Fortnightly Review

Management of atopic eczema

P M McHenry, H C Williams, E A Bingham on behalf of a Joint Workshop of the British Association of Dermatologists and the Research Unit of the Royal College of Physicians of London

Atopic eczema is a common disease affecting 5-15% of schoolchildren and 2-10% of adults.[1-2] Patients with atopic eczema account for 10-20% of all referrals to dermatologists and about 30% of dermatological consultations in general practice.[3] There is reasonable evidence to support a substantial increase in the prevalence of atopic eczema over the past 30 years,[4] although the reasons for this increase are unclear. The clinical expression of atopic dermatitis probably results from an interplay between genetic, immunological, and environmental factors.[5,6] The multifactorial aetiology of atopic eczema needs to be stressed as the perception that eczema is exclusively caused by food allergies or house dust mite often dominates the lives of patients and their families.

In a recent survey of members of the National Eczema Society over half of respondents said that their eczema interfered with their life and two thirds said that their expectations of their initial consultation with their general practitioner or hospital consultant had been only partly met.[7] Although this survey may not be representative of all patients with eczema, it suggests that the management of these patients could be improved.

This article suggests a framework for good practice in managing atopic eczema based on a consensus of opinion formed at a joint workshop of the British Association of Dermatologists and the research unit of the Royal College of Physicians of London. The importance of explanation and education of the patient is stressed, and with good compliance most people with eczema should respond well to first line treatment.

Summary points

- Time for explanation and education is essential
- Adequate amounts of emollients should be prescribed, and these should be used liberally and frequently
- When prescribing topical corticosteroids the age of the patient, the site to be treated, and the extent of the disease are important considerations
- Deterioration in previously stable eczema may be due to secondary bacterial or viral infection or to development of a contact dermatitis
- Attempts to eradicate the house dust mite are not currently recommended
- Dietary restriction is of little or no benefit in adults, and in children it is worth trying only in selected infants under professional supervision
- Evidence for the therapeutic value of evening primrose oil remains inconclusive
- PUVA or UVB may be helpful in selected patients

Department of Dermatology, Robertson Building, University of Glasgow, Glasgow G12 8QQ
P M McHenry, *clinical lecturer*

Department of Dermatology, University Hospital, Queen's Medical Centre, Nottingham
H C Williams, *senior lecturer*

Department of Dermatology, Royal Victoria Hospital, Belfast
E A Bingham, *consultant dermatologist*

Participants in the workshop are listed at the end of the article.

Correspondence to:
Dr McHenry.

BMJ 1995;310:843-7

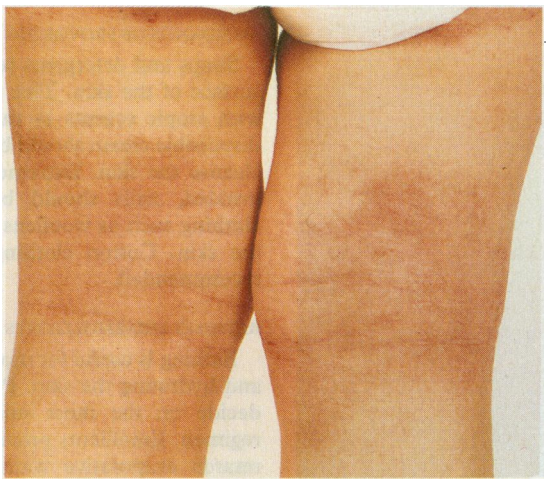

FIG 1—*Atopic eczema affecting the flexures*

Diagnosis

Atopic eczema is usually diagnosed on clinical grounds, based on the patient's history, family history, and the appearance of the eruption (box 1).[8] Figure 1 shows the typical features of atopic eczema. A skin biopsy is generally not helpful. If there is doubt about the diagnosis other conditions such as scabies (burrows in finger webs) or immunodeficiency states (recurrent systemic or ear infections, petechiae) should be considered. The presence of lymphadenopathy may cause alarm but is usually secondary to extensive skin disease in otherwise healthy patients.

History and examination

As even mild eczema can be associated with severe morbidity a comprehensive history and examination is important (box 2). In children a full immunisation history should be taken as vaccinations such as mumps, measles, and rubella and pertussis may have been omitted without good reason. It is also important to take a dietary history as parents of children with atopic eczema often experiment with dietary restriction.[9]

Box 1—Diagnostic criteria for atopic eczema

Must have

An itchy skin condition (or report of scratching or rubbing in a child)

Plus three or more of the following:

- History of itchiness in skin creases such as folds of the elbows, behind the knees, fronts of ankles, or around neck (or the cheeks in children under 4 years)
- History of asthma or hay fever (or history of atopic disease in a first degree relative in children under 4 years)
- General dry skin in the past year
- Visible flexural eczema (or eczema affecting the cheeks or forehead and outer limbs in children under 4 years)
- Onset in the first two years of life (not always diagnostic in children under 4 years)

The extent, location, and severity of eczema should be noted. Bacterial infection is suggested by the presence of crusting or weeping. Grouped, punched out erosions, or less often vesiculation, generally indicate infection with herpes simplex (fig 2). Children with chronic severe eczema should have their weight and height measured regularly.

Investigations

So far no data have shown any benefit from routine estimation of the total serum IgE concentration or identification of specific IgE antibodies to common allergens such as house dust mite, pollens, or food mix using skin prick testing or the radioallergosorbant test (RAST). These tests are unable to predict the outcome of avoiding appropriate antigens.[10] In addition, 15% of apparently healthy people have raised IgE titres while 20% of patients with clear clinical evidence of atopic eczema do not have raised IgE titres or a positive radioallergosorbant test.[11] In older patients in whom there is diagnostic difficulty, measuring total serum IgE may sometimes be useful.

Deterioration in patients with previously stable or mild atopic eczema may be due to secondary bacterial or viral infection or to development of contact dermatitis. Bacteriological swabs are not routinely indicated but may be necessary if patients do not respond to treatment in order to identify antibiotic resistant strains of *Staphylococcus aureus* and detect additional streptococcal infection. If herpes simplex infection is suspected swabs should be sent for virological screening and a smear sent for electron microscopy if this service is available.

Patch testing should be considered not only in patients whose condition has deteriorated but also in those who seem unresponsive to treatment as sensitisation to topical treatments, including steroids, have been reported in atopic eczema.[12]

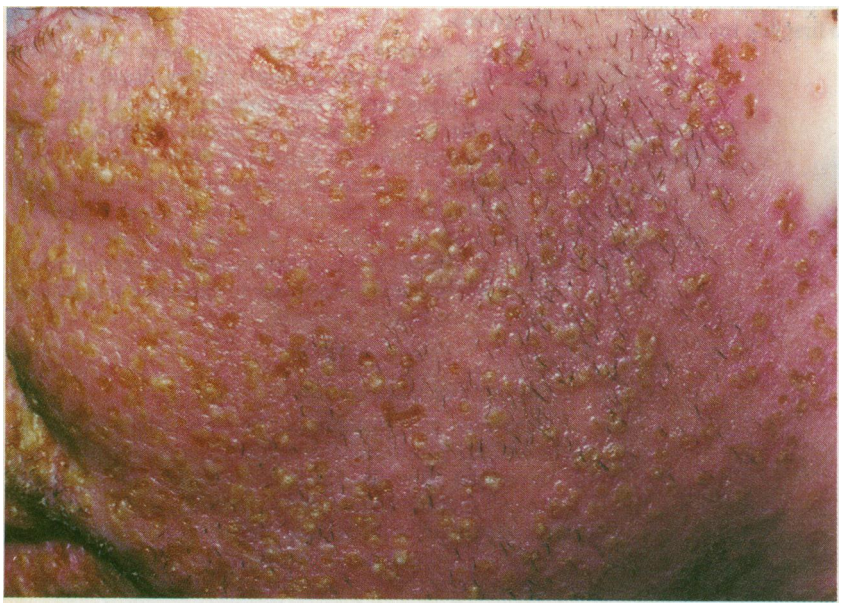

FIG 2—*Herpes simplex infection with multiple discrete vesicles and erosions*

First line treatment

EXPLANATION AND DISCUSSION

One of the most important aspects in the management of atopic eczema is to allow adequate time for explanation and discussion. Explanation and education regarding the application of topical preparations and the quantity to use is essential. A practice or clinic nurse should demonstrate how to apply the treatment, and patients should be given written information to reinforce the issues discussed. The information should be factual, non-controversial, and available in different languages. The National Eczema Society is an excellent source of information and support for patients and their families. Adolescents should be advised to choose careers in which exposure to irritants is unlikely.

Box 2—History and examination

The following factors should be inquired about:

- Aggravating factors such as exposure to irritants
- Sleep disturbance
- Coexisting atopic disease
- Family history of atopic disease
- Immunisations in children
- Previous treatments
- Use of steroids other than topical
- Dietary manipulation and adequacy of diet
- Effect on school work, career, or social life
- Most distressing thing for the patient or family
- Patient's or family's expectations from treatment

A full skin examination should be carried out:

- Record the extent and severity of eczema
- Look for evidence of clinical infection
- Nails should be kept short

A growth chart should be completed and updated in children with chronic severe eczema

AVOIDANCE OF PROVOKING FACTORS

Soaps and detergents remove natural lipid from the surface of the skin. This is undesirable in all patients with atopic eczema as they already have dry skin. A dispersible cream should be used as a soap substitute to cleanse the skin. Extremes of temperature should be avoided, nails should be kept short, and irritant clothing such as woollens should not be worn next to the skin. Cotton clothing is more comfortable and recommended.

BATHING AND EMOLLIENTS

Bathing is useful for most patients for both cleansing and hydrating the skin. Patients should be allowed to decide on the most suitable bath oil and bathing regimen. Emollients provide a surface lipid film which retards evaporative water loss from the epidermis. They are most effective when applied after bathing as

this is when the water content of the skin is greatest. Emollients should be reapplied to exposed areas such as the hands and face at regular intervals throughout the day as the lipid film also provides some protection against external irritants.

In general the more oily the preparation, the better the emollient effect. However, adults, and adolescents in particular, often find the most greasy preparations too messy for routine use, and some patients prefer to use different emollients for the face and body. The doctor's role is to help patients find an emollient that is effective and cosmetically acceptable for them in order to ensure regular use. Sufficient quantities of emollient should be prescribed to allow it to be applied liberally at least twice a day. If emollients are being applied to the whole body children will require at least 250 g per week and adults 500 g per week.

INFECTION

Antibiotics are important for treating overt secondary bacterial infection in patients with atopic eczema. Flucloxacillin is usually the most appropriate antibiotic for treating *S aureus*, which is the commonest pathogen. Phenoxymethylpenicillin should be given if β haemolytic streptococci are isolated. Erythromycin may be used when there is resistance to flucloxacillin or in patients with a penicillin allergy. Use of topical antibiotics should be restricted to limited areas. They are generally not ideal for treating bacterial infections in patients with atopic eczema as patients often have widespread secondary infection. Treatment of staphylococcal carrier sites prophylactically (such as the nose, axillae, and perineum) with topical antibiotics may be appropriate in patients with recurrent infected eczema.

Eczema herpeticum responds to oral acyclovir, and the drug should be given early in the course of the disease. In ill feverish patients, the acyclovir should be given intravenously.

TOPICAL CORTICOSTEROIDS

Topical corticosteroids are the mainstay of treatment for atopic eczema and can be used safely if certain precautions are taken. Use and abuse of topical steroids has caused considerable confusion and controversy and has resulted in the undertreatment of many patients with atopic eczema. Lack of adherence to treatment may often be traced back to patients' or parents' fears of steroids.[13] It is therefore important to explain the different potencies and the benefits and risks of topical corticosteroids. The basic principle is to use the least potent preparation required to keep the eczema under control, and when possible the corticosteroids should be stopped for short periods.

To minimise potential side effects when prescribing topical corticosteroids it is important to consider the age of the patient, the site to be treated, the extent of the disease, the type of preparation, and the method of application.

Age—For most children with mild to moderate eczema 1% hydrocortisone ointment is adequate. It does not cause systemic side effects related to percutaneous absorption unless used extravagantly on very small babies. Stronger preparations should not be prescribed for infants in primary care. In older children moderately potent steroids may be needed for short periods to gain control of the disease. Children who are not responding to 1% hydrocortisone and who are requiring more potent corticosteroids frequently should be referred for a specialist opinion. In adults the use of mild or moderately potent corticosteroids as classified in the *British National Formulary*[14] is unlikely to cause systemic or local cutaneous side effects. Preparations in the very potent and potent categories should be used with caution for limited periods only.

Site—Corticosteroid absorption is increased at certain sites such as the face and flexures, particularly in the presence of eczema. On the face, the principal risk is the development of permanent telangiectasia, and in general only 1% hydrocortisone should be used here in all age groups. Long term use of topical steroids in the eyelid area has been associated with the development of glaucoma.[15,16] Topical corticosteroids, including 1% hydrocortisone, should be used with caution at this site, particularly if there is a personal or family history of glaucoma.[17] Care should be taken, especially in adolescence, to avoid striae atrophicae when using more potent preparations in other high risk sites such as the breasts, abdomen, upper arms, and thighs. These can result in permanent disfigurement. On the palms and soles potent preparations may be used for a longer period as only a small area is being treated and percutaneous absorption is reduced.

Extent of eczema—The potential for systemic absorption increases with the extent and activity of the eczema. The main risk is suppression of the pituitary adrenal axis with possible interference of growth in children. It is important to monitor the number, strength, and size of tubes used between visits. This can indicate both excessive use and underuse of topical preparations.

Type of preparation—Generally ointment bases are preferable to cream bases. The occlusive effect of ointments results in better penetration of the corticosteroid and the incidence of irritant and hypersensitivity reactions is reduced. This is mainly because preservatives are required in creams but not in ointments.

Methods of application—Treatment should not be applied more than twice daily, and some of the newer preparations require only once daily application. The large variation in the amounts of topical steroids used by different patients can be minimised by specifying the quantity in terms of fingertip units, where one fingertip unit equals 0·5 g.[18] Used intermittently, wet wrap bandaging may be useful, especially in younger children but this requires consultant supervision because of the risk of pituitary adrenal suppression.[19] On the palms and soles, or to limited very thickened lichenified areas of eczema, the effectiveness of topical steroids can be enhanced by the use of impermeable or semipermeable films. The widespread use of polythene occlusion of topical steroids to treat eczema is not recommended.

ICHTHAMMOL AND TAR

The principal tars used for treatment of atopic eczema in Britain are ichthammol and coal tar. Ichthammol is a derivative of shale and is less irritant than coal tars and may be applied as an ointment (such as 1% ichthammol in zinc ointment) or in the form of paste bandages, which can be particularly useful for healing lichenified eczema. Coal tar solution is generally preferred to crude coal tar and in a strength of 1-10% may be added to a variety of cream, ointment, or paste bases or it can be added to the bath.

ANTIHISTAMINES

The therapeutic value of antihistamines seems to reside principally in their sedative properties, and they are useful as a short term adjuvant to topical treatment during relapses associated with severe pruritus. Non-sedating antihistamines have little or no value in atopic eczema.[20,21] The value of antihistamines may be progressively reduced as a result of tachyphylaxis,[22] and long term use is not recommended. Night time use of sedative antihistamines, taken an hour or so before bedtime, should be considered in any patient with atopic eczema who has difficulty getting to sleep, who wakes regularly during the night, or who scratches

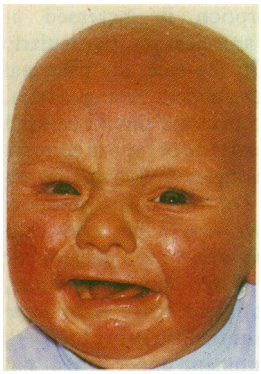

FIG 3—*Eczema can cause considerable suffering for the patients and their families. Reproduced with permission*

while asleep. Daytime use should be avoided. Large doses of antihistamines may be required in children.

PSYCHOLOGY

Atopic eczema may cause considerable suffering for patients (fig 3) and their families. Sharing knowledge and experiences with other patients or parents can help reduce feelings of helplessness and isolation. The National Eczema Society is invaluable for facilitating this support. Patients with eczema may also be helped by various cognitive behavioural techniques such as relaxation therapy or self hypnosis. Access to a clinical psychologist is recommended.

Community-hospital interface

Most people with eczema will respond well to first line management and do not require referral to a specialist. Failure to respond to treatment is an indication for referral to a hospital specialist (box 3).

Specialists should start with first line treatment measures again, reinforcing any aspects in which there was lack of compliance. A period as an inpatient may help overcome flares. If patients still fail to respond second line treatment should be started by the specialist. Box 4 gives recommendations for the hospital service.

Second line treatment

ALLERGEN AVOIDANCE

Although house dust mites may have an important role in atopic eczema,[23 24] evidence for the benefits of eradicating mites is not strong,[25] and currently there are no effective measures for complete eradication. However, research is advancing rapidly and may clarify the role of house dust mites in atopic eczema. With our present knowledge attempts to eradicate the house dust mite are not recommended.

The role of foods in initiating or perpetuating atopic eczema has been extensively investigated but without reaching a conclusion.[26 27] A trial of dietary manipulation may be indicated when a patient's history is strongly suggestive of a specific food allergy or when widespread active eczema is not responding to first line treatment. In general, dietary restriction is of little or no benefit in adults with atopic eczema, and in children it is probably infants who benefit most.[26 27] In infants a four to six week trial excluding egg and milk with the introduction of a hydrolysate infant formula may be justified, followed by a supervised rechallenge. Professional dietetic advice and supervision is recommended.

Immediate hypersensitivity or type I reactions to foods can sometimes occur in patients with eczema, ranging from contact urticaria to anaphylaxis. It is important that parents and doctors recognise such reactions and that the precipitating substance is avoided.

PHOTOTHERAPY AND PHOTOCHEMOTHERAPY

Psoralens plus ultraviolet A (PUVA) and to a lesser extent ultraviolet B have been found helpful in selected patients with atopic eczema.[28 29] Some concern exists, however, about the long term adverse effects such as premature skin aging and cutaneous malignancies, particularly with PUVA,[30] and it remains to be seen whether the benefits outweigh the risks. Narrow band ultraviolet B (312 nm) has recently been introduced, and this may prove safer than PUVA but equally effective.[31]

Box 3—Indications for referral to a specialist

- Diagnostic doubt
- Failure to respond to maintenance treatment with mildly potent steroids in children or moderately potent steroids in adults
- Second line treatment required or dietary manipulation being tried
- When specialist opinion would be valuable in counselling patients and family

Third line treatment

Systemic corticosteroids have a limited but definite role in tiding occasional patients with severe atopic eczema over crises. The decision to use systemic steroids should never be taken lightly, and they should not be considered for maintenance treatment until all other avenues have been explored. It is particularly important to try to avoid oral corticosteroids during rapid adolescent growth, roughly 11-16 years in girls and 13-18 years in boys, to reduce the risk of permanent growth retardation.

Box 4—Recommendations for hospital service

- Maximum waiting time of six weeks for first appointment
- Ask patients to bring all treatments with them at first visit
- System in place which allows the patient to have rapid access
- Trained nursing staff available with sufficient time to demonstrate treatments
- Access to patch testing facilities
- Access to a dietitian
- Access to a phototherapy unit
- Access to a clinical psychologist
- Opportunity for admission to hospital under the care of a dermatologist or paediatrician, or both

No conclusions can be drawn from the data on evening primrose oil. Two large trials have not shown any evidence of benefit,[32 33] but other studies have reported benefit, particularly for patients with moderate or severe eczema.[34 35] If evening primrose oil is tried adequate doses should be given—160-320 mg daily in children aged 1-12 years and 320-480 mg in adults for three months. If no benefit is noted after three months it is unlikely to be helpful.

Several other drugs such as azathioprine,[36] cyclosporin,[37 38] Chinese herbal medicines,[39 40] and immunomodulators such as interferons[41] and thymopentin[42] have been reported to be effective in atopic eczema, but these are still very experimental. Hepatotoxicity has been reported after administration of Chinese herbs.[43] Patients wishing to try Chinese herbs should be advised to have regular liver function tests. Scientific evidence to support the use of homoeopathic remedies in atopic eczema is still awaited.

Future developments

Since no treatment exists with proved benefit on the natural course of atopic eczema, prevention is desirable. Evidence for the role of breast feeding[44 45] and for maternal avoidance of allergens during pregnancy and lactation in protecting against atopy is conflicting.[46-48] A recent intervention study in which infants at high risk of developing atopic disease (born to atopic parents) were randomised to allergen avoidance regimens (by breast feeding mothers avoiding allergenic foods and by reducing house dust mite

populations) showed a reduction in expression of allergic disease (including eczema) at 12 months.[49] It will be interesting to see if these effects persist, and further confirmatory work will be required.

Conclusions

The main aim in the management of patients with atopic eczema is to provide an acceptable quality of life until remission occurs. Good communication is essential, and it is important that the message is consistent from all of the health care team. Specific outcome measures should be identified at the outset of treatment. These will vary because of the wide variation in patients' perception of their disease but could include improvement in itch, loss of sleep, time off work or school, understanding of the disease, social interaction, or clinical scoring of severity. The dermatology life quality index[50] or similar questionnaires may be useful for assessing outcome.

Although a cure is unrealistic, most patients with atopic eczema can reasonably expect to get good control of their eczema if managed properly. Around 75% of children with atopic eczema are clear of eczema by their early teens,[4] but relapses may occur and clearance figures for adults are not available.

Background papers discussed at the workshop are available on request from the Royal College of Physicians: definitions and epidemiology (H C Williams), pathogenesis (M H A Rustin), the value of investigations in management (R M MacKie), paediatric audit measures (T J David), treatment (D J Atherton), measurement of disease activity and outcome (A Finlay), special aspects of management in adults (R A C Graham-Brown), patient education (J Harper), what patients would like (CM Funnell).

Other participants in the workshop were R Allen (Nottingham), E A Bingham (Belfast), S M Breathnach (London), A Hopkins (chairperson, London), C T C Kennedy (Bristol), R Lansdowne (London), J Launer (London), R Lever (Glasgow), F Regelous (London), V Shaw (London), N B Simpson (chairperson, Newcastle), K Spowart (London), J Warner (Southampton).

The workshop was funded by the Royal College of Physicians of London. Special thanks are due to Drs N Simpson, A Hopkins, and D Atherton for initiating and organising the workshop.

The figures are provided courtesy of Dr R S Lever, consultant dermatologist, Western Infirmary, Glasgow.

1 Rajka G. *Essential aspects of atopic dermatitis.* Berlin: Springer-Verlag, 1989:5-7.
2 Johnson ML, Johnson KG, Engel A. Prevalence, morbidity and cost of dermatologic diseases. *J Am Acad Dermatol* 1984;11:930-6.
3 Rook AR, Savin JA, Wilkinson DS. The prevalence, incidence and ecology of diseases of the skin. In: Rook AR, Wilkinson DS, Ebling FJG, Champion RH, Bunton JL, eds. *Textbook of dermatology.* 4th ed. London: Blackwell, 1986:40.
4 Williams HC. Is the prevalence of atopic eczema increasing? *Clin Exp Dermatol* 1992;17:385-91.
5 Schultz-Larsen F. Genetic aspects of atopic eczema. In: Ruzicka T, Ring J, Pryzbilla B, eds. *Handbook of atopic eczema.* London: Springer-Verlag, 1991:15-26.
6 Bos JD, Kapsenberg ML, Sillevis Smitt JH. Pathogenesis of atopic eczema. *Lancet* 1994;343:1338-41.
7 Long CC, Collard R, Funnell CM, Finlay AY. What do members of the National Eczema Society really want? *Clin Exp Dermatol* 1993;18:516-22.
8 Williams HC, Burney PGJ, Pembroke AC, Hay RH. The UK working party's diagnostic criteria for atopic dermatitis. III. Independent hospital validation. *Br J Dermatol* 1994;131:406-17.
9 Webber SA, Graham-Brown RAC, Hutchinson PE, Burns DA. Dietary manipulation in childhood atopic dermatitis. *Br J Dermatol* 1989;121:91-8.
10 David TJ. Conventional allergy tests. *Arch Dis Child* 1991;66:281-2.
11 Juhlin L, Johansson SGO, Bennich H, Hogman C, Thyresson N. Immunoglobulin E in dermatoses. *Arch Dermatol* 1969;100:12-6.
12 Maucher OM, Faber M, Knipper H, Kirchner S, Schopf E. Kortikoidallergie. *Hautarzt* 1987;38:577-82.
13 David TJ. Steroid scare. *Arch Dis Child* 1987;62:876-8.
14 Joint Formulary Committee. *British National Formulary.* No 27. London: British Medical Association, Royal Pharmaceutical Society of Great Britain, 1994:412.
15 Aggarwal RK, Potamitis T, Chong NHV, Guarro M, Shah P, Kheterpal S. Extensive visual loss with topical facial steroids. *Eye* 1993;7:664-6.
16 Cubey RB. Glaucoma following the application of corticosteroid to the skin of the eyelids. *Br J Dermatol* 1976;95:207-8.
17 Howell JB. Eye diseases induced by topically applied steroids. *Arch Dermatol* 1976;112:1529-30.
18 Long CC, Finlay AY. The finger tip unit—a new practical measure. *Clin Exp Dermatol* 1991;16:444-7.
19 Goodyear HM, Spowart K, Harper JI. "Wet wrap" dressings for the treatment of atopic eczema in children. *Br J Dermatol* 1991;125:604.
20 Berth-Jones J, Graham-Brown RAC. Failure of terfenadine in relieving the pruritus of atopic dermatitis. *Br J Dermatol* 1989;121:635-7.
21 Wahlgren C-F, Hagermark O, Bergstrom R. The antipruritic effect of a sedative and a non-sedative antihistamine in atopic dermatitis. *Br J Dermatol* 1990;122:545-51.
22 Kemp JP. Tolerance to antihistamines: is it a problem? *Ann Allergy* 1989;63:621-3.
23 Platts-Mills TAE, Mitchell EB, Rowntree S, Chapman MD, Wilkins SR. The role of house dust mite allergens in atopic dermatitis. *Clin Exp Dermatol* 1983;8:233-47.
24 Norris PG, Schofield O, Camp RDR. A study of the role of house dust mite in atopic dermatitis. *Br J Dermatol* 1988;118:435-40.
25 Colloff MJ, Ayres J, Carswell F, Howarth PH, Merrett TG, Mitchell GB, *et al.* The control of allergens of dust mites and domestic pets: a position paper. *Clin Exp Allergy* 1992;22 (suppl 2):1-28.
26 Atherton DJ, Sewell M, Soothill JF, Wells RS. A double blind controlled cross-over trial of antigen avoidance diet in atopic eczema. *Lancet* 1978;i:401-3.
27 Neild VS, Marsden RA, Bailes JA, Bland JM. Egg and milk exclusion diets in atopic eczema. *Br J Dermatol* 1986;114:117-23.
28 Jekler J, Larko O. UVB phototherapy for atopic dematitis. *Br J Dermatol* 1988;119:697-705.
29 Atherton DJ, Carabott F, Glover MT, Hawk JL. The role of psoralen photochemotherapy (PUVA) in the treatment of atopic eczema in adolescents. *Br J Dermatol* 1988;118:791-5.
30 Stern RS, Laird N, Melski J, Parrish JA, Fitzpatrick TB, Bleich HL. Cutaneous squamous cell carcinoma in patients treated with PUVA. *N Engl J Med* 1984;310:1156-61.
31 George SA, Bilsland DJ, Johnson BE, Ferguson J. Narrow band (TL-01) UVB air conditioned phototherapy for chronic severe adult atopic dermatitis. *Br J Dermatol* 1993;128:49-56.
32 Bamford JTM, Gibson RW, Renier CM. Atopic eczema unresponsive to evening primrose oil (linolenic and gamma-linolenic acids) *J Am Acad Dermatol* 1985;13:959-65.
33 Berth-Jones J, Graham-Brown RAC. Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993;341:1557-60.
34 Wright S, Burton JL. Oral evening primrose seed oil improves atopic eczema. *Lancet* 1982;ii:1120-2.
35 Stewart JCM, Morse PF, Moss M, Horrobin DF, Burton JL, Douglas WS, *et al.* Treatment of severe and moderately severe atopic dermatitis with evening primrose oil (Epogam); a multi-centre study. *J Nutr Med* 1991;2:9-15.
36 Younger IR, Harris DWS, Colver GB. Azathioprine in dermatology. *J Am Acad Dermatol* 1992;25:281-6.
37 Munro CS, Higgins EM, Marks JM, Daly BM, Freidmann PS, Shuster S. Cyclosporin A in atopic dermatitis. *Br J Dermatol* 1991;124:43-8.
38 Sowden JM, Berth-Jones J, Ross JS, Motley RJ, Marks R, Finlay AY, *et al.* Double-blind, controlled, crossover study of cyclosporin in adults with severe refractory atopic dermatitis. *Lancet* 1991;338:137-40.
39 Sheehan M, Atherton DJ. A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema. *Br J Dermatol* 1992;126:179-84.
40 Sheehan MP, Rustin MHA, Atherton DJ, Buckley C, Harris DJ, Brostoff J, *et al.* Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis: results of a double-blind placebo-controlled study. *Lancet* 1992;340:13-7.
41 Boguniewicz M, Jaffe HS, Izu A, Sullivan MJ, York D, Geha RS, *et al.* Recombinant gamma interferon in treatment of patients with atopic dermatitis and elevated IgE levels. *Am J Med* 1990;88:365-70.
42 Leung DY, Hirsch RL, Schneider L, Moody C, Takaoka R, Li SH, *et al.* Thymopentin therapy reduces the clinical severity of atopic dermatitis. *J Allergy Clin Immunol* 1990;85:927-33.
43 Graham-Brown RAC. Toxicity of Chinese herbal remedies. *Lancet* 1992;340:673.
44 Burr ML. Does infant feeding affect the risk of allergy? *Arch Dis Child* 1983;58:561-5.
45 Golding J, Peters TJ. The epidemiology of childhood eczema. *Paediatr Perinatal Epidemiol* 1987;1:67-9.
46 Chandra RK, Puri S, Suraiya C, Cheema PS. Influence of natural food antigen avoidance during pregnancy and lactation on incidence of atopic eczema in infants. *Clin Allergy* 1986;16:563-9.
47 David TJ. Infection and prevention:current controversies in childhood atopic eczema: a review. *J R Soc Med* 1989;82:820-2.
48 Lilja G, Dannaeus A, Foucard T, Graff-Lonnevig V, Johansson SG, Oman H. Effects of maternal diet during late pregnancy and lactation on the development of atopic diseases in infants up to 18 months of age—in vivo results. *Clin Exp Allergy* 1989;19:473-9.
49 Arshad SH, Matthews S, Gant C, Hide D. Effect of allergen avoidance on allergic disorders in infancy. *Lancet* 1992;339:1493-7.
50 Finlay AY, Khan GK. Dermatology life quality index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;19:210-6.

(Accepted 11 January 1995)