2010 Annual Evidence Update on Atopic Eczema

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Welcome to the fourth Annual Evidence Update on Atopic Eczema produced by NHS Evidence - skin disorders, with the results of a search for new guidelines and systematic reviews published or indexed since the last Annual Evidence Update in September 2009. There is also a "what's new" analysis, discussing the new evidence and its implications for clinical practice.

2010 Annual Evidence Update on Atopic Eczema - Introduction

Introduction by Professor Hywel Williams (Clinical Lead) and Dr Douglas Grindlay (Information Specialist), NHS Evidence - skin disorders

Welcome

Welcome to the 2010 Annual Evidence Update on Atopic Eczema from NHS Evidence - skin disorders. This is a summary of important new evidence published or indexed since our 2009 Annual Evidence Update. As regular readers will know, the Annual Evidence Update searches for new evidence in the form of guidelines and systematic reviews. We use systematic reviews as our core evidence source for Annual Evidence Updates because of the well-known hazards in interpreting the results of single research studies (see, for example, Ioannidis 2005). Although NHS Evidence - skin disorders is aimed at healthcare professionals, we hope that many people with eczema, and also parents and carers, will also find some of the information of interest.

So what's in our Annual Evidence Update on Atopic Eczema?

Lots of interesting new information is the short answer, on topics such as consumption of organic foods, silk clothing, links with ADHD, and bleach baths, to mention but a few. There is even some information on treatment of atopic dermatitis in dogs thrown in for good measure and general interest. We suggest you start with our "What's new?" commentary which is a guide for busy health care professionals on the new evidence and its potential implications for clinical practice. We would like to express our special thanks to Dr Kave Shams (Specialist Registrar and UK Dermatology Clinical Trials Network Fellow) for helping us to put the "What's new" section together this year.

There is no need to read the whole commentary if the topic of the systematic review does not interest you, but we do commend you to read the "bottom line" summary section on how the evidence might change everyday clinical practice.

This year, we have gone even further in terms of trying to distill down the clinical implications in our "bottom line" table by trying to summarise the content of systematic review of guideline in one or two sentences, followed by a statement of what action we would take as clinicians as a result of reading and critically appraising the new evidence. You may disagree with our interpretation of the new evidence, which is fine—the important thing is to identify the evidence so that all can make an informed choice about its utility.

The citations we found have been listed under relevant headings in our Results, with links to PubMed or free full text where available, should you wish to read more deeply.

Filling important research gaps

We hope you enjoy this Annual Evidence Update, but if you feel that important questions about atopic eczema have not been answered, please send these to us using our DUETs submission form so that we can consider including them in the atopic eczema topic of DUETs, the UK Database of Uncertainties about the Effects of Treatments. Documenting such uncertainties will help future researchers and funders to prioritise and fill those important gaps—and there are lots of important gaps to fill.

Lost track of what was said in previous Annual Evidence Updates?

This is now our fourth Annual Evidence Update on Atopic Eczema, and some of the themes such as risk of brain tumours, hydrolyzed milk formulas and calcineurin inhibitors have appeared before. So if you are struggling to remember what we said before about systematic reviews in these topics, you can visit our previous Annual Evidence Updates here. Shortened versions of our previous commentaries have also appeared as review papers published in the journal *Clinical and Experimental Dermatology*. Or if you are looking for a "map" of all systematic reviews on atopic eczema done to date, organised by categories such as epidemiology, prevention, topical and systemic treatments etc., then you can find them all in one place here.

Hywel Williams and Douglas Grindlay, 13th September 2010

2010 Annual Evidence Update on Atopic Eczema - Results

A literature search was carried out to identify **new guidelines and systematic reviews** relating to atopic eczema (atopic dermatitis) that have been published or indexed since the 2009 Annual Evidence Update on Atopic Eczema.
The result of this search is the **2010 Annual Evidence Update on Atopic Eczema**.

Search period
January 2009 was set as the limit for earliest publication date in this year's searches, to allow for any delays in indexing of citations in the bibliographic databases used (which might mean the citations were not found in the searches for the previous Annual Evidence Update in August 2009).
All the searches were carried out for the last time on 24th August, 2010.

Sources Searched
The following sources were searched:

- Ovid MEDLINE (using SIGN MEDLINE systematic review filter)
- Ovid EMBASE (using SIGN EMBASE systematic review filter)
- PubMed (using PubMed Clinical Queries systematic review filter)
- Cochrane Library
- NHS Evidence - skin disorders

All citations found in the searches were hand searched by reading the titles and abstracts to identify systematic reviews and potential systematic reviews relevant to atopic eczema. For all potential systematic reviews where there was still some doubt, the full texts were then read to ensure that they were indeed systematic reviews.
The definition of a systematic review from the Glossary of Cochrane Collaboration Terms on the Cochrane Collaboration website was used:
“A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.”

RESULTS
One guideline and 18 new systematic reviews judged of direct relevance to the topic of atopic eczema and its treatment were identified. Two papers on canine atopic dermatitis have also been included for interest.
The citations for these systematic reviews are listed below, arranged by topic. Within each topic, the citations are presented in alphabetical order of first author. Links to PubMed abstracts or free full text, where available, are provided.
Please note that the inclusion of citations in this list does not imply endorsement. NHS Evidence - skin disorders does not accept responsibility for the content or quality of included studies.
A number of citations were identified as possible systematic reviews for the Annual Evidence Update in the initial searches, but were subsequently excluded on the grounds of a lack of a clear systematic review methodology or for other reasons. These citations are listed at the end of this page under the heading "Excluded references", with the reasons for exclusion.

UK Guidelines
No new UK guidelines identified

Overseas guidelines

National Institute of Allergy and Infectious Diseases.
Guidelines for the Diagnosis and Management of Food Allergy (draft).
Bethesda, MD: National Institute of Allergy and Infectious Diseases, 2010.
Link to full text

Epidemiology and causes

Chen C, Xu T, Chen J, Zhou J, Yan Y, Lu Y, Wu S.
Allergy and risk of glioma: a meta-analysis.
European Journal of Neurology 2010 Aug 16. [Epub ahead of print]
Link to PubMed abstract
Note: PubMed, Cochrane Library and EMBASE searched.

Linabery AM, Jurek AM, Duval S, Ross JA.
The association between atopy and childhood/adolescent leukemia: a meta-analysis.
American Journal of Epidemiology 2010;171(7):749-64. Epub 2010 Mar 12.
Link to full text
Note: PubMed and Cochrane Database of Systematic Reviews searched.

Monteiro L, Souza-Machado A, Menezes C, Melo A.
Association between allergies and multiple sclerosis: a systematic review and meta-analysis.
Acta Neurologica Scandinavica 2010 Apr 29. [Epub ahead of print]
Link to PubMed abstract
Note: MEDLINE only searched.

Schmitt J, Buske-Kirschbaum A, Roessner V.
Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review.
Allergy 2010 Aug 17. [Epub ahead of print]
Link to PubMed abstract
Note: PubMed and PsycINFO searched.

Schram ME, Tedja AM, Spijker R, Bos JD, Williams HC, Spuls PI.
Is there a rural/urban gradient in the prevalence of eczema? A systematic review.
British Journal of Dermatology 2010;162(5):964-73. Epub 2010 Mar 16.
Link to PubMed abstract
Note: MEDLINE and EMBASE searched.

Prevention

Alexander DD, Cabana MD.
Partially hydrolyzed 100% whey protein infant formula and reduced risk of atopic dermatitis: a meta-analysis.
Journal of Pediatric Gastroenterology and Nutrition 2010;50(4):422-30.
Link to PubMed abstract
Note: MEDLINE only searched.

Alexander DD, Schmitt DF, Tran NL, Barraj LM, Cushing CA.
Partially hydrolyzed 100% whey protein infant formula and atopic dermatitis risk reduction: a systematic review of the literature.
Nutrition Reviews 2010;68(4):232-45.
Link to PubMed abstract
Note: MEDLINE only searched.

Chafen JJS, Newberry S, Riedl M, Bravata DM, Maglione M, Suttorp M, Sundaram V, Paige NM, Towfigh A, Hulley BJ, Shekelle PG.
Prevalence, natural history, diagnosis, and treatment of food allergy: a systematic review of the evidence. Rand Health Working Paper WR-757-1.
Santa Monica, CA: RAND Corporation, 2010.
Link to full text
Note: PubMed, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials and World Allergy Organization Journal searched.

Chafen JJS, Newberry SJ, Riedl MA, Bravata DM, Maglione M, Suttorp MJ, Sundaram V, Paige NM, Towfigh A, Hulley BJ, Shekelle PG.
Diagnosing and managing common food allergies: a systematic review.
JAMA 2010;303(18):1848-56.
Link to PubMed abstract
Link to DARE abstract
Note: PubMed, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and Cochrane Central Register of Controlled Trials searched.

Dangour AD, Lock K, Hayter A, Aikenhead A, Allen E, Uauy R.
Nutrition-related health effects of organic foods: a systematic review.
American Journal of Clinical Nutrition 2010;92(1):203-10. Epub 2010 May 12.
Link to PubMed abstract
Note: PubMed, ISI Web of Science, CAB Abstracts and EMBASE searched.

Kremmyda LS, Vlachava M, Noakes PS, Diaper ND, Miles EA, Calder PC.
Atopy risk in infants and children in relation to early exposure to fish, oily fish, or long-chain omega-3 fatty acids: a systematic review.
Clinical Reviews in Allergy & Immunology 2009 Dec 9. [Epub ahead of print]
Link to PubMed abstract
Note: MEDLINE and EMBASE searched. This reference has been included in the Results for scrutiny as it is called a systematic review in the title, but it lacks a methodology section and there are no details of search terms and selection criteria.

Szajewska H, Horvath A.
Meta-analysis of the evidence for a partially hydrolyzed 100% whey formula for the prevention of allergic diseases.
Current Medical Research and Opinion 2010;26(2):423-37.
Link to PubMed abstract
Link to DARE abstract
Note: Cochrane Library, MEDLINE, EMBASE and CINAHL searched.

Treatment - emollients
Tarr A, Iheanacho I.
Should we use bath emollients for atopic eczema?
BMJ 2009;339:b4273.
Link to PubMed (no abstract)
Note: PubMed, Cochrane Library, Clinical Evidence and Current Clinical Trials database searched.

Treatment - topical calcineurin inhibitors
Chen SL, Yan J, Wang FS.
Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a meta-analysis of randomized clinical trials.
Journal of Dermatological Treatment 2010;21(3):144-56.
Link to PubMed abstract
Note: Ovid, Cochrane Library, MEDLINE and National Knowledge Infrastructure (CNKI) searched.

Fleischer AB Jr, Boguniewicz M.
An approach to pruritus in atopic dermatitis: a critical systematic review of the tacrolimus ointment literature.
Journal of Drugs in Dermatology 2010;9(5):488-98.
Link to PubMed abstract
Note: PubMed only searched.

Treatment – antibacterial treatments
Bath-Hextall FJ, Birnie AJ, Ravenscroft JC, Williams HC.
Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review.

British Journal of Dermatology 2010;163(1):12-26. Epub 2010 Mar 5.
Link to PubMed abstract
Note: Updated, journal version of 2008 Cochrane Review, with 5 extra RCTs. Cochrane Skin Group Specialised Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and metaRegister of Current Controlled Trials searched.

Treatment – occlusive therapy
Braham SJ, Pugashetti R, Koo J, Maibach HI.
Occlusive therapy in atopic dermatitis: overview.
Journal of Dermatological Treatment 2010;21(2):62-72.
Link to PubMed abstract
Note: PubMed and EMBASE searched.

Treatment – specialised clothing
Vlachou C, Thomas KS, Williams HC.
A case report and critical appraisal of the literature on the use of DermaSilk in children with atopic dermatitis.
Clinical and Experimental Dermatology 2009;34(8):e901-3.
Link to PubMed abstract
Note: MEDLINE, EMBASE and Cochrane Controlled Trials Register searched.

Canine atopic dermatitis – INCLUDED FOR INTEREST
Olivry T, DeBoer DJ, Favrot C, Jackson HA, Mueller RS, Nuttall T, Prélaud P; International Task Force on Canine Atopic Dermatitis.
Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis.
Veterinary Dermatology 2010;21(3):233-48. Epub 2010 Apr 23.
Link to PubMed abstract

Olivry T, Foster AP, Mueller RS, McEwan NA, Chesney C, Williams HC.
Interventions for atopic dermatitis in dogs: a systematic review of randomized controlled trials.
Veterinary Dermatology 2010;21(1):4-22.
Link to PubMed abstract

EXCLUDED REFERENCES
Cao Y, Liao M, Huang X, Mo Z, Gao F.
Meta-analysis of genome-wide linkage studies of atopic dermatitis.
Dermatitis 2009;20(4):193-9.
Link to PubMed abstract
Note: Covers similar ground to two systematic reviews included in 2009 Annual Evidence Update that had wider searches.

Carbone A, Siu A, Patel R.
Pediatric atopic dermatitis: a review of the medical management.
Annals of Pharmacotherapy 2010 Jul 13. [Epub ahead of print]
Link to PubMed abstract
Note: Insufficient details of methodology, narrow search and unusual focus of results.

Klemens C, Berman D, Mozurkewich E.
A meta-analysis of perinatal omega-3 fatty acid supplementation on inflammatory markers, allergy, atopy, and asthma in infancy and childhood.
American Journal of Obstetrics and Gynecology 2009;201(6 SUPPL. 1):S178.
(No PubMed abstract)
Note: Conference abstract only—lacks full methodology.

Desai M, Axelrod D.
Acetaminophen use and risk of rhinitis and eczema in schoolchildren: a meta-analysis.
Journal of Allergy and Clinical Immunology 2010;125(2 SUPPL. 1):AB172.
(No PubMed abstract)

Note: Conference abstract only—lacks full methodology.

Ip S, Chung M, Raman G, Trikalinos TA, Lau J.
A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries.
Breastfeeding Medicine 2009;4 Suppl 1:S17-30.
Link to PubMed abstract
Note: Summary of a systematic review included in 2008 Annual Evidence Update.

Ker J, Hartert TV.
The atopic march: what's the evidence?
Annals of Allergy, Asthma & Immunology 2009;103(4):282-9.
Link to PubMed abstract
Note: Insufficient details of methodology.

Langan SM.
Flares in childhood eczema.
Skin Therapy Letter 2009;14(8):4-5.
Link to PubMed abstract
Note: Summary of a systematic review included in 2007 Annual Evidence Update.

Lipozencic J, Wolf R.
The diagnostic value of atopy patch testing and prick testing in atopic dermatitis: facts and controversies.
Clinics in Dermatology 2010;28(1):38-44.
Link to PubMed abstract
Note: No methodology given.

Rehal B, Armstrong A.
Health outcome measures in atopic dermatitis: a systematic review of trends in disease severity and quality-of-life instruments 1999-2009.
Journal of Investigative Dermatology 2010;130:S59.
(No PubMed abstract)
Note: Conference abstract only—lacks full methodology.

Schnopp C, Ring J, Mempel M.
The role of antibacterial therapy in atopic eczema.
Expert Opinion on Pharmacotherapy 2010;11(6):929-36.
Link to PubMed abstract
Note: No methodology given.

Simpson EL.
Atopic dermatitis: a review of topical treatment options.
Current Medical Research and Opinion 2010;26(3):633-40.
Link to PubMed abstract
Note: Insufficient details of methodology; author states it is not a systematic review.

Spergel JM.
From atopic dermatitis to asthma: the atopic march.
Annals of Allergy, Asthma & Immunology 2010;105(2):99-106. Epub 2010 Jan 22.
Link to PubMed abstract
Note: No methodology given.

van der Aa LB, Heymans HS, van Aalderen WM, Sprikkelman AB.
Probiotics and prebiotics in atopic dermatitis: review of the theoretical background and clinical evidence.
Pediatric Allergy and Immunology 2010;21(2 Pt 2):e355-67. Epub 2009 Jul 2.
Link to PubMed abstract
Link to DARE abstract
Note: Insufficient details of methodology.

Walling HW, Swick BL.
Update on the management of chronic eczema: new approaches and emerging treatment options.
Clinical, Cosmetic and Investigational Dermatology 2010;3:99-117.
Link to full text
Note: Insufficient details of methodology.

2010 Annual Evidence Update on Atopic Eczema - Commentary

"What's new?" — a tour of the 2010 Annual Evidence Update on Atopic Eczema with the busy clinician in mind

Professor Hywel Williams, Clinical Lead for NHS Evidence - skin disorders and Co-ordinating Editor of the Cochrane Skin Group, and Dr Kave Shams, Dermatology Registrar, Southern General Hospital, Glasgow

GUIDELINE

Diagnosis and management of food allergy

In last year's Annual Evidence Update, we included German guidelines on the investigation and management of food allergy which failed to connect recommendations with the evidence sufficiently [1]. This year, guidelines on the diagnosis and management of food allergies in general have been published in draft form by the National Institute of Allergy and Infectious Diseases (NIAID) in the USA (Link to full text). Due to the increasing public health concerns and reports of increased prevalence of food allergies, these guidelines set out to provide advice to healthcare workers on how to approach food allergies in a clinical setting. The methodology is fairly well described, and the quality of evidence behind the various recommendations stated.

One of the great challenges of the new US guidelines is the lack of a consistent definition of food allergy in the supporting literature. The section dealing with the definition of food allergy is especially well explained and comprehensively discussed, including the need to recognise non-IgE mediated food allergy. The authors place great emphasis on the importance of an adequate history in the diagnosis of food allergy. They then advocate skin-prick testing or testing for specific circulating IgE, whilst stressing that positivity of either without a supporting history is not diagnostic of a food allergy. The guidelines also highlight the over-reporting of allergies when examining studies that use parental self-report. We anticipate the publication of UK guidelines by the National Institute of Health and Clinical Excellence (NICE) on this very topic in early 2011 (Link). In the interim, the US guidelines are a helpful guide to this often controversial area of medicine.

EPIDEMIOLOGY AND CAUSES

Reduced risk of glioma?

In our 2008 Annual Evidence Update, we reported the findings of a well-reported systematic review and meta-analysis by Linos *et al*. [2] which showed a reduced risk of glioma in those with atopic diseases, in particular atopic eczema. No such association was found between atopy and meningioma. The possibility that the risk of glioma is reduced in atopic conditions has now been explored further in a well-reported meta-analysis by Chen *et al*. published in 2010 and included in this year's Annual Evidence Update (Link to PubMed abstract). The methodology is well explained, with quality rating of included studies and various sensitivity and subgroup analyses being used to test the robustness of the findings. The authors include twelve studies (ten case-control and two cohort studies) involving 61,090 participants, of whom 6,408 had glioma. Five new case control studies that were not included in the earlier review are identified. The review again demonstrates a lower risk of glioma in individuals with allergic conditions in general (Odds Ratio [OR] 0.60; 95% Confidence Interval [CI] 0.52-0.61) and also for those with eczema (OR 0.69; 95% CI 0.62-0.78), an estimate which is very similar to that found by Linos *et al*. but with slighter tighter confidence intervals. Of note is that Chen *et al*. performed a subgroup analysis excluding those studies in whom proxy reporting of allergic disease was used, a procedure which did not alter the observed association.

However, as with most reviews this year, there is a high degree of variation in terms of the definition of the different atopic diseases in the included studies. The reduced risk is, however, evident across the various study types irrespective of methodology. Possible explanations for how gliomas and atopic diseases are related remain largely speculative, although a protective effect of high levels of IgE has been suggested. Disease associations like this can usually only be determined by observational studies, which are more prone to bias than experimental studies. However, the reduced

risk of gliomas in those with atopic diseases, including eczema, seems consistent between two well-reported, independent systematic reviews.

Reduced risk of leukaemia?

Leukaemia is the commonest cancer in under 20-year-olds, and its incidence is rising. Atopic disease, which is also increasing in prevalence, has been suggested as a possible risk factor, and a new systematic review by Linabery *et al*. aims to summarise existing data about such a possible association (Link to full text). The review is generally well written, but limits eligible studies to those studying subjects under 19 years of age, without providing an explanation for this cut-off. The authors include ten case-control studies of 6,592 cases with leukaemia and 24,171 controls in a meta-analysis which shows an inverse relation between acute lymphoblastic leukaemia (ALL) and atopy/allergy (OR 0.69; 95% CI 0.54-0.89), i.e. opposite to the hypotheses that atopy is a risk factor for leukaemia. The five studies that include information on eczema specifically also show a reduced risk of ALL (OR 0.74; 95% CI 0.58-0.96). There is no association in this analysis between specific atopic conditions and acute myeloid leukaemia (AML) or leukaemias overall.

We are encouraged by the authors' very open and comprehensive discussion of potential sources of bias in this paper, in which they conclude that caution should be given when interpreting the results, given the modest number of studies, substantial heterogeneity between them, residual confounding and potential for exposure misclassification. The absolute risk of leukaemia is very small even in the presence of atopic disease, so even if a possible reduced risk of leukaemia with eczema is confirmed in future larger prospective studies, it is not going to alter clinical practice. The possible inverse association may provide a valuable insight into the pathogenesis of both conditions. The possible reduced risk of leukaemia in those with atopy was first highlighted in a limited systematic review by Wang & Diepgen [3] and along with the reduction of glioma risk discussed above, there may be something in atopy reducing the risk of some forms of cancer, for reasons which are still unclear.

Association with multiple sclerosis?

Interest has also been shown in a potential link between allergies and multiple sclerosis (MS). In terms of immune response, allergic diseases are classified as predominantly following a Th2 pattern, whereas MS follows a Th1 pattern. Some have suggested that the Th1 and Th2-driven diseases may co-exist, and may even interact to affect disease progression. A well-reported systematic review by Monteiro and colleagues (Link to PubMed abstract) looks at the possible association between allergic disease and MS, and includes ten studies from an initial yield of 1,010. The ten studies are all either case-control or cross-sectional studies, and include 2,764 cases with MS and 262,620 controls. Meta-analysis reveals no association between MS and allergic diseases (OR 0.91; 95% CI 0.68-1.23), nor is there an association with asthma, allergic rhinitis or eczema (OR 0.93; 95% CI 0.71-1.23). Although the authors quality rate the studies, little attention is given to how eczema was defined and whether such people were truly atopic, which could give rise to mis-classification and lack of associations in observational studies.

Overall, the review shows that there is no good evidence at present to support an increased or inverse association with any of the allergic diseases and MS. We read with interest in the discussion that MS, much like allergic disease, is more prevalent in geographical areas with improved hygiene/sanitation, which happens to be the subject of another review detailed below.

Increased risk of attention-deficit/hyperactivity disorder?

The fact that the prevalence of attention-deficit/hyperactivity disorder (ADHD) and eczema have both risen over recent decades led Schmitt and colleagues (Link to PubMed abstract) to explore a possible causal link, given that it is at least plausible that sleep disturbance from eczema could contribute to behavioral problems in an affected child. Their systematic review is well-reported, and includes twenty observational studies covering 170,175 individuals. Only one of the studies is prospective, the rest being mainly cross-sectional in design. Six of the studies show a consistent positive association between eczema and reported ADHD, and one study suggests that the association is strongest for those with sleeping problems. Twelve studies show a positive association between asthma and ADHD, which is partly confounded by eczema. Hay fever and raised IgE levels do not show any association with ADHD. The authors conclude that eczema, but not other atopic diseases, appears to be independently related to ADHD.

Whilst we concur that there does appear to be an association between eczema/sleep disturbance and reported ADHD in the observational studies reported to date, we are sceptical that such a relationship is a causal one. We have both experienced dealing with children with severe eczema who illustrate a range of behavioural experiences, such as not being able to sit still due to constant scratching—a

manifestation of eczema that could be labeled as ADHD, which improves drastically as the eczema is treated. What is important therefore, in order to separate cause from effect, is to look at those studies that separate eczema from subsequent ADHD in time, i.e. cohort studies. Only one cohort study with a 49% follow up rate was included in the study, which shows only a weak association (OR 1.19; 95% CI 0.88–1.61) between infant onset eczema and ADHD after adjustment for confounders and other co-morbidities, but not for “eczema ever” or ADHD reported at the age of 10 years.
Schmitt *et al*. are at pains to point out the limitations of the current data. In addition to the inability to determine the time order of events or infer causality, they also point out that methods for diagnosing the atopic diseases were generally poor and highly variable. Often parental reports were utilized, which will introduce reporting bias given that itchy children will often be perceived as overactive. Failure to adjust for other confounding factors was also a problem. We view this study as providing good grounds for exploring the hypothesis that eczema is associated with sleep disturbance and may be a specific risk factor for ADHD, e.g. through large prospective studies with clear definitions of the two conditions. In the meantime, we would counsel caution in labeling children with eczema who fidget and don’t pay attention as having ADHD—treat their eczema aggressively and see how their behavior changes.

Urban/rural prevalence gradients
The rising incidence of eczema, positive social class gradient and the observation that eczema is commoner in migrants when compared to their country of origin all point to a strong role of environmental factors for disease expression in eczema. Several authors have commented that eczema is a disease of urbanisation, which may be related to the commonly discussed hygiene hypothesis, i.e. improved hygiene and reduced infections lead to a skewing of the immune system towards allergic disease. Schram et al. (Link to PubMed abstract) seek to explore whether eczema is commoner in urban versus rural areas in a well-reported systematic review. Out of the 268 initial articles, 26 were eventually included, all of which were published between 1982 and 2009 and most of which were prospective cohort studies. Overall, 19 studies show a higher risk of eczema in urban areas, with 11 of these being statistically significant. In contrast, six studies show a reduced risk of eczema in urban areas. This trend towards lower risk of eczema in urban areas is stronger when analyzing studies conducted in 'developing' countries only.
These findings are limited due to considerable heterogeneity between the identified studies, and therefore a pooled risk was not calculated. Discrepancies between the studies were frequently encountered in terms of the definition of eczema, the definition of 'urban' and 'rural', the patient population, and the sample size. Most of the studies also fail to take into account the fact that people may move into, as well as out of, an area. Furthermore, as the authors point out, the urban and rural populations in many places may be genetically distinct. Although the review supports the idea that urbanization is a risk factor for eczema, larger scale, good quality studies are needed before we will encourage our patients with eczema to move to the countryside.

PREVENTION

Hydrolyzed whey formulas
Cow’s milk protein is the most commonly encountered food allergen in infants who are not breastfed. Hydrolyzing the cow’s milk protein in formula feeds reduces their molecular weight and their allergenicity, which is why hydrolyzed formulas are used for infants with established cow’s milk protein allergy. It is less clear whether hydrolyzed milk formulas used from birth prevent the development of eczema when compared with cow’s milk formulas, which is the focus of a 2010 review by Alexander & Cabana (Link to PubMed abstract). We note that the lead author is funded by Nestlé (which is one of the world’s leading manufacturers of hydrolyzed whey formulas), and that an almost identical review has been (overtly) published by the same team in a different journal, as discussed below.
The search strategies, exclusion and inclusion criteria are quite well described in the review by Alexander & Cabana, although only MEDLINE was searched. They include a total of 18 studies, the majority of which are small, and which are either unblinded or single-blind. They performed "an extensive and critical review" of the studies and chose six which they found to be "methodologically superior and more informative" for a separate meta-analysis. The study selection process is poorly explained and may be a significant source of inclusion bias. Furthermore, the six studies include only four different infant populations between them, and they also include populations at higher risk of eczema (positive family history), which may have skewed the results.
All of the studies included in the meta-analysis show a reduced risk of atopic eczema in children fed partially hydrolyzed formulas as compared to standard cow’s milk formula (Relative Risk [RR] 0.55;

95% CI 0.4-0.76). These data are from the time point closest to when the infant was fed partially hydrolyzed formula, but the analysis suggests the risk reduction is sustained to the age of 3, albeit narrowly (RR 0.76; 95% CI 0.57-1).
Even though a previous Cochrane Review [4] found some evidence of eczema prevention for extensively hydrolyzed formula milk when compared against partially hydrolyzed formula milks, that review did not find any evidence to support prevention of eczema (or indeed any other allergic diseases) through partially hydrolyzed milk formulas when compared with cow's milk formulas, as suggested in the Alexander & Cabana review. We have significant reservations about this review due to the possible bias introduced by study selection and the role of the sponsors. We agree with the authors that breast-feeding is the most effective and appropriate method to nourish infants, and this will remain the principal advice we give all of our patients.
As noted above, our literature search picked up a duplicate publication by Alexander in 2010, again sponsored by Nestlé (Link to PubMed abstract). The search strategy is identical (except for searching "through" March rather than April 2009), and so are the identified studies (again 18 in number). This time, however, methodology and quality assessment of studies are better described. Despite using the same studies, the authors chose to undertake a narrative approach rather than attempt a meta-analysis. It is also interesting that despite the content being largely the same, the lead author has no less than four new co-authors in the duplicate publication, with Cabana being dropped.
Nestlé then complete their hat-trick of reviews by funding a third, almost identical meta-analysis conducted in the same year, covering the same research question as above, by Szajewska & Horvath (Link to PubMed abstract). Study search strategies are very well described, and this time four databases were searched. This review only includes studies which evaluate partially hydrolyzed formulas produced by Nestlé, on the basis that the production methods may yield disparate products. The authors also chose to include what they call "quasi-RCTs", i.e. studies that do not use a truly random method for allocation of study participants—a potential source of bias. They identified 15 trials (one of which is an unpublished study provided by Nestlé), studying 12 populations. The study methods are well described, although excluded studies are only available on request, which is rather unusual. Rather than pooling data from all studies, the authors chose to stratify studies into different age groups. Thus the risk reductions obtained stem from between two and five studies for each age group. In our view, this is a limitation of this review since the meta-analyses are generally performed utilising only two or three studies.
The largest number of studies included in a meta-analysis by Szajewska & Horvath is five (for the 3-6 month age group) and shows a relative risk of 0.48 (95% CI 0.23-1.0), in terms of all allergic diseases in general when partially hydrolyzed milk formula is used rather than cow's milk formula. Incidence of eczema is also consistently lower in those fed hydrolyzed rather than standard formulas, although the effect diminished with increasing infant age and was lost by 24 to 36 months. The quality of many of the included studies is poor. Almost all included studies have inadequate sequence generation, unclear allocation concealment and unclear or absent blinding. Although the review is reasonably well reported, we are not able to draw any clear conclusions from the data since the risk of bias from included studies is so high.
Perhaps partially hydrolyzed formulas can prevent eczema when compared with standard formulas in those who are unable to breastfeed, but better studies are needed along with an updated independent Cochrane systematic review.

Food allergy
Food "allergy' is a popular topic amongst patients and parents of children with eczema. We have commented on reviews of diet and dietary supplements in eczema in previous years. This year, an extensive systematic review by Chafen *et al*. (Link to full text) aims to evaluate evidence relating to the prevalence, diagnosis, management and prevention of all aspects of food allergy in order to inform the US National Institute of Allergy and Infectious Diseases Guidelines discussed at the start of this commentary. A shorter version has also been published in *JAMA* (Link to PubMed abstract).
The methodological quality of this systematic review by Chafen *et al*. is high overall. Search strategies and criteria for study selection, quality assessment and data analysis are all presented in detail. Unfortunately, only English language papers are included which may have introduced some bias. The authors identified 182 studies which met their inclusion criteria, but then limited these to 72 studies (studies with data on allergies to cow's milk, hen's egg, peanut, tree nut, fish and shellfish, as these together reportedly account for more than 50% of food allergies). These studies include one meta-analysis on incidence and prevalence, 18 studies on diagnosis and 53 studies on management and prevention.

The review draws attention to a significant lack of consensus as to how a food allergy should be defined, and how food allergies should be diagnosed. Only 82% of included studies incorporate any definition of food allergy and a mere 49% require distinction of food allergy from food intolerance, pharmacologic and toxin-mediated reactions. Direct comparison between studies is thus difficult, and the bulk of the review is narrative and qualitative rather than quantitative in nature. The authors present a long list of various studies evaluating various diets, compounds and other interventions and their effect on the manifestations of atopy and allergies. We agree with the review authors that it is hard to draw firm conclusion for clinical practice from the presented data, which largely is due to the great heterogeneity of the included studies and diverse topics covered. In addition to acting as a repository for all the food allergy studies for those interested in the evidence base to date, perhaps the most important aspect of this review is the call for clearer definitions of food allergy, and for standardisation in testing methods and quantification. Until such basic definitions are agreed, the evidence base for food allergy in conditions such as eczema will remain muddy.

Organic foods

There is increasing demand for organically produced foods, and often a perception that they have added health effects beyond conventional foods. A well-reported systematic review by Dangour *et al*. (Link to PubMed abstract), sponsored by the UK Food Standards Agency, aims to assess the possible health effects of consuming organic produce. Unlike many other reviews this year, these authors also include foreign language papers, and helpfully performed a pre-publication repeat search to ensure the review was as up-to-date as possible. They examined the full-text version of 45 studies out of 91,989 identified after their initial searches, and include a total of 12 studies (six trials, one cohort study, one cross sectional study and four reports of animal studies and cell lines) in the final review, three of which were identified in hand searches of reference lists.

Overall, this review finds a very heterogenous group of studies, which fail to show any evidence of differences in nutrition-related health outcomes resulting from exposure to organic as opposed to conventionally produced foodstuffs. However, one included study, a birth cohort study of 2,764 infants followed to the age of 2 years in the Netherlands, reported a 36% reduction in eczema risk for those children who had consumed strictly organic dairy products [5]. Although interesting, this finding needs to be interpreted with caution, as it is likely that consumption of organic foods is highly correlated with other health-seeking behaviours. Diagnosis of eczema was based on parental report only, raising the possibility of reporting bias. Other exposures and outcomes such as asthma and sensitisation were explored, all of which failed to find any association. So the Dangour *et al*. review cannot be considered to have found any robust evidence for a health benefit of organic foods, but one of the included studies has generated a hypothesis that organic dairy produce could reduce eczema risk that could perhaps be tested in a future clinical trial.

Fish oils

There are two principal types of polyunsaturated fatty acids, omega-3 and omega-6. The former has been suggested to decrease the risk of atopic diseases in children, whilst the latter may increase such risk. In a 2009 systematic review, Kremmyda *et al*. (Link to PubMed abstract) aim to evaluate the possible association between exposure to fish/fish-oil and infant/childhood atopic disease. Whilst the review is strong in terms of scope and explanation of possible mechanisms of polyunsaturated fatty acids and inflammation in atopic disease, the methods of the systematic review itself are poorly specified, with merely a declaration of searched databases and search dates. The selected studies are highly variable in design, and include cohort studies (prospective and retrospective), cross-sectional studies and case-control studies. All five observational studies included in the review that assess the effect of maternal fish intake during pregnancy on atopic disease in offspring show a beneficial effect in terms of atopic disease, but intake during lactation does not appear to confer any benefit. Of the fourteen observational studies looking at the association between fish intake in infancy and childhood and atopic disease, nine show a beneficial effect from fish intake, three show no benefit and two show a negative association. The rate of atopic diseases in the studies varies considerably depending on country and disease definition.

The review then gives a detailed narrative description of five randomized controlled trials (RCTs) that evaluate the possible benefits of fish oil supplementation in pregnancy or lactation in relation to subsequent atopic disease. Although no meta-analysis was done, the studies collectively show that fish oil supplementation during pregnancy and lactation results in offspring obtaining more omega-3 polyunsaturated fatty acids, along with immunologic changes in cord blood and reduced sensitization to common food allergens. The long-term effects on atopic diseases are less clear, with some studies

showing reduced prevalence and severity of eczema in infancy, with a possible persistence until adolescence, along with reduction in hay fever and asthma.
A further five RCTs evaluate the possible benefits of fish oil supplementation during infancy and childhood on atopic disease outcomes. Again, it is clear that fish oil supplementation resulted in improved omega-3 polyunsaturated fatty acid levels in the infants and children along with some immunologic changes in peripheral blood. But it is less clear if these changes are associated with any clinical benefit and whether they persist as other factors take over in later life.
Overall, the results from this review by Kremmyda *et al*. have to be interpreted with caution given the lack of description of methods, which may have resulted in missed studies and over-reliance on poor quality studies alongside better ones. Given the wide range of related questions posed in this review, it is not surprising that included studies are heterogeneous in terms of quality, design, study population, methods of ascertaining food histories and definitions of outcome measures. Results from the observational studies of increased fish intake during pregnancy suggest some benefit in preventing atopic disease, which are partly corroborated by RCTs of fish oil supplementation during pregnancy. Given that fish oils do little harm and may have other long term benefits, there is certainly scope for discussing increased fish intake or fish oil supplementation with pregnant mothers with atopic disease if they "want to do something", although the current evidence is not strong enough to make such an intervention a treatment recommendation. The evidence from observational and intervention studies of increased fish intake or fish oil supplementation for infants is less convincing at present, and much larger studies with clearer clinical outcomes that are measured throughout the lives of offspring are needed to make clearer policy recommendations.

ECZEMA TREATMENTS

Bath emollients

Emollients are widely used in the management of dry skin in eczema in the belief that they restore defective skin barrier function. Emollients may be applied directly to the skin, and may also be part of "complete emollient therapy" whereby creams, ointments, bath emollients and soap substitutes are all used concurrently. The use of bath emollients currently forms part of the NICE guidelines on the management of atopic eczema in children (Link). Tarr & Iheanacho (Link to PubMed) searched for RCTs and systematic reviews but failed to identify any published trials specifically evaluatinh the efficacy of bath emollients in eczema. Nor did they find any studies comparing bath emollients to directly applied emollients, or studies evaluating the additional benefit of "complete emollient therapy" over other regimens. The methodology of this review, done on behalf of the *Drug and Therapeutics Bulletin* and published in the British Medical Journal “Uncertainties Page” series (which does not allow much space) is inevitably lacking in detail, e.g. no information of search terms or search dates is provided. Nonetheless, the paper highlights an area of clinical uncertainty where high quality, adequately powered studies are very much needed—especially given the large sums of NHS spending (£15.5 million in England alone in 2008) that bath emollients account for.
Few would argue against that direct application of emollients is a sensible part of eczema treatment, but the additional value of bath emollients is questionable. Bath emollients may never achieve an adequate emollient concentration and much ends up down the drain rather than on the skin. Worse still, their use may divert attention away from direct application of emollients in the belief that the bath emollient has done the job.

Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCIs), including tacrolimus and pimecrolimus, alter T-cell function and are now established topical treatment options for people with atopic eczema. Although readers might feel we have "done TCIs to death" in previous Annual Evidence Updates, there is always reason to visit new systematic reviews which uncover new studies, especially those which deal with comparative efficacy against topical corticosteroids, or those that deal with safety concerns. An independent systematic review of TCI efficacy and safety in children with eczema by Chen and colleagues published in 2010 (Link to PubMed abstract) identifies 20 RCTs that include a total of 6,288 children with moderate to severe eczema. The review methodology is well explained in Cochrane style and uses Cochrane software to conduct and present the results. However, the search strategies used are not given. The primary outcome assessed was physician’s global assessment (PGE) or the investigator’s global assessment (IGA). We will not describe the placebo-controlled studies as they have been covered before and because they are of little interest to clinicians who wish to know how the treatments compare with existing treatment options.

With regards to topical tacrolimus, there is no significant difference between 0.03% and 0.01% tacrolimus in three studies where these are compared (OR 0.9; 95% CI 0.55-1.46). This result should not be interpreted as meaning that the two concentrations are equivalent, as this does not concord with clinical experience and the confidence interval for the limited number of studies is very wide. Comparison between 0.03% tacrolimus and 1% hydrocortisone acetate at 3 weeks in two similar studies suggests superiority of the tacrolimus preparation (OR 3.49; 95% CI 2.47-4.94), which is not that surprising.
With regards to topical 1% pimecrolimus versus corticosteroids (potent on trunk, mild on face), two trials that include 961 children/infants suggest a possible superiority of pimecrolimus at 6 months (OR 1.59; 95% CI 1.20-2.11), but not at 12 months (OR 1.31; 95% CI 0.97-1.77).
The authors also compare studies of 1% pimecrolimus versus 0.03% or 0.1% tacrolimus. Two out of the three trials of 0.03% tacrolimus versus pimecrolimus 1% found evidence of superiority of the tacrolimus preparation, and another trial shows that 0.1% tacrolimus is more effective than 1% pimecrolimus.
A useful summary of common adverse events reported in included trials is given in the review, although these vary a great deal from 15-84% with 0.03% tacrolimus, 13-39% with 0.1% tacrolimus and 5-86% with 1% pimecrolimus cream. We do not feel it is possible to recommend one over another based on these data in terms of likelihood of adverse events, and in terms of the really critical issues of long-term safety. In particular, concerns about possible carcinogenicity are not covered by any new data in the review.
The second review of topical calcineurin inhibitors, by Fleischer & Boguniewicz (Link to PubMed abstract), has a narrower focus, evaluating the effects of tacrolimus on pruritus in atopic eczema. The lead author is on an advisory board of Astellas, the manufacturer of tacrolimus, who also funded the review and provided advice on data accuracy. Search terms are stated, but only PubMed was searched, leaving doubts about missed studies. There does not appear to be any form of quality assessment of the 23 studies included in the review. Five studies compare tacrolimus to vehicle, and not surprisingly show a reduction of pruritus. Four studies evaluate the long-term, anti-pruritic effects of tacrolimus, but none of the studies include any statistical analyses on the presented data. Four studies compare topical calcineurin inhibitors with topical steroids, but no statistical analyses are presented. The review is therefore rather limited in its ability to say very much about the comparative efficacy of tacrolimus for itching.
The authors then go on to criticise the FDA's 'black box warning' concerning topical calcineurin inhibitors and the possible link to skin cancer and lymphoma, based on previous epidemiological studies and the RCT data in their review. Although we agree that there is no evidence for a causal link between the use of topical calcineurin inhibitors and cancer, the short-term nature of the studies included in this review (longest period of follow up for instance is 30 months) means that it has little power to detect rare long term adverse effects.

Antibacterial treatments

Most readers will be aware of how eczema can develop overt secondary infection and of the pro-inflammatory effects of *Staphylococcus aureus* in non-infected eczema through direct chemical and superantigen mechanisms. Yet a Cochrane Review published in 2008 [6] found no clear evidence of benefit for topical antibiotics, systemic antibiotics and other anti-staphylococcal therapies for clinically infected and non-infected eczema. Failure to find any positive evidence of benefit in a bunch of small, poorly reported studies does not mean that interventions do not work, and is perhaps more a reflection of the poor evidence base that exists. The Cochrane Review has now been updated with a further five RCTs in a 2010 paper by Bath-Hextall *et al*. published in the *British Journal of Dermatology* (Link to PubMed abstract). The update failed to find any new evidence that contradicted the conclusions of the original Cochrane Review and concludes that the continued use of antistaphylococcal interventions should be questioned, especially in non-infected eczema, until better and longer-term studies show clear evidence of clinical benefit.
One new study included in the update deserves special mention because of the public interest it has created. Thirty one children with moderate/severe eczema and clinical infection were pre-treated with oral cefalexin for 2 weeks and then randomized to bath water with added bleach plus nasal mupirocin ointment vs. normal bath water and nasal vehicle ointment. The study reports greater improvements in clinical scores (EASI) in the bleach/mupirocin group at 1 and 3 months when compared with the placebo group. It is unclear, however, if the claimed benefits for bleach plus mupirocin are due to the marked differences in baseline disease severity, differences in the use of co-treatments such as topical corticosteroids during the study, or a failure to undertake an intention-to-treat analysis. A more detailed critique of the study is available elsewhere [7], and although we have too many concerns

about the study to suggest that bleach baths can be used in clinical practice, another trial with a stronger design would be worthwhile.

Use of bandages

Occlusion therapy using wet or dry bandages/wraps is quite well established in the treatment of eczema. At the very least, they may reduce scratching or infection of affected skin, which often exacerbates skin inflammation. Wet wraps entail the addition of moisturisers/emollients, sometimes with the addition of therapeutic agents such as corticosteroids. Occlusive therapy for eczema is the topic of a 2010 review by Braham and colleagues (Link to PubMed abstract). Search terms are provided, and two databases (PubMed and EMBASE) were searched. Non-English language studies were excluded. The authors identified 18 studies, 14 of which address wet-wrap techniques, but only five of which are RCTs. Four studies compare wet-wraps with conventional application of treatment, and two of these studies find a greater benefit with wet-wraps.

Four studies look at dry occlusion; one of these is a RCT, which shows a greater improvement in the control group. The authors conclude that there does not appear to be a benefit of dry occlusion in the treatment of atopic eczema, which is perhaps too bold given that only one RCT has been included, with the three remaining studies including a non-controlled study, a study of microbial colonisation and another examining lichen simplex chronicus. Instead we propose we need further RCTs are needed to better evaluate the place of dry occlusion in eczema.

Of note is that several of the studies show that wet wraps, where steroids are used, affect systemic cortisol levels. The changes were transient, and the clinical significance is unclear, but it highlights the need for caution when using potent steroids over larger areas under occlusion. Increased counts of skin bacteria or clinical infection are reported in all of the dry occlusion studies and in four of the 14 studies that used wet-wraps, but any summative remarks are difficult in the presence of such varied study populations, interventions and outcomes.

Much of the lengthy discussion is used by the authors to offer various pieces of practical advice. We do however feel that many of the suggestions lack a good evidence base. This is perhaps more of a criticism of the lack of data in the literature, rather than this review itself.

Overall, the studies in this review are all fairly small and the topical agents used, treatment duration, type of occlusive and indications for treatment vary too greatly to provide useful guidance. Furthermore, blinding is always challenging with physical treatments. It is hard to make comparisons between different regimens, and it is difficult to recommend one type of treatment over another based on this review.

Specialised clothing

Various forms of occlusive clothing are often used in eczema management, especially when combined with topical treatment. More recently, silk clothing has been marketed as a means of improving eczema. One such type of clothing, named DermaSilk, is made from woven silk which is impregnated with an antibacterial agent (AEGIS AEM 5772/5) and is sold as an effective treatment of dermatitis for all age groups. Vlachou and colleagues (Link to PubMed abstract) highlight a case report of a 5-year-old boy with severe eczema in whom the mother felt that DermaSilk helped. Yet when the authors conducted a systematic review of literature, evidence for the use of such clothing was lacking. Only two small randomized and two non-randomized studies were identified which included 99 patients in total.

In the largest non-randomized single blind study, DermaSilk is compared to cotton clothing in children with eczema. Eczema severity reduced from 43 to 30 using the ScorAD index ($P < 0.01$) at day 7, in the Dermasilk group and a change from 47 to 46 in the control group, but the authors fail to provide the difference in change of score between the two groups, which is the whole point of the exercise. A smaller study presented in the article compares DermaSilk alone with DermaSilk coated with AEGIS AEM 5772/5, and fails to show a significant difference between the two fabrics in terms of reducing microbiological cultures for *Staphylococcus aureus*. The studies are too few and are of too poor quality to make any comments on the possible value of DermaSilk.

The systematic review of evidence was not well described, and it should have specified inclusion/exclusion criteria and quality rated the included studies formally. Overall, we feel inadequacies of the included trials make it difficult to justify the use of DermaSilk in the clinic, and our practice will not be altered based on current evidence. We do however welcome larger, better quality studies to clarify any existing assertions of a clinical benefit.

For interest – eczema in dogs

The removal of the family dog from the home in order to improve a sufferer's eczema in the absence of clear and reproducible worsening of disease is probably not a good idea as tolerance soon develops, and because a previous systematic review has failed to show any association at a population level between dog exposure in early life and eczema research, with some studies showing a possible protective effect [8]. It is therefore intriguing to read how dogs can be affected by atopic eczema too, and how many parallels there are between human and canine eczema.
A systematic review of RCTs examining treatment of atopic eczema in dogs, by Olivry *et al*. (Link to PubMed abstract) appeared in the last year. The quality of the systematic review is very high, and in many respects more rigorous than many of the reviews this year of human studies, as it was based on Cochrane methods. As in human dermatology, good quality evidence is scarce in the veterinary setting. The authors found a total of 49 RCTs that include 2,126 dogs, and found some evidence of benefit for topical tacrolimus (3 RCTs), topical triamcinolone (1 RCT), oral glucocorticoids (5 RCTs), oral ciclosporin (6 RCTs), subcutaneous recombinant gamma-interferon (1 RCT) and subcutaneous allergen-specific immunotherapy (3 RCTs). One high-quality RCT shows that an oral essential fatty acid supplement could reduce prednisolone consumption by approximately half. Interestingly, dogs do not suffer from the same renal toxicity from ciclosporin as humans, so it is used more widely.
This review formed the basis of the high quality 2010 guidelines on the treatment of canine atopic eczema by the International Task Force on Canine Atopic Dermatitis (Link to PubMed abstract). We were fascinated by how similar the treatments are for our canine friends, in terms of topical/systemic treatments but also in terms of risk reduction methods—including the use of omega-3 and 6 fatty acids and environmental measures, such as reduction of house dust mites. Some advocated treatment measures (such as effective flea control) thankfully remain unique to dogs—at least for now.

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2010 Annual Evidence Update on Atopic Eczema - Summary points and implications for practice

Summary points, and will the new evidence change our clinical practice?

Professor Hywel Williams, Clinical Lead for NHS Evidence - skin disorders and Co-ordinating Editor of the Cochrane Skin Group, and Dr Kave Shams, Dermatology Registrar, Southern General Hospital, Glasgow

GUIDELINE

Food allergy: The US National Institute of Allergy and Infectious Diseases has produced extensive, high quality draft guidelines on the management of food allergy. The advice on food allergy is still limited by lack of clear definitions and a poor evidence base. The guidelines emphasise the importance of taking a good clinical history of food allergy before proceeding to skin-prick or RAST tests, and of the need to be aware of non-IgE mediated food allergy.
Action: We will continue to ask all our eczema patients (especially younger children) about symptoms suggestive of immediate and delayed food allergy to foods such as egg, milk, fish, citrus and nuts. We will not blindly order "allergy tests" on patients, as positive tests have a low predictive value.

CAUSES OF ECZEMA

Risk of cancer: Some evidence points to a possible reduced risk of glioma and acute leukaemia in people who have had eczema in childhood, the reasons for which are unclear.
Action: Given that most of our messages are doom and gloom, this observation of a possible health benefit of having eczema is perhaps worth mentioning to some parents who feel despondent about eczema.
Risk of multiple sclerosis: There is no clear evidence to support an increased or decreased risk of multiple sclerosis in eczema and other atopic diseases.
Action: None, especially as we were not aware of the possibility of an association in the first place.
Attention deficit hyperactivity disorder (ADHD): Although some cross sectional studies suggest a possible association between reported eczema and ADHD, we are not convinced it is a true association at this stage and large prospective studies are needed to disentangle cause and effect.
Action: We shall be cautious accepting that children who are restless because of undertreated eczema have ADHD. We shall treat the underlying eczema aggressively and see how the behaviour improves.
Living in the city: Most studies in developed countries looking at whether eczema is commoner in urban as opposed to rural locations suggest an increased risk of disease expression in urban areas.
Action: The evidence is not strong enough to recommend our patients to move to “a place in the country”.

PREVENTION

Hydrolyzed milk formulas: Although a recent systematic review sponsored by the manufacturers of hydrolyzed milk formulas has suggested that partially hydrolyzed formulas from birth may prevent eczema to some degree, compared with standard cow’s milk formula, we would like to see an independent Cochrane Review update on this topic.
Action: We will continue to advise parents that breast-feeding is the most effective and appropriate method to nourish infants, and that mothers who cannot breastfeed can use conventional formula milk. If their child does develop cow’s milk allergy, then a hydrolyzed milk formula is appropriate.
Organic foods: There is no robust evidence that consumption of organic foods reduces the risk of eczema. One cohort study from the Netherlands has suggested that consumption of strictly organic dairy products may reduce eczema risk in infants, a finding that needs to be tested in new studies.
Action: We will not be recommending organic foods during infancy if parents do not choose to buy them.
Fish oils for pregnant mothers: Observational and intervention studies evaluating increased fish intake or fish supplementation during pregnancy suggest a possible reduction in subsequent eczema prevalence and severity.
Action: Although the evidence is not strong enough yet to inform guidelines, the possibility of increasing fish intake or of fish oil supplementation during pregnancy may be something to discuss with families with allergic disease, given the safety and other health benefits of fish oils.
Fish oils for infants: The evidence to support increased fish intake or fish oil supplementation in infant diets to prevent or reduce the severity of subsequent eczema is not so strong.
Action: Hold off the extra fish fingers for now.

ECZEMA TREATMENT

Food allergy: A very large, well conducted systematic review on food allergy has highlighted the confusion around the topic. The review calls for clearer definitions of food allergy, and for standardisation in testing methods and quantification.
Action: We shall continue to consider the possibility of food allergy in those with eczema, especially in infants, but we remain unclear about the best method of diagnosing such food allergy.
Bath emollients: Although few would question the value of emollients in the dry skin associated with eczema, the evidence showing any additional value of bath emollients is questionable because they may never achieve an adequate emollient concentration, much ends up down the drain rather than on the skin, and their use may divert attention away from direct application of emollients in the belief that the bath emollient has done the job.
Action: Whilst we would not actively stop a child from using bath emollients if they like them, we recommend more attention is paid to direct application of emollients after bathing rather than what is put in the bath.
Topical tacrolimus and pimecrolimus: Some comparative efficacy evidence shows that both 0.03% and 0.1% tacrolimus ointment is more effective than 1% pimecrolimus, with a similar range of short-term adverse events.
Action: It is still unclear whether 0.03% tacrolimus is any better than pimecrolimus. We will continue to use either for children with eczema within their licensed indications, and swap from one to the other if the child fails to notice any benefit or reports troublesome burning which lasts more than a week.
Silk clothing: Two small studies have evaluated specialised silk clothing for children with eczema. No clear positive findings were shown and both studies had significant flaws.
Action: We do not recommend that parents are advised to purchase silk clothing for children with eczema and we really need some better studies addressing this issue. If children with eczema try silk clothing and like it, then it is up to families whether they buy it.
Bandages: The evidence base for occlusive therapy with dry or wet-wrap bandages with or without emollients or topical corticosteroids is increasing, but the studies still differ too much in terms of who is studied, and how the occlusive therapy is used, to make any strong recommendations, especially with regards to dry bandages. Wet-wraps as an adjunctive treatment for refractory eczema appear to be useful, but concerns about skin infection and the clinical significance of enhanced absorption of topical corticosteroids require bigger and better studies.
Action: We will continue to use wet-wrap bandages over topical corticosteroids for short periods of up to one week for acute flares of uninfected and heavily excoriated limb eczema that does not respond to conventional topical corticosteroids and emollients.
Antistaphylococcal interventions including bleach baths: There is still no clear evidence that anti-staphylococcal treatments are useful in eczema.
Action: We will continue to use short courses of oral antibiotics for children with overtly infected eczema. We will not use or recommend topical corticosteroid/antibiotic combinations, antibacterial or silver textiles, bleach baths or long term antibiotics in people with clinically infected or non-infected eczema until better evidence becomes available.

2010 Annual Evidence Update on Atopic Eczema - DUETs uncertainties update

UK DUETs uncertainties update

Dr Douglas Grindlay, Information Specialist, NHS Evidence - skin disorders

Introduction

NHS Evidence – skin disorders is involved in collecting and collating uncertainties about the effects of treatments for skin disorders, to be added to the UK Database of Uncertainties about the Effects of Treatments (DUETs).
DUETs has been established to publish treatment uncertainties that cannot currently be answered reliably by referring to up-to-date systematic reviews of existing research evidence. These uncertainties can then be used to inform future research.
DUETs draws on three main sources to identify uncertainties about the effects of treatments:

- Patients', carers' and clinicians' questions about the effects of treatments;
- Research recommendations in reports of systematic reviews and clinical guidelines;
- Ongoing research, both systematic reviews in preparation and new 'primary' studies.

In 2007 a set of uncertainties was added to the DUETs database on atopic eczema, derived from published systematic reviews and from questions submitted by health professionals and patients. These uncertainties have been reviewed each year and have now been reviewed again in the light of the new systematic reviews found in this year's Annual Evidence Update on Atopic Eczema. Please click here to view the updated UK DUETs module on atopic eczema.
Please note that DUETs is a work in process. If you have identified any uncertainties on atopic eczema or other skin disorders—clinical questions that are not answered by existing systematic reviews—then do please let us know. You can contact us via our DUETs feedback form.

Newly added uncertainty

Partially hydrolyzed whey protein formula for preventing atopic eczema in infants

Reviewed and updated uncertainties

Will breast feeding reduce the chances of a baby developing atopic eczema? (Patient question)
Exclusive breast-feeding for preventing atopic eczema in infants at high risk for the development of atopy
Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing atopic eczema in the child
Exclusion diets for preventing atopic eczema in infants at high risk for the development of atopy
Omega 3 and omega 6 fatty acids for prevention of atopic eczema
Role of diet in triggering atopic eczema (Patient question)
Exclusion diets for treating established atopic eczema
Bath emollients for atopic eczema
Are topical tacrolimus and pimecrolimus for atopic eczema safe or can they cause lymphoma or skin cancer? (Patient question)
Long-term safety of pimecrolimus and tacrolimus for atopic eczema
Topical pimecrolimus compared to mild corticosteroids for atopic eczema
Interventions to reduce Staphylococcus aureus in the management of atopic eczema
Efficacy and safety of wet-wraps for long-term treatment of atopic eczema
Safety of wet-wrap dressings with diluted topical corticosteroids, in particular 'new generation' topical corticosteroids versus established corticosteroids
Specialised clothing for reducing or preventing atopic eczema

Removed uncertainties
None

Systematic reviews on atopic eczema - INDEX PAGE

This is the index page for a **mapping by topic of systematic reviews on atopic eczema** published from 2000 onwards (the date of the HTA monograph *Systematic review of treatments for atopic eczema*).
The systematic reviews are those found in the searches for the Skin Disorders Specialist Library's Annual Evidence Updates on Atopic eczema for 2007, 2008, 2009 and 2010.

Systematic reviews on atopic eczema - Epidemiology

This is a mapping by topic of **systematic reviews on the epidemiology of atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.

Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of the diagnosis (Chapter 3), assessment of severity, psychological and psychosocial wellbeing and quality of life (Chapter 4), epidemiology (Chapter 5) and identification and management of trigger factors (Chapter 6) in atopic eczema in this age group.

Aetiology	2009	Meta-analysis of genome-wide linkage studies of atopic dermatitis
	2009	Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systemati review and meta-analysis
	2009	Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disea
	2007	Toward a major risk factor for atopic eczema: meta-analysis of filaggrin polymorphism data
	2005	Atopic dermatitis and the 'hygiene hypothesis': too clean to be true?
	2004	How atopic is atopic dermatitis?
Risk factors	2010	Is there a rural/urban gradient in the prevalence of eczema? A systematic review
	2008	Caesarean delivery and risk of atopy and allergic disease: meta-analyses
	2008	A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis
	2006	What causes worsening of eczema? A systematic review
	2004	No epidemiological evidence for infant vaccinations to cause allergic disease
Co-morbidities	2010	Allergy and risk of glioma: a meta-analysis
	2010	Association between allergies and multiple sclerosis: a systematic review and meta-analysis
	2010	Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review
	2010	The association between atopy and childhood/adolescent leukemia: a meta-analysis
	2008	Alexithymia and dermatology: the state of the art
	2007	Atopy and risk of brain tumors: a meta-analysis
	2007	Risk of developing asthma in young children with atopic eczema: A systematic review
Diagnosis	2008	Diagnostic criteria for atopic dermatitis: a systematic review
	2006	What is meant by a "flare" in atopic dermatitis? A systematic review and proposal
Severity & outcome measures	2007	What are the best outcome measurements for atopic eczema? A systematic review
	2003	Measuring atopic dermatitis severity in randomized controlled clinical trials: what exactly are we measuring?
	2000	Outcome measures of disease severity in atopic eczema
Disease impact	2008	The socioeconomic impact of atopic dermatitis in the United States: a systematic review
	2008	Sleep disruptions in parents of children and adolescents with chronic illnesses: prevalence, causes and consequences
	2008	A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids

Systematic reviews on atopic eczema - Prevention

This is a mapping by topic of **systematic reviews on the prevention of atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.

Maternal dietary exclusions	2010	Diagnosing and managing common food allergies: a systematic review
	2010	Prevalence, natural history, diagnosis, and treatment of food allergy: a systematic review of the evidence
	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2006	Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treati atopic disease in the child *(Cochrane Review)*
	2000	Systematic review of treatments for atopic eczema
Breastfeeding	2010	Diagnosing and managing common food allergies: a systematic review

	2010	Prevalence, natural history, diagnosis, and treatment of food allergy: a systematic review of the evidence
	2009	Exclusive breastfeeding and incident atopic dermatitis in childhood: a systematic review and meta-analysis of prospective cohort studies
	2009	The long-term effects of breastfeeding on asthma and atopic disease
	2009	A systematic review of the importance of milk TGF-beta on immunological outcomes in the infant and young child
	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2007	Breastfeeding and maternal and infant health outcomes in developed countries
	2004	The optimal duration of exclusive breastfeeding: a systematic review
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2002	Optimal duration of exclusive breastfeeding *(Cochrane Review)*
	2001	Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies
Formulas	2010	Partially hydrolyzed 100% whey protein infant formula and reduced risk of atopic dermatitis: a meta-analysis
	2010	Partially hydrolyzed 100% whey protein infant formula and atopic dermatitis risk reduction: a systematic review of the literature
	2010	Meta-analysis of the evidence for a partially hydrolyzed 100% whey formula for the prevention of allergic diseases
	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2007	The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review
	2006	Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants *(Cochrane Review)*
	2006	Soy formula for prevention of allergy and food intolerance in infants *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Weaning	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2006	Systematic review of the relationship between early introduction of solid foods to infants and the development of allergic disease
	2004	The optimal duration of exclusive breastfeeding: a systematic review
	2002	Optimal duration of exclusive breastfeeding *(Cochrane Review)*
Diet	2010	Diagnosing and managing common food allergies: a systematic review
	2010	Prevalence, natural history, diagnosis, and treatment of food allergy: a systematic review of the evidence
	2010	Nutrition-related health effects of organic foods: a systematic review
	2010	Atopy risk in infants and children in relation to early exposure to fish, oily fish, or long-chain omeg 3 fatty acids: a systematic review
	2009	Omega 3 and 6 oils for primary prevention of allergic disease: systematic review and meta-analysi
	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Probiotics	2008	Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis
	2007	Probiotics in infants for prevention of allergic disease and food hypersensitivity *(Cochrane Revie*
	2005	Probiotics for atopic diseases
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Prebiotics	2007	Prebiotics in infants for prevention of allergic disease and food hypersensitivity *(Cochrane Revie*
Pets	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2007	The role of furry pets in eczema: a systematic review
Avoidance of other aeroallergens	2008	Systematic review and evidence-based consensus guideline on prevention of allergy and atopic eczema of the German Network on Allergy Prevention (ABAP)
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report

Systematic reviews on atopic eczema - Topical treatments

This is a mapping by topic of **systematic reviews on topical treatments for atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.

Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of emollients (Section 7.1), topical corticosteroids (Section 7.2), topical calcineurin inhibitors (Section 7.3), dry bandages and medicated dressings, including wet wrap therapy (Section 7.4), antihistamines and other pruritics (Section 7.5) and treatment for associated infections (Section 7.6) in atopic eczema in this age group.

Emollients	2009	Should we use bath emollients for atopic eczema?
	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Occlusive therapies	2010	Occlusive therapy in atopic dermatitis: overview
	2006	Efficacy and safety of 'wet-wrap' dressings as an intervention treatment in children with severe and/or refractory atopic dermatitis: a critical review of the literature
Topical corticosteroids	2007	Established corticosteroid creams should be applied only once daily in patients with atopic eczema
	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2005	Topical corticosteroids for atopic eczema: clinical and cost effectiveness of once-daily vs. more frequent use
	2004	Clinical and cost-effectiveness of once-daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation
	2003	Eumovate (clobetasone butyrate 0.05%) cream: A review of clinical efficacy and safety
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Coal tar	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Topical doxepin	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Pimecrolimus	2010	Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a met analysis of randomized clinical trials
	2009	Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis
	2007	Topical pimecrolimus for eczema *(Cochrane Review)*
	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2006	Review of pimecrolimus cream 1% for the treatment of mild to moderate atopic dermatitis
	2005	Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatiti meta-analysis of randomised controlled trials
	2005	The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation
	2004	Topical calcineurin inhibitors in the treatment of atopic dermatitis: a meta-analysis of current evidence
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Tacrolimus	2010	Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a met analysis of randomized clinical trials

	2010	An approach to pruritus in atopic dermatitis: a critical systematic review of the tacrolimus ointmen literature
	2009	Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis
	2008	Meta-analysis of tacrolimus ointment for atopic dermatitis in pediatric patients
	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2007	Efficacy and tolerability of topical tacrolimus in the treatment of atopic dermatitis: a systematic review of randomized controlled trials (Li *et al.*, *Journal of Clinical Dermatology* 2007; 36: 757-60)
	2005	Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatiti meta-analysis of randomised controlled trials
	2005	The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation
	2004	Topical calcineurin inhibitors in the treatment of atopic dermatitis: a meta-analysis of current evidence
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Cipamfylline cream	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Topical ciclisporin	2000	Systematic review of treatments for atopic eczema
Lithium succinate ointment	2000	Systematic review of treatments for atopic eczema
Topical disodium cromoglycate	2000	Systematic review of treatments for atopic eczema
Nedocromil sodium cream	2000	Systematic review of treatments for atopic eczema
Topical tiacrilast	2000	Systematic review of treatments for atopic eczema
Platelet-activating factor antagonist	2000	Systematic review of treatments for atopic eczema
Salbutamol ointment	2000	Systematic review of treatments for atopic eczema
Topical antibiotics & antiseptics	2010	Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review
	2008	Interventions to reduce Staphylococcus aureus in the management of atopic eczema *(Cochrane Review)*
	2007	A systematic review of the safety of topical therapies for atopic dermatitis
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Topical antibiotic-corticosteroid combinations	2010	Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review
	2008	Interventions to reduce Staphylococcus aureus in the management of atopic eczema *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Antibacterial bath additives	2010	Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review
	2008	Interventions to reduce Staphylococcus aureus in the management of atopic eczema *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Silver textiles	2010	Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review
	2008	Interventions to reduce Staphylococcus aureus in the management of atopic eczema *(Cochrane Review)*

Systematic reviews on atopic eczema - Phototherapy

This is a mapping by topic of **systematic reviews on phototherapy for atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of phototherapy in atopic eczema in this age group (Section 7.8).

Broadband UVA	2007	Phototherapy in the management of atopic dermatitis: a systematic review
	2000	Systematic review of treatments for atopic eczema
UVA1	2007	Phototherapy in the management of atopic dermatitis: a systematic review
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
Combined UVAB	2007	Phototherapy in the management of atopic dermatitis: a systematic review
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Narrowband UVB	2007	Phototherapy in the management of atopic dermatitis: a systematic review
	2005	Narrowband UVB phototherapy in skin conditions beyond psoriasis
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non corticosteroids
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
PUVA	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report

Systematic reviews on atopic eczema - Dietary treatments for established eczema

This is a mapping by topic of **systematic reviews on dietary treatments for established atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of management of trigger factors, including dietary exclusions and modifications, in atopic eczema in this age group (Section 6.3).

Probiotics	2009	Probiotics for the treatment of eczema: a systematic review
	2008	Efficacy of probiotics in the treatment of pediatric atopic dermatitis: a meta-analysis of randomized controlled trials
	2008	Probiotics for treating eczema (Cochrane Review)
	2008	Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis
Dietary supplements	2004	Oral essential fatty acid supplementation in atopic dermatitis-a meta-analysis of placebo-controlled trials
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Dietary restrictions	2010	Diagnosing and managing common food allergies: a systematic review
	2010	Prevalence, natural history, diagnosis, and treatment of food allergy: a systematic review of the evidence
	2009	Dietary exclusions for improving established atopic eczema in adults and children: systematic revie
	2008	Dietary exclusions for established atopic eczema (Cochrane Review)
	2006	What causes worsening of eczema? A systematic review
	2004	Dietary treatment of childhood atopic eczema/dermatitis syndrome (AEDS)
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema

Systematic reviews on atopic eczema - Psychological and educational interventions

This is a mapping by topic of **systematic reviews on psychological and educational interventions for atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of behavioural therapies (Section 7.10), education (Section 8.1) and adherence to therapy (Section 8.2) in atopic eczema in this age group.

Psychological interventions	2007	Psychological and educational interventions for atopic eczema in children *(Cochrane Review)*
	2007	The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analy
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Educational interventions	2007	Psychological and educational interventions for atopic eczema in children *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Nurse-led clinics	2006	Nurse-led clinics reduce severity of childhood atopic eczema: a review of the literature

Systematic reviews on atopic eczema - Psychological and educational interventions

This is a mapping by topic of **systematic reviews on psychological and educational interventions for atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of behavioural therapies (Section 7.10), education (Section 8.1) and adherence to therapy (Section 8.2) in atopic eczema in this age group.

Psychological interventions	2007	Psychological and educational interventions for atopic eczema in children *(Cochrane Review)*
	2007	The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analy
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Educational interventions	2007	Psychological and educational interventions for atopic eczema in children *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Nurse-led clinics	2006	Nurse-led clinics reduce severity of childhood atopic eczema: a review of the literature

Systematic reviews on atopic eczema - Complementary and alternative therapies

This is a mapping by topic of **systematic reviews on complementary and alternative therapies for atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of complementary therapies in atopic eczema in this age group (Section 7.9).

Chinese herbal medicine	2007	Systemic treatment of severe atopic eczema: a systematic review
	2005	Chinese herbal medicine for atopic eczema *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Evening primrose oil	2006	A meta-analysis of randomized, placebo-controlled clinical trials of Efamol evening primrose oil in atopic eczema. Where do we go from here in light of more recent discoveries?
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Borage oil	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Homeopathy	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Massage	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Hypnotherapy & biofeedback	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2002	Complementary/alternative medicine in dermatology: evidence-assessed efficacy of two diseases and two treatments
	2000	Systematic review of treatments for atopic eczema
Bioresonance	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema

Systematic reviews on atopic eczema - Other interventions for established eczema

This is a mapping by topic of **systematic reviews on other (mainly physical) interventions for established atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.
Please see also the full version of the 2007 NICE Clinical Guideline "Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years". This includes a systematic review of management of trigger factors in atopic eczema in this age group (Section 6.3).

House dust mite reduction	2006	What causes worsening of eczema? A systematic review
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Pet removal	2007	The role of furry pets in eczema: a systematic review
Avoidance of other aeroallergens	2006	What causes worsening of eczema? A systematic review
Avoidance of detergent enzymes	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema
Water softeners	2000	Systematic review of treatments for atopic eczema
Specialised clothing	2010	Interventions to reduce Staphylococcus aureus in the management of atopic eczema: an updated Cochrane review
	2009	A case report and critical appraisal of the literature on the use of DermaSilk in children with atopic dermatitis
	2008	Interventions to reduce Staphylococcus aureus in the management of atopic eczema *(Cochrane Review)*
	2003	AAD Guidelines of Care for Atopic Dermatitis: Technical Report
	2000	Systematic review of treatments for atopic eczema

[Link to National Eczema Week (National Eczema Society)]

2010 Annual Evidence Update on Atopic Eczema - Methodology

A literature search was carried out to identify new guidelines and systematic reviews relating to atopic eczema (atopic dermatitis) that have been published or indexed since the 2009 Annual Evidence Update on Atopic Eczema. The results are the **2010 Annual Evidence Update on Atopic Eczema** from NHS Evidence - skin disorders.
This webpage describes the search strategies used and the criteria for inclusion in the Annual Evidence Update.

Search period

The search for the 2010 Annual Evidence Update on Atopic Eczema was for citations published or indexed in 2009 or 2010 and not included in the 2009 Annual Evidence Update.
January 2009 was set as the limit for earliest publication date in most of the searches, to allow for any delays in indexing of citations in the bibliographic databases used (which might mean the citations were not found in the searches for the previous Annual Evidence Update in August 2009).
In the case of PubMed, the search was refined by searching for records *indexed* in the PubMed database in 2009 and 2010 (using the "edat" command), which would find any citations published before 2009 but indexed late and hence not found in last year's search.
All the searches were carried out for the last time on 24th August, 2010.

Sources Searched

The following sources were searched:
Ovid MEDLINE (using SIGN MEDLINE systematic review filter)
Ovid EMBASE (using SIGN EMBASE systematic review filter)
PubMed (using PubMed Clinical Queries systematic review filter)
Cochrane Library
NHS Evidence - skin disorders

The search of PubMed was carried out as an insurance to ensure that no systematic reviews were missed using MEDLINE and EMBASE, especially as PubMed tends to be more up to date than and so is better for finding new citations.
The search of the Cochrane Library was also carried out as an insurance, to find relevant citations in the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment Database. The intention was to confirm that nothing of relevance was missed in the searches of MEDLINE, EMBASE and PubMed.
The search of NHS Evidence - skin disorders was to find new guidelines and also gave a confirmatory search for new Cochrane Reviews and DARE abstracts.

Systematic review filters

The SIGN systematic review filters developed for Ovid implementations of MEDLINE and EMBASE were used as they provide a reasonable balance between specificity and sensitivity. Details of the SIGN systematic review filters can be found on the following webpage:
http://www.sign.ac.uk/methodology/filters.html

Details of the PubMed Clinical Queries systematic review filter and its validation can be found via the following links:
http://www.nlm.nih.gov/bsd/pubmed_subsets/sysreviews_strategy.html
http://www.nlm.nih.gov/bsd/pubmed_subsets/sysreviews_sources.html

Search Strategies

The search terms were chosen to find citatations that used either "atopic eczema", "atopic dermatitis" or "neurodermatitis" as the disease name.

SIGN MEDLINE systematic review filter:
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations & Ovid MEDLINE
1. Meta-Analysis/
2. meta analy$.tw.
3. metaanaly$.tw.
4. meta analysis.pt.
5. (systematic adj (review$1 or overview$1)).tw.
6. exp Review Literature/
7. or/1-6
8. cochrane.ab.
9. embase.ab.
10. (psychlit or psyclit).ab.
11. (psychinfo or psycinfo).ab.
12. (cinahl or cinhal).ab.
13. science citation index.ab.
14. bids.ab.
15. cancerlit.ab.
16. or/8-15
17. reference list$.ab.
18. bibliograph$.ab.
19. hand-search$.ab.
20. relevant journals.ab.
21. manual search$.ab.
22. or/17-21
23. selection criteria.ab.
24. data extraction.ab.
25. 23 or 24
26. review.pt.
27. 25 and 26
28. comment.pt.
29. letter.pt.
30. editorial.pt.
31. animal/
32. human/
33. 31 not (31 and 32)
34. or/28-30,33
35. 7 or 16 or 22 or 27
36. 35 not 34
37. atopic.mp. [mp=ti, ot, ab, nm, hw]
38. dermatitis.mp. [mp=ti, ot, ab, nm, hw]
39. 37 and 38
40. eczema.mp. [mp=ti, ot, ab, nm, hw]
41. neurodermatitis.mp. [mp=ti, ot, ab, nm, hw]
42. 39 or 40 or 41
43. 36 and 42
44. limit 43 to yr="2009 - 2010"

SIGN EMBASE systematic review filter:
Ovid EMBASE
1. exp Meta Analysis/
2. ((meta adj analy$) or metaanalys$).tw.
3. (systematic adj (review$1 or overview$1)).tw.
4. or/1-3
5. cancerlit.ab.
6. cochrane.ab.
7. embase.ab.

8. (psychlit or psyclit).ab.
9. (psychinfo or psycinfo).ab.
10. (cinahl or cinhal).ab.
11. science citation index.ab.
12. bids.ab.
13. or/5-12
14. reference lists.ab.
15. bibliograph$.ab.
16. hand-search$.ab.
17. manual search$.ab.
18. relevant journals.ab.
19. or/14-18
20. data extraction.ab.
21. selection criteria.ab.
22. 20 or 21
23. review.pt.
24. 22 and 23
25. letter.pt.
26. editorial.pt.
27. animal/
28. human/
29. 27 not (27 and 28)
30. or/25-26,29
31. 4 or 13 or 19 or 24
32. 31 not 30
33. atopic.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
34. dermatitis.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
35. 33 and 34
36. eczema.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
37. neurodermatitis.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
38. 35 or 36 or 37
39. 38 and 32
40. limit 39 to yr="2009 - 2010"

PubMed using Clinical Queries systematic review filter:
((eczema) OR (atopic AND dermatitis) OR (neurodermatitis)) AND 2009 : 2010[edat] AND systematic[sb]

Cochrane Library and NHS Evidence - skin disorders:
eczema OR dermatitis OR neurodermatitis

Identification of systematic reviews

All citations found in the searches were hand searched by reading the titles and abstracts to identify systematic reviews and potential systematic reviews relevant to atopic eczema. A particularly careful analysis of the methods was made to identify citations with a systematic review methodology. For all potential systematic reviews where there was still some doubt, the full texts were then read to ensure that they were indeed systematic reviews.
To determine systematic reviews, the definition of a systematic review from the Glossary of Cochrane Collaboration Terms on the Cochrane Collaboration website was used:
“A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.”

The final decision on whether a citation was a systematic review and relevant to atopic eczema was made by Professor Hywel Williams, Clinical Lead for NHS Evidence - Skin Disorders and Co-ordinating Editor of the Cochrane Skin Group.