

Emollients, education and quality of life: the RCPCH care pathway for children with eczema

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ABSTRACT

Objectives The Royal College of Paediatrics and Child Health (RCPCH) Science and Research Department was commissioned by the Department of Health to develop national care pathways for children with allergies. The eczema pathway focuses on defining the competences to improve the equity of care received by children with eczema.

Method The eczema pathway was developed by a multidisciplinary working group and was based on a comprehensive review of evidence. The pathway was reviewed by a broad group of stakeholders including paediatricians, allergists, dermatologists, specialist nurses, dietician, patients' representatives and approved by the Allergy Care Pathways Project Board and the RCPCH Clinical Standards Committee. It was also reviewed by a wide range of stakeholders.

Results The results are presented in three sections: the evidence review, mapping and the core knowledge document. The various entry points to the ideal pathway of care are defined from self-care through to follow-up. There is considerable emphasis on good skin care and when allergy problems should be dealt with. The pathway algorithm and associated competences can be downloaded from <http://www.rcpch.ac.uk/allergy/eczema>.

Conclusions Effective eczema management is holistic and encompasses an assessment of severity and impact on quality of life, treatment of the inflamed epidermal skin barrier, recognition and treatment of infection and assessment and management of environmental and allergy triggers. Patient and family education which seeks to maximise understanding and concordance with treatment is also important in all children with eczema.

INTRODUCTION

Disease definition

Atopic eczema (atopic dermatitis) is an itchy inflammatory skin condition with skin creases (flexures), characterised by poorly demarcated erythema (redness) accompanied by surface change such as swelling (oedema), scratch marks (excoriations) and sometimes weeping in the acute stage and skin thickening (lichenification) in the chronic stage.¹ Initial consensus-based criteria were useful in listing the clinical features of eczema,² and these were later refined into a list of reliable and

valid discriminators (table 1).³⁻⁴ Healthcare professionals should also be aware that in Asian, African and African-Caribbean children, atopic eczema may present differently. It can cause skin darkening as opposed to skin reddening (erythema) and can affect the extensor surfaces rather than the flexures. Discoid (circular) or follicular (around hair follicles) patterns of eczema may also be more common as well as gross thickening (lichenification) of the skin.⁵ The cellular mechanisms of eczema have been reviewed elsewhere.⁶

Although frequently referred to as having 'atopic' eczema, some children with the clinical phenotype do not have demonstrable immunoglobulin (IgE)-mediated sensitivity to allergens,⁷ leading the World Allergy Organization to propose that the term 'eczema' alone is used to denote the clinical phenotype which may or not be atopic. While the presence or absence of atopy does not help our clinical predictive ability to diagnose eczema,⁸⁻⁹ it does tend to correlate with eczema severity, with atopic sensitisation being more prevalent in patients with more severe disruption of their skin barrier problems particularly in infants with atopic mechanisms contributing to skin inflammation in some but not all patients.⁷

Disease severity and quality of life

Most cases of childhood eczema in any given community are mild (84%) with infrequent flares and minimal disruption to sleep and daily activities. Moderate and severe eczema, which affect 14% and 2% of the population, respectively, may significantly impact quality of life and psychosocial function.¹⁰ Specific aspects affected include itch and its associated sleep loss (causing considerable family disturbance), social stigmatisation, the need for special clothing and bedding, avoidance of activities (eg, swimming) and the need for frequent applications of topical treatments and visits to healthcare professionals.¹¹ Several cost of illness studies suggest a high economic burden for eczema,¹² with overall costs comparable to those of asthma.¹³ Family stress related to the care of children with moderate or severe eczema may be significantly greater than that of type 1 diabetes, mainly owing to sleep deprivation, employment loss, time to care for eczema and financial costs.¹⁴

Table 1 Diagnostic criteria for children with eczema

Atopic eczema should be diagnosed when a child has an itchy skin condition plus three or more of the following:

Visible flexural dermatitis involving the skin creases, such as the bends of the elbows or behind the knees (or visible dermatitis on the cheeks and/or extensor areas in children aged ≤ 18 months)

Personal history of flexural dermatitis (or dermatitis on the cheeks and/or extensor areas in children aged ≤ 18 months)

Personal history of dry skin in the past 12 months

Personal history of asthma or allergic rhinitis (or history of atopic disease in a first-degree relative for children aged under 4 years)

Onset of signs and symptoms under the age of 2 years

A holistic approach should be taken into account when assessing eczema severity which includes an assessment of skin severity together with its impact on a child's sleep, everyday activities and psychosocial wellbeing. (table 3) There is not necessarily a direct relationship between the severity of eczema and its impact on quality of life. Although several disease severity scales exist, only three (SCORing atopic dermatitis (SCORAD), eczema area and severity index (EASI) and Patient Oriented Eczema Measure (POEM)) have been shown to perform reasonably well to standard psychometric scale requirements.¹⁵ The POEM is the only one that has been derived from patients for patients.¹⁶ Validated tools for assessing quality of life in infants and children with eczema include the Children's Dermatology Life Quality Index,¹⁷ Infant's Dermatitis Quality of Life index¹⁸ and Dermatitis Family Impact Questionnaire.^{19–20}

Disease prevalence

The International Study of Asthma and Allergies in Childhood (ISAAC) has shown that eczema symptom prevalence varies from around 2% to 20% around the world, with the UK, Scandinavia and Australia having some of the highest rates.^{20–21} ISAAC time trends data suggest that eczema has been increasing worldwide over the past 10 years, especially in developing countries and in younger children.²² The reasons for such a rapid increase are still unclear, but they cannot be explained by genetics, though epigenetic events may be involved.

Natural history and aetiology

Eczema commonly starts in the first years of life²³ with onset before the age of 2 years in 80% of cases. Adult onset eczema in hospital-based studies occurs in only 10% of patients.²⁴ Studies of representative populations suggest that around 60% of childhood cases of eczema are free of symptoms by early adolescence,^{23–25} although up to 50% may recur in adulthood.²⁶ Approximately one-third of patients with eczema persist with eczema into adult life. Risk factors for eczema persistence are disease of early onset, severe widespread disease in infancy, concomitant asthma or hay fever and a family history of eczema.²³

Patients with eczema are at higher risk of developing asthma. Sensitisation to food and inhalant allergens in infancy appears to predict the onset of allergic airways disease in childhood and asthma persistence at age of 20 years, raising the concept of 'the allergic or atopic march', an observed progression of allergic symptoms in some but not all patients.^{27–29} In the German Multicentre Allergy Study all participants with eczema and IgE sensitisation to at least one food allergen at the age of 12 months had allergic airways disease by

5 years of age.³⁰ Coexistence of early onset wheezing with early onset eczema in this study conferred a greater risk for asthma at 7 years than in those infants with eczema but no history of early wheeze, suggesting co-manifestation of two phenotypes at an early age rather than an allergic march.^{31–32}

There is good evidence to suggest that genetic factors are an important predisposition to eczema.³³ Twin studies³⁴ have shown a much higher concordance for monozygotic (85%) than for dizygotic twins (21%). The most consistent genetic markers for eczema are those coding for filaggrin protein, a hygroscopic protein that is key to helping to maintain the barrier function of the skin and which may explain much of the associated dryness of eczema.³⁵

Environmental factors

Environmental factors are also likely to be critical in determining disease expression in eczema given the large increase of disease prevalence over a short time,²² the positive social class gradient³² and the fact that migrants coming from a country with low disease prevalence seem to develop higher rates in their adopted country.³⁶ The observed inverse association between the prevalence of eczema and family size, has led to the 'hygiene hypothesis'.³⁷ The possible link between reduced microbial or helminth exposure in modern society and increased eczema is a complex one which has been reviewed elsewhere.³⁸

Bacterial infections of the skin are more common in patients with eczema and play an integral role in eczema pathogenesis.³⁹ Damage to the epidermal skin barrier from inflammation and scratching allows bacterial colonisation with *Staphylococcus aureus* in 90% of patients with eczema compared with 30% of unaffected individuals.

Viral infections of the skin are also higher in patients with eczema. Eczema herpeticum is an uncommon generalised (or locally widespread) vesicular eruption caused by the herpes simplex virus. It is important to recognise and initiate hospital treatment immediately for eczema herpeticum as this can cause significant mortality if left untreated.

Trigger factors for eczema

For those with established eczema, a plethora of other potential environmental factors for exacerbating eczema have been suggested including exposure to irritants (eg, soaps, shampoos), rough clothing (eg, wool), contact allergens, food and inhalant allergens, microbes and climatic factors.^{39–40} Inhalant allergens (eg, house dust mite, pollens and animal dander) can trigger eczema exacerbations in allergic patients.⁴¹

Food allergy

Hospital-based studies have shown the presence of food allergy in approximately 30% of children with moderate to severe eczema, proven by blinded oral provocation challenge testing.^{42–50} Most common food allergens are cows' milk, hens' eggs, nuts, soya, wheat and fish. The risk is greatest in infants and young children with eczema, whose disease is of early onset (within the first 12 months).^{51–53} In infants with mild intermittent eczema and in children whose eczema developed after their first birthday, the likelihood of food allergy is much reduced.

METHOD

The pathway method is described separately in this supplement.⁵⁴

RESULTS

Evidence review

A total of 625 titles and abstracts were screened by the project manager and the Eczema Working Group Chair (figure 1). Thirty-six systematic reviews and/or primary papers and nine guidelines were identified for appraisal; handsearching the reference lists of appraised papers identified a further five papers. The critical appraisal resulted in the inclusion of 13 systematic reviews and/or primary papers and seven clinical practice guidelines.

The evidence review found that atopic dermatitis is frequently the first manifestation of an atopic diathesis. Between 30% and 50% of children with atopic dermatitis will eventually develop allergic rhinitis or asthma later in childhood.²⁷ An additional study found that one in three children with eczema later develop asthma.²⁸ Eczematous reactions to food can only be diagnosed by taking into account the patient's history, the degree of sensitisation and the clinical relevance of the sensitisation.⁵⁵ Oral food challenge tests are frequently required to obtain an accurate diagnosis of food allergy. There is little benefit in adopting exclusion diets in unselected cases of atopic eczema but it may be appropriate to trial if there is a clinical history of reactions to foods,⁵⁶ or a clinical history and allergy tests that strongly support the diagnosis of food allergy. Infants with severe atopic eczema are more likely overall to benefit from amino acid-based or extensively hydrolysed cows' milk formula, particularly when associated with symptoms of gut dysmotility or failure to thrive.⁵⁷

The best patient eczema severity measures were found to be SCORAD, EASI and POEM.¹⁵ In addition to measuring skin manifestations, quality of life should be assessed and psychological interventions were found to significantly ameliorate eczema severity, itching intensity and scratching.⁵⁸

The literature clearly demonstrates that education and training of children and parents and its role in improving the regular use of emollients.^{59 60} Other studies indicate that written information should be given to parents and that doctors

should try to improve partnership during consultations.⁶¹ In support of this the benefits of nurse-led clinics, compared with care from a doctor, were associated with increased patient satisfaction, longer consultations resulting in improved patient education and similar health outcomes. There were no studies identified comparing nurse-led and doctor-led clinics in the management of eczema.⁶²

Mapping

The national Royal College of Paediatrics and Child Health (RCPCH) care pathway can be downloaded from <http://www.rcpch.ac.uk/allergy/eczema>. This pathway was been developed around the competences required to diagnose and optimally manage eczema.^{62 64} These competences have not been assigned to specific health professionals or settings in order to encourage flexibility in service delivery. However, it is envisaged that the provision of optimal care at all NHS levels will require close liaison between different health professional groups including doctors, nurses, pharmacists and dietitians. All health professionals should have paediatric training in line with the principles outlined in the Children's National Service Framework.⁶⁵

The pathways recommend the stepped approach to management,⁵ using emollients even when the atopic eczema is clear (table 2). Management can then be stepped up or down,

Table 2 Stepped approach to treatment

Mild atopic eczema	Moderate atopic eczema	Severe atopic eczema
Emollients	Emollients	Emollients
<i>Mild potency:</i> topical corticosteroids	<i>Moderate potency:</i> topical corticosteroids	<i>Potent:</i> topical corticosteroids
	Topical calcineurin inhibitors	Topical calcineurin inhibitors
	Bandages	Bandages
		Phototherapy
		Systemic therapy

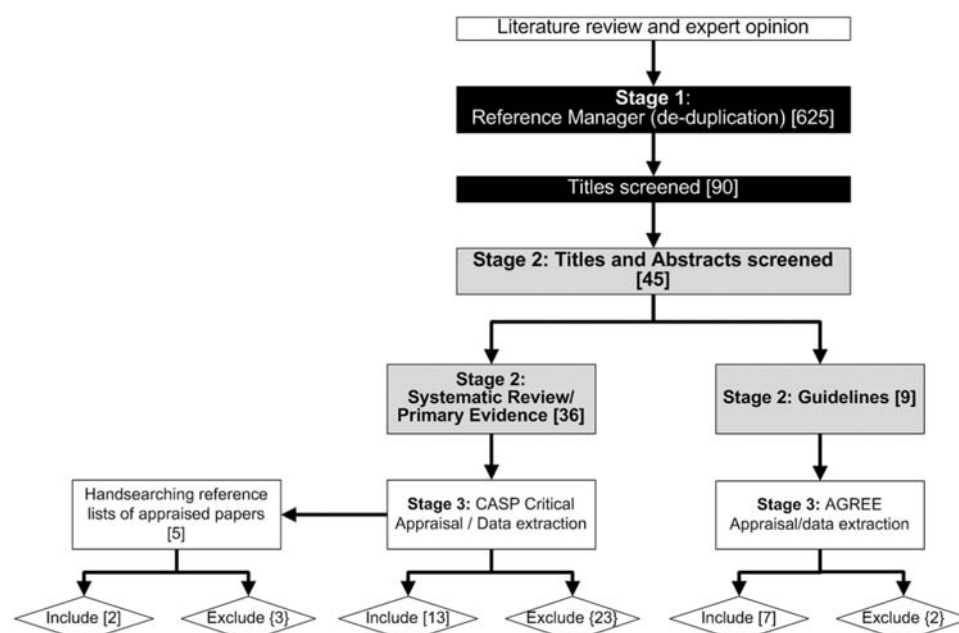


Figure 1 Methodology of evidence review. CASP, Critical Appraisal Skills Programme.

Table 3 NICE holistic assessment⁵

Skin/physical severity		Impact on quality of life	
Clear	Normal skin, no evidence of active atopic eczema	None	No impact on quality of life
Mild	Areas of dry skin, infrequent itching (with or without small areas of redness)	Mild	Little impact on everyday activities, sleep and psychosocial wellbeing
Moderate	Areas of dry skin, frequent itching, redness (with or without excoriation and localised skin thickening)	Moderate	Moderate impact on everyday activities and psychosocial wellbeing, frequently disturbed sleep
Severe	Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking and alteration of pigmentation)	Severe	Severe limitation of everyday activities and psychosocial functioning, nightly loss of sleep

There is not necessarily a direct relationship between the severity of the atopic eczema and the impact of the atopic eczema on quality of life.

according to the severity of symptoms, with the addition of the other treatments.

External review

A total of 13/53 (25%) of invited organisations responded, providing 78 comments. All comments were reviewed by the Eczema Working Group and the pathway was approved by the Allergy Care Pathways Project Board and the RCPCH Clinical Standards Committee.

Core knowledge document

The core knowledge document for this pathway is the National Institute for Health and Clinical Excellence guideline for atopic eczema in children.⁵

DISCUSSION

The wide variation across the UK in the provision of care for children with allergic conditions is described elsewhere.⁵ Effective eczema management requires a holistic assessment of its severity and impact on the child and family's psychosocial functioning and quality of life. Severity can vary from one area of the body to another and does not need to be severe to harm a child's psychosocial well-being.

Initial management of eczema

Initial treatment should focus on repairing the skin barrier through the use of emollients for moisturising, washing and bathing. Inflamed skin requires a stepped approach to treatment, in which the potency of topical steroids used at each step is tailored to the severity of the eczema, body site and age of child.⁵ Topical calcineurin inhibitors are used as second line treatments, within their licensed indications, for the treatment of moderate to severe eczema.

Oral antibiotics are recommended for the treatment of obviously infected eczema (weeping, pustules, crusts, atopic eczema failing to respond to treatment, rapidly worsening atopic eczema, fever, malaise). Suspicion of secondary infection of eczema with herpes simplex virus should prompt rapid assessment and treatment. Eczema herpeticum is a medical emergency requiring same day hospital treatment and should be suspected

in the presence of rapidly worsening, painful eczema, clustering of small blisters, punched out circular erosions or crusts of uniform appearance and possible fever, lethargy and distress.

Advice regarding the management of eczema should be given in verbal and written format in language that is easy to understand. Education which seeks to maximise understanding and concordance with treatment is important in all children with eczema. It is important to highlight that eczema is usually a chronic disease, and that measurement of treatment impact should include long-term measures such as number of well controlled weeks or number of disease flares prevented⁶⁶ rather than short-term reduction of composite disease scores, the clinical interpretability of which can be obscure.¹⁶ This is currently lacking in many cases.

Assessment of trigger factors

A clinical history which seeks to identify trigger factors for eczema is recommended, especially when eczema is responding poorly to treatment or where there is a continuous daily requirement for potent or moderately potent steroids in an infant or young child. In the older child, the association of allergic rhinitis (hayfever) or asthma with eczema should raise the possibility of associated inhalant allergies. Treatment with a non-sedating antihistamine in patients allergic to tree or grass pollen who experience flares of eczema within the pollen season, may be beneficial. House dust mite allergy is commonly associated with eczema. However, evidence that current house dust mite reduction measures are effective in reducing eczematous inflammation is limited.⁶⁷

In the young infant the association of gut symptoms with eczema or severe eczema responding poorly to topical treatments should raise the possibility of food allergy. For bottle fed infants under 6 months a 6–8 week trial of an extensively hydrolysed or amino acid formula should be offered in place of a cows' milk formula. In breastfed infants the mother should be offered a trial of an allergen-specific exclusion diet for 6 weeks, although the evidence that this is beneficial is limited.⁵

The overall prevalence of food allergy in infants and young children with moderate to severe eczema is 30%.^{42–50} The perceived prevalence of suspected food allergy in eczema, however, is much greater and self-imposed exclusion diets are common with up to 75% of patients trying food exclusions.⁶⁸ This puts individuals at risk of nutritional deficiencies and may unnecessarily restrict their lifestyle even further. In particular, infants who are breastfed beyond 6 months without monitoring or vitamin supplementation are susceptible to vitamin D deficiency, rickets, iron deficiency, anaemia and other vitamin deficiencies. Frequently, the diagnosis of food allergy can be excluded thus allowing the child's diet to be liberated.

An accurate diagnosis of food allergy is made by interpreting the allergy tests in the face of a thorough clinical history. This requires an understanding of the different presentations of food allergy (IgE-mediated and non-IgE-mediated), natural history and performance of tests. Competences for making these assessments are defined within the pathway and we hope that they guide treatment.

Where food allergy is confirmed, specific dietary avoidance should be implemented together with an assessment of the child's nutritional requirements for any dietary restriction imposed for longer than 4 weeks. Dietary management can be an effective strategy for the treatment of eczema in children where an allergen-specific diagnosis has been confirmed.^{56 69} More research in this area needs to be conducted.

CONCLUSION AND CLINICAL IMPLICATIONS

This eczema care pathway is designed to guide patients, carers and healthcare professionals in the optimal management of eczema in infants and children. Each step of the guideline details the appropriate competences required to make an accurate clinical diagnosis, thus enabling initiation of effective treatment for eczema. Where the appropriate competences are not available onward referral is recommended. The approach is holistic and encompasses an assessment of severity and impact on quality of life, treatment of the inflamed epidermal skin barrier, recognition and treatment of infection and assessment and management of environmental and allergic triggers.

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REFERENCES

- Aoki T, Fukuzumi T, Adachi J, *et al*. Re-evaluation of skin lesion distribution in atopic dermatitis. Analysis of cases 0 to 9 years of age. *Acta Derm Venereol Suppl (Stockh)* 1992;**176**:19–23.
- Hanifin JM, Rajka G. Diagnostic Features of Atopic Dermatitis. *Acta Derm Venereol* 1980;**92**:44–7.
- Williams HC, Burney PG, Pembroke AC, *et al*. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation. *Br J Dermatol* 1994;**131**:406–16.
- Breninkmeijer EE, Schram ME, Leeflang MM, *et al*. Diagnostic criteria for atopic dermatitis: a systematic review. *Br J Dermatol* 2008;**158**:754–65.
- NICE. Atopic Eczema in Children. National Institute for Health and Clinical Excellence 2007.
- Bieber T. Atopic dermatitis. *N Engl J Med* 2008;**358**:1483–94.
- Flohr C, Johansson SG, Wahlgren CF, *et al*. How atopic is atopic dermatitis? *J Allergy Clin Immunol* 2004;**114**:150–8.
- Hanifin JM. Atopiform dermatitis: do we need another confusing name for atopic dermatitis? *Br J Dermatol* 2002;**147**:430–2.
- Johansson SG, Bieber T, Dahl R, *et al*. Revised Nomenclature for Allergy for Global Use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol*. 2004;**113**:832–6.
- Emerson RM, Williams HC, Allen BR. Severity distribution of atopic dermatitis in the community and its relationship to secondary referral. *Br J Dermatol* 1998;**139**:73–6.
- Herd RM. The morbidity and cost of atopic dermatitis. In: Williams HC, ed. *Atopic Dermatitis*. Cambridge: Cambridge University Press 2000:85–95.
- Mancini AJ, Kaulback K, Chamlin SL. The socioeconomic impact of atopic dermatitis in the United States: a systematic review. *Pediatr Dermatol* 2008;**25**:1–6.
- Verboom P, Hakkaart-Van L, Sturkenboom M, *et al*. The cost of atopic dermatitis in the Netherlands: an international comparison. *Br J Dermatol* 2002;**147**:716–24.
- Kemp AS. Cost of illness of atopic dermatitis in children: a societal perspective. *Pharmacoeconomics* 2003;**21**:105–13.
- Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? A systematic review. *J Allergy Clin Immunol* 2007;**120**:1389–98.
- Charman C, Williams H. Outcome measures of disease severity in atopic eczema. *Arch Dermatol* 2000;**136**:763–9.
- Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol* 1995;**132**:942–9.
- Lewis-Jones M, Finlay A, Dykes P. Measurement of the impact of atopic dermatitis on infant's and their families lives. *Br J Dermatol* 1999;**141**(Suppl 55):105–6.
- Lawson V, Lewis-Jones MS, Finlay AY, *et al*. The family impact of childhood atopic dermatitis: the Dermatitis Family Impact Questionnaire. *Br J Dermatol* 1998;**138**:107–13.
- Cardiff University. Quality of Life: Overview. Cardiff. 2011. <http://www.dermatology.org.uk/quality/quality-life.html> (accessed 15 February 2011)
- Odhambo JA, Williams HC, Clayton TO, *et al*. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *J Allergy Clin Immunol* 2009;**124**:1251–8.e23.
- Williams H, Stewart A, von Mutius E, *et al*. Is eczema really on the increase worldwide? *J Allergy Clin Immunol* 2008;**121**:947–54.e15.
- Williams HC, Wuthrich B. The natural history of atopic dermatitis. In: Williams HC, ed. *Atopic Dermatitis*. Cambridge: Cambridge University Press 2000:41–59.
- Wahn U, Warner J, Simons FE, *et al*. IgE antibody responses in young children with atopic dermatitis. *Pediatr Allergy Immunol* 2008;**19**:332–6.
- Rystedt I. Long term follow-up in atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1985;**114**:117–20.
- Lammintausta K, Kalimo K, Raitala R, *et al*. Prognosis of atopic dermatitis. A prospective study in early adulthood. *Int J Dermatol* 1991;**30**:563–8.
- Eichenfield LF, Hanifin JM, Beck LA, *et al*. Atopic dermatitis and asthma: parallels in the evolution of treatment. *Pediatrics* 2003;**111**:608–16.
- van der Hulst AE, Klip H, Brand PL. Risk of developing asthma in young children with atopic eczema: a systematic review. *J Allergy Clin Immunol* 2007;**120**:565–9.
- Rhodes HL, Thomas P, Sporik R, *et al*. A birth cohort study of subjects at risk of atopy: twenty-two-year follow-up of wheeze and atopic status. *Am J Respir Crit Care Med* 2002;**165**:176–80.
- Kulig M, Bergmann R, Niggemann B, *et al*. Prediction of sensitization to inhalant allergens in childhood: evaluating family history, atopic dermatitis and sensitization to food allergens. The MAS Study Group. Multicentre Allergy Study. *Clin Exp Allergy* 1998;**28**:1397–403.
- Illi S, von Mutius E, Lau S, *et al*. The natural course of atopic dermatitis from birth to age 7 years and the association with asthma. *J Allergy Clin Immunol* 2004;**113**:925–31.
- Williams H, Flohr C. How epidemiology has challenged 3 prevailing concepts about atopic dermatitis. *J Allergy Clin Immunol* 2006;**118**:209–13.
- van den Oord RA, Sheikh A. Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis. *BMJ* 2009;**339**:b2433.
- Larsen FS, Holm NV, Henningsen K. Atopic dermatitis. A genetic-epidemiologic study in a population-based twin sample. *J Am Acad Dermatol* 1986;**15**:487–94.
- Rodríguez E, Baurecht H, Herberich E, *et al*. Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disease. *J Allergy Clin Immunol* 2009;**123**:1361–70.e7.
- Burrell-Morris C, Williams HC. Atopic dermatitis in migrant populations. In: Williams HC, ed. *Atopic Dermatitis*. Cambridge: Cambridge University Press 2000:169–82.
- Williams HC, Strachan DP, Hay RJ. Childhood eczema: disease of the advantaged? *BMJ* 1994;**308**:1132–5.
- Flohr C, Pascoe D, Williams HC. Atopic dermatitis and the 'hygiene hypothesis': too clean to be true? *Br J Dermatol* 2005;**152**:202–16.
- Langan SM, Williams HC. What causes worsening of eczema? A systematic review. *Br J Dermatol* 2006;**155**:504–14.
- Langan SM, Silcocks P, Williams HC. What causes flares of eczema in children? *Br J Dermatol* 2009;**161**:640–6.
- Shah D, Hales J, Cooper D, *et al*. Recognition of pathogenically relevant house dust mite hypersensitivity in adults with atopic dermatitis: a new approach? *J Allergy Clin Immunol* 2002;**109**:1012–18.
- Sampson HA. Role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol* 1983;**71**:473–80.
- Sampson HA, McCaskill CC. Food hypersensitivity and atopic dermatitis: evaluation of 113 patients. *J Pediatr* 1985;**107**:669–75.
- Isolauri E, Turjanmaa K. Combined skin prick and patch testing enhances identification of food allergy in infants with atopic dermatitis. *J Allergy Clin Immunol* 1996;**97**:9–15.
- Burks AW, James JM, Hiegel A, *et al*. Atopic dermatitis and food hypersensitivity reactions. *J Pediatr* 1998;**132**:132–6.
- Eigenmann PA, Sicherer SH, Borkowski TA, *et al*. Prevalence of IgE-mediated food allergy among children with atopic dermatitis. *Pediatrics* 1998;**101**:E8.
- Niggemann B, Sialaff B, Beyer K, *et al*. Outcome of double-blind, placebo-controlled food challenge tests in 107 children with atopic dermatitis. *Clin Exp Allergy* 1999;**29**:91–6.
- Eigenmann PA, Calza AM. Diagnosis of IgE-mediated food allergy among Swiss children with atopic dermatitis. *Pediatr Allergy Immunol* 2000;**11**:95–100.
- Niggemann B, Binder C, Dupont C, *et al*. Prospective, controlled, multicenter study on the effect of an amino-acid-based formula in infants with cow's milk allergy/intolerance and atopic dermatitis. *Pediatr Allergy Immunol* 2001;**12**:78–82.

50. **Roehr CC**, Reibel S, Ziegert M, *et al.* Atopy patch tests, together with determination of specific IgE levels, reduce the need for oral food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 2001;**107**:548–53.
51. **Hill DJ**, Heine RG, Hosking CS, *et al.* IgE food sensitization in infants with eczema attending a dermatology department. *J Pediatr* 2007;**151**:359–63.
52. **Hill DJ**, Hosking CS. Food allergy and atopic dermatitis in infancy: an epidemiologic study. *Pediatr Allergy Immunol* 2004;**15**:421–7.
53. **Hill DJ**, Sporik R, Thorburn J, *et al.* The association of atopic dermatitis in infancy with immunoglobulin E food sensitization. *J Pediatr* 2000;**137**:475–9.
54. **Warner JO**, Lloyd K. Shared learning for chronic conditions: a methodology for developing the Royal College of Paediatrics and Child Health (RCPCH) care pathways for children with allergies. *Arch Dis Child* 2011;**96**(Suppl 2):i1–i5.
55. **Werfel T**, Erdmann S, Fuchs T, *et al.* Approach to suspected food allergy in atopic dermatitis. Guideline of the Task Force on Food Allergy of the German Society of Allergology and Clinical Immunology (DGAKI) and the Medical Association of German Allergologists (ADA) and the German Society of Pediatric Allergology (GPA). *J Dtsch Dermatol Ges* 2009;**7**:265–71.
56. **Bath-Hextall F**, Delamere FM, Williams HC. Dietary exclusions for established atopic eczema. *Cochrane Database Syst Rev* 2008;**1**:CD005203.
57. **Hill DJ**, Murch SH, Rafferty K, *et al.* The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review. *Clin Exp Allergy* 2007;**37**:808–22.
58. **Chida Y**, Steptoe A, Hirakawa N, *et al.* The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analysis. *Int Arch Allergy Immunol* 2007;**144**:1–9.
59. **Szczepanowska J**, Reich A, Szepietowski JC. Emollients improve treatment results with topical corticosteroids in childhood atopic dermatitis: a randomized comparative study. *Pediatr Allergy Immunol* 2008;**19**:614–18.
60. **Levy ML**. Atopic dermatitis: understanding the disease and its management. *Curr Med Res Opin* 2007;**23**:3091–103.
61. **Gore C**, Johnson RJ, Caress AL, *et al.* The information needs and preferred roles in treatment decision-making of parents caring for infants with atopic dermatitis: a qualitative study. *Allergy* 2005;**60**:938–43.
62. **Moore E**, Williams A, Manias E, *et al.* Nurse-led clinics reduce severity of childhood atopic eczema: a review of the literature. *Br J Dermatol* 2006;**155**:1242–8.
63. RCPCH. A Framework of Competences for Level 3 Training in Paediatric Immunology, Infectious Diseases and Allergy (Online), 2010. http://www.rcpch.ac.uk/doc.aspx?id_Resource=4355 (accessed 5 Oct 2009).
64. Skills for Health. Competence Application Tools (Online), 2009. https://tools.skillsforhealth.org.uk/competence/searchResults?keywords=allergy&level%5B%5D=1&level%5B%5D=2&level%5B%5D=3&level%5B%5D=4&adv_search.x=4&adv_search.y=8 (accessed 5 Oct 2009).
65. Department of Health. National Service Framework for Children, Young People and Maternity Services (Online) 2007. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/Browsable/DH_4867287 (accessed 9 Sep 2011).
66. **Langan SM**, Thomas KS, Williams HC. What is meant by a “flare” in atopic dermatitis? A systematic review and proposal. *Arch Dermatol* 2006;**142**:1190–6.
67. **Sheikh A**, Hurwitz B, Nurmatov U, *et al.* House dust mite avoidance measures for perennial allergic rhinitis. *Cochrane Database Syst Rev* 2010;**7**:CD001563.
68. **Johnston GA**, Bilbao RM, Graham-Brown RA. The use of dietary manipulation by parents of children with atopic dermatitis. *Br J Dermatol* 2004;**150**:1186–9.
69. **Fiocchi A**, Bouygue GR, Restani P, *et al.* Accuracy of skin prick tests in IgE-mediated adverse reactions to bovine proteins. *Ann Allergy Asthma Immunol* 2002;**89**:26–32.