dr Stephen Wedderburn</i>	<i>General Practitioner, Aberdeen</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

## 16.3 CONSULTATION AND PEER REVIEW

### 16.3.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 1 October 2009 and was attended by **xx** representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

### 16.3.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees,

who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. **The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.**

SIGN is very grateful to all of these experts for their contribution to the guideline.

Title and full name                      *Job title, Work place, City*

Title and full name                      *Job title, Work place, City*

Title and full name                      *Job title, Work place, City*

Title and full name                      *Job title, Work place, City*

Title and full name                      *Job title, Work place, City*

### 16.3.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

Dr Keith Brown                              *Chair of SIGN; Co-Editor*

Dr Safia Qureshi                              *SIGN Programme Director; Co-Editor*

Dr Sara Twaddle                              *Director of SIGN; Co-Editor*

# Abbreviations

<b>APT</b>	Atopy patch test
<b>CADIS</b>	
<b>CDLQ</b>	
<b>CI</b>	Confidence interval
<b>DBPCFC</b>	Double-blind placebo-controlled food challenge
<b>DFI</b>	
<b>DLQI</b>	
<b>FTU</b>	Fingertip usage
<b>HA</b>	Hydrocortisone acetate
<b>HPA</b>	Hypothalamic-pituitary-adrenal
<b>IDQoLI</b>	
<b>MD</b>	Mean difference
<b>NPV</b>	Negative predictive value
<b>PPV</b>	Positive predictive value
<b>RCTs</b>	Randomised controlled trials
<b>RR</b>	Relative risk
<b>SCORAD</b>	
<b>SIGN</b>	Scottish Intercollegiate Guidelines Network
<b>SPT</b>	Skin prick test
<b>TCI</b>	Topical calcineurin inhibitor
<b>TCS</b>	Topical corticosteroid
<b>WMD</b>	Weight mean difference
<b>WWT</b>	Wet wrap treatment

# Annex 1

## Key questions used to develop the guideline

Standard paragraph to cover how KQs are written (PICO etc) and what they are used for – search strategy etc.

### THE KEY QUESTIONS USED TO DEVELOP THE GUIDELINE

#### ASSESSMENT AND DIAGNOSIS

##### Key question

Inclusion/ exclusion criteria	See guideline section
----------------------------------	--------------------------

1. Which criteria are most useful in considering the diagnosis and severity of atopic eczema in primary care?

Compare:

- a. diagnostic criteria (clinical signs/symptoms)
  - b. validated severity measures ( SCORAD)
  - c. syndromic associations eg Wiskott-Aldrich syndrome, anhidrotic ectodermal dysplasia, phenylketonuria etc
  - d. Co-morbidities - (scabies, herpes simplex, fungal/bacterial/viral infections, contact dermatitis – including to medicaments, steroids, cosmetics) and exacerbating environmental factors, psychological consequences
  - e. Quality of life issues (an indication of severity/coping – group to list? Domestic, occupations, family dynamics, etc.
2. What factors make the use of emollients more effective for atopic eczema reducing symptoms of atopic eczema?

Compare:

- a. greasiness - creams vs lotions vs ointments
  - b. With or without the additional use of antiseptic
  - d. Amount prescribed
  - e. Application technique (frequency, before/after other topical preparations – corticosteroids, tacrolimus)
  - f. Side effects (stinging)
  - g. patient choice
  - h. bath / shower gels, soap substitutes etc
3. What factors are important to consider for maximum

benefit when applying topical corticosteroids in the treatment of patients with atopic eczema?

Consider:

- a. Potency groups
- b. Potential side effects – influence of body site eg flexures, face & occlusion
- c. Evidence for risk of side effects – “safe” amounts in different settings – adult/child, scalp in infants
- d. Application technique
- e. “Finger tip units”
- f. Antibiotic/steroid combinations
- g. Before/after/with emollient
- h. Frequency of application - once or twice daily
- i. “Step down” regimes
- j. Long-term steroid regimes
- k. Prescribing advice – amount, duration, monitoring repeat prescriptions
- l. what is the role for systemic corticosteroids in treating atopic eczema?

4. What is the evidence that systemic antihistamines are beneficial in the treatment of patients with atopic eczema?

5. What is the evidence that antimicrobial measures are beneficial in the treatment of patients with atopic eczema?

- a. Is there evidence that swabbing affected skin or potential sites of staph and/or strep carriage influences outcome?
- b. Is there evidence that daily bathing is beneficial?
- c. What is the evidence for topical antiseptics are beneficial
- d. What is the evidence for topical antibiotics are beneficial
- e. What is the evidence for systemic short courses of antibiotics
- f. Evidence for prolonged courses
- g. Treatment for staph and/or strep carriage (reservoirs of disease – patient, family, pets)

6a. What is the evidence that occlusive dressings are beneficial in the treatment of patients with atopic eczema, in terms of efficacy?

b. What is the evidence they reduce itch or topical steroid requirement, patient satisfaction ?

Include: Wet wraps, paste bandages, tubular bandages, tubifast, ichthammol,

7. What is the most appropriate usage of topical calcineurin inhibitors (tacrolimus/pimecrolimus) in the management of patients with atopic eczema?

Compare:

- a. Tacrolimus vs/or pimecrolimus
- c. Potential side effects
- d. Frequency/duration
- e. Long-term strategy

8. What is the evidence for the influence of dietary modification in the management of patients with atopic eczema?

Consider:

- a. Food allergy investigation – including “if and when”
- b. Empirical/exclusion diets
- c. Maternal diet during pregnancy/breast feeding
- d. Weaning/ introduction of food

9. What is the evidence for the management of environmental factors in the control of atopic eczema symptoms?

Consider:

- a. House dust mites
- b. Contact with pets/pollen
- c. Irritant contact (eg washing powders, fabric softeners, fragrance avoidance)
- d. Clothing fibre/choice of textiles
- e. Humidity/temperature/air conditioning
- f. Workplace irritants (nb Catering, nursing, hairdressing, mechanics – previous eczema history etc)
- g. Are patients with an eczema history more prone to workplace irritant experience

10. What is the evidence for the safety and efficacy of, complementary and/or alternative or adjuvant therapies in the management of patients with atopic eczema?

- a. Chinese herbal medicine
- b. Japanese herbal medicine
- c. Dead Sea treatment/spa therapy
- d. Acupuncture
- e. Hypnotherapy
- f. Homeopathy
- g. Reflexology
- h. "British" herbal therapy /herbal medicine / phytotherapy
- i. Psychological and relaxation therapies

11. Are the following routes of delivering patient treatment information effective in improving care, self management and concordance in patients with atopic eczema?

Compare:

- a. Written treatment plans
- b. Patient information leaflets (career guidance)
- c. Role of primary healthcare team in education
- d. Other (websites, support groups)?
- e. Information retention factors

## Annex 2 Emollients

### Why?

Emollients are a necessary part of the treatment of atopic eczema as they replace the natural surface oils which tend to be deficient in this condition and which are essential in preventing irritant materials, infection and allergy-inducing substances from entering the skin. Treatment with emollients should be maintained after the inflammation has resolved.

### Which?

Emollients come in a variety of forms:

- Bath additives and shower products
- Soap substitutes
- Leave-on emollients

Some emollients may contain an antiseptic preparation for use when the skin is, or could become, infected.

There is a very wide choice of emollients (creams, ointments, lotions and sprays), most of which can be purchased over-the-counter as well as being available on prescription. By and large, the greasier the emollient the more effective it is. Ointments are generally greasy, but take longer to absorb into the skin and are less pleasant to use than creams. Lotions are readily absorbed, quicker to apply to large areas of the body and can be applied with less friction to the skin. Personal preference is perhaps the most important factor in determining the best emollient, as an individual is unlikely to use a product in sufficient quantity if it is not entirely acceptable to them. Thus, it is a good idea for patients themselves to sample the different types available and to inform their doctor of their choice.

### When?

Emollients should be applied liberally and frequently, the more the better, but at least 2-4 times a day when the skin is dry. Ideally, they should be applied after bathing. If a topical steroid or topical calcineurin inhibitor is also being used, it is recommended that there is a gap of at least half an hour between the applications of emollient and anti-inflammatory agent. It is a good idea to carry a small sample of emollient (in handbag, pocket or satchel) for use during the day. As greasy emollients may mark and stick to clothing, it is often more convenient to apply ointments at night and to use lighter preparations during the day.

### How?

Leave-on emollients should be applied in adequate quantities, sufficient to completely cover dry and inflamed areas. For children this may be up to (and occasionally more than) 500 g each week, and adults may require double this amount. The emollient should be applied smoothly in the general direction of body hair. Shower and bath preparations should be used with water at a comfortable, rather than hot, temperature: The amounts to be used will be found in the instructions that come with the preparations. Soap substitutes should be used when washing.

Emollients can become infected with bacteria, and so it is desirable not to share them with others. The use of pump dispensers minimises the risk of microbial contamination, and if the emollient is in a pot the required amount should be removed with a clean spoon or spatula.

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