

Eczema and allergy: how useful is allergy testing?

Heather Godwin RGN,
RSCN, HV, BA(Hons)
PGCE, eczema research
nurse, Great Ormond
Street Hospital for
Children NHS Trust,
London

Abstract

Aim: To determine the value of allergy testing using skin prick tests and specific immunoglobulin E measurements (spIgE) to identify allergies in children with eczema (atopic dermatitis) and to correlate these findings with the clinical history.

Method: This was a retrospective study of 100 children with moderate to severe eczema attending hospital for treatment. In each child a detailed clinical history of allergy was documented and the severity of atopic dermatitis assessed by the research nurse. Skin prick tests were carried out using grass pollen, house-dust mite and egg-white allergens. Blood tests were taken for total IgE and spIgE responses to these allergens. A control group of 100 children with no history of allergy was also included for comparison.

Results: More than two thirds of the children (68 per cent) had a high total IgE (>1000kU/l). SpIgE tests to grass and house-dust mite were shown as the most frequent finding although statistically poor in association with the clinical history. Allergy to these airborne allergens was found to be more common in the older age group of children, whereas egg-white allergy was seen more commonly in the younger age group.

Conclusion: There is no one diagnostic test for allergy in children with atopic dermatitis. The results of these tests in combination with the clinical history provide a more accurate assessment of the child's allergy status. Children with moderate to severe eczema have a high incidence of associated allergy. Skin prick tests and spIgE proved helpful but neither was exclusively better than the other for diagnosis. The clinical nurse specialist is able to make a valuable contribution to the family through offering support and carrying out allergy tests.

It is well recognised that children with eczema are more susceptible to allergic reactions to a wide range of food and inhalant allergens than those without eczema. Identifying potential aggravating factors of eczema is an integral part of management to help to control the skin condition and to prevent the unnecessary introduction of restrictive diets and activities. In some children the cause of the allergy is obvious but for many it is not clear and the question of allergy testing arises.

As part of a Medical Research Council (MRC)-funded research project at Great Ormond Street Hospital to identify the genes that cause eczema, children were recruited from outpatients with a history of eczema, asthma and allergy. Tests carried out included skin prick tests (SPTs) and blood tests for total and spIgE, together with a history of allergic reactions. The information gained provides evidence of the association between eczema severity and allergy and the accuracy of these tests. The experience of this undertaking also highlights the nurse's role in managing children with eczema.

Background

Eczema is a worldwide medical problem, affecting 15 to 20 per cent of children in the UK. It is predominantly a disease of childhood with more than 80 per cent of sufferers developing signs and symptoms in the first year of life (Flohr and Williams 2006). The diagnosis of eczema is usually obvious but there are validated diagnostic criteria originally described by Hanifin and Rajka (1980) and subsequently modified by the UK Working Party (Williams *et al* 1994), which enable universal consistency in the diagnosis of eczema. As children get older eczema improves and by adolescence most do not have eczema as a clinical problem, although some aspects persist into adult life, such as a sensitive skin and a predisposition to allergy (Williams and Wüthrich 2000, Flohr and Williams 2006). A proportion of children with eczema will also develop asthma and chronic rhinitis/hay fever (Flohr and Williams 2006).

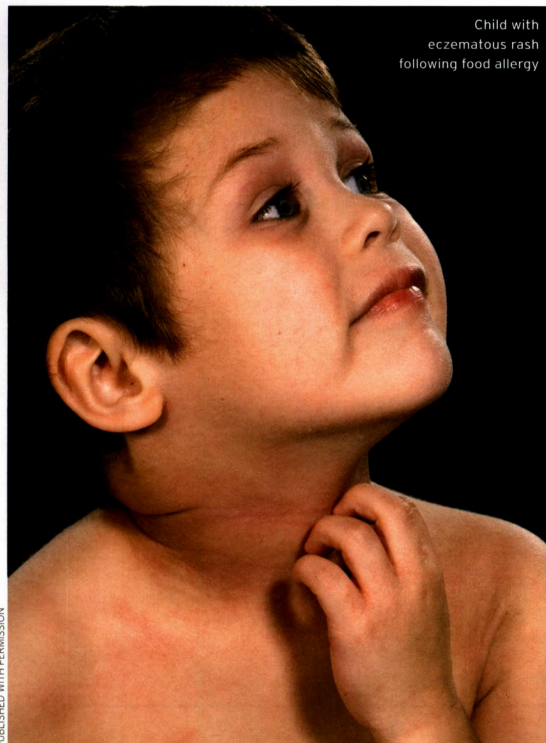
Eczema is thought to arise as a result of an interaction between certain genes and environmental factors (Moffatt *et al* 2006). It is primarily a genetic

Key words

- Children: eczema
- Allergy
- Nurse specialists

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Child with
eczematous rash
following food allergy

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disorder, with a strong family history of eczema, asthma or hayfever occurring in affected families and a high incidence occurring in identical twins compared with non-identical twins (Moffatt *et al* 2006, Van Eredewegh 2002). However, on a day-to-day basis eczema is triggered and aggravated by various factors, in particular in response to certain allergens. For most children with mild eczema, which is readily treatable with simple topical medications, allergy is not usually a significant problem. In our experience allergy can be a major associated issue for those children with moderate to severe eczema.

To diagnose allergy, there are a number of different tests available but there is no one gold standard or agreed accurate test for all allergens. Some say an important component of diagnosing allergy is having a positive clinical history together with one positive allergy test (Ewan and Clark 2005, Roberts 2005). Alternatively and in the absence of a positive history, Smits *et al* (2003) and Niggemann *et al* (2000) state that two positive allergy tests are needed to confirm a specific allergy. The allergy tests available are: specific immunoglobulin E measurements (spIgE)

measurement from blood; skin prick tests; patch testing; and food challenge (Roehr 2001, Fiocchi *et al* 2004, Holgate and Lack 2004). The latter is undoubtedly the most useful for food allergens but not practical for first-line investigation.

Differing views exist regarding the reliability of allergy testing particularly in children with eczema (Roberts 2005, Kunz and Ring 2000). Hansen *et al* (2004) showed the most accurate test for whole-egg allergy was the SPT while Cantani and Micera (2003) found SPTs were more reliable for inhalant allergens than food allergens. Kunz and Ring (2000) report inconsistency in sensitivity and specificity and false positive and negative results have been reported in spIgE tests (Holgate and Lack 2004).

Eczema is associated with a susceptibility to allergy in the form of intermediate hypersensitivity reactions (Holgate and Lack 2004). Common allergens include: eggs, cows milk, house-dust mites (HDM), grass, cats, dogs, horses and moulds (Flohr and Williams 2006). This type of allergic response is mediated by IgE. IgE can be detected in the serum and is associated with the release of histamine and other mediators of inflammation as an allergic response to allergens such as pollen or foods. This can be manifested as allergic rhinitis, asthma or skin irritation (Reeves and Todd 1991). In children with eczema, food allergy is seen as an itchy red skin with an urticarial rash occurring soon after ingestion (David 2006). Eighty per cent of children with eczema have a raised total IgE, but approximately 10 per cent of children with eczema are within the normal range, a proportion of whom have no spIgE responses to common allergens (Moffatt *et al* 2006). The higher the IgE, the more likely the individual is to having allergy as a significant problem; however some children with a normal IgE can also have problems with allergy.

Our study did not include patch testing or food challenges but it is important to note that these are acknowledged as further tests that can be used (Hon *et al* 2007, Niggemann *et al* 2000, Roehr *et al* 2001). Skin patch tests are recommended by Niggemann *et al* (2000) as a valuable adjunct to allergy testing for identifying late phase allergic reactions particularly in children with eczema. Food challenge is suggested by some to provide a more definitive test (Ewan and Clark 2005, Niggemann *et al* 2000, Smits *et al* 2003).

The nursing contribution to allergy testing is a growing area in hospitals and general practice (Hodges *et al* 2007, Walker 2007). However, there is a dearth of information on testing children with eczema. The nurse specialist plays an important role in investigating these children and supporting their families.

Allergy tests

Skin prick test: A drop of a solution containing the allergen is applied to the skin and a lancet used to prick the skin. The allergen will bind to the IgE on mast cells causing degranulation and the release of histamine. This manifests as a weal and flare reaction, the diameter of which can be measured (Alk Abello 2001).

IgE: Total IgE is a non-specific test which indicates the potential for each individual to develop allergic reactions; with higher levels seen in allergic children and adults. The levels tend to rise initially with age in childhood and then plateau or decrease in adult life (Owby 1996).

Radioallergosorbent test (RAST): A measure of spIgE responses to a panel of allergens from a blood sample taken from the patient. The process involves an allergy-impregnated disc being incubated with the patients' serum. Allergen spIgE, if present, will bind to the allergen. The disc is then incubated again with radiolabelled anti-IgE and the radioactivity measured to give the level of spIgE present (Todd and Spickett 2005). SpIgE is the IgE value specific to particular allergens (Kunz and Ring 2000).

Patch testing: Carried out by using allergens incorporated in petroleum jelly. This is left in contact with the skin for 48 hours, which allows the antigen-presenting Langerhans cells in the skin to take up the antigen and recruit T cells. The test is read at three and five days indicating the delay required to recruit and stimulate the T cells. A positive reaction will show erythema, oedema and sometimes blistering. Patch testing is used to investigate delayed type hypersensitivity reactions giving rise to contact dermatitis (Todd and Spickett 2005). This is not considered to be a routine investigation for the diagnosis of atopic dermatitis, but can be helpful if there is any suspicion of there being a contact allergy, for example to the topical medication being applied to the skin. Having made that statement there are some investigators who have found doing routine patch tests in children with eczema to the common atopic allergens, as previously listed, informative. This is now referred to as the atopy patch test. This investigation was not used in our project.

Eczema severity score

Assessing eczema severity can be done by a variety of scoring methods, for example SCORAD (European task force on Atopic Dermatitis) (1993), EASI (Cherill *et al* 1998) and SASSAD (Berth-Jones 1996). The method used in our research was the Rajka and Langeland standard modified Hanifin criteria (Lewis-Jones and Charman 2006). This grades eczema into three categories: mild, moderate and severe. These are accounted for by measuring the intensity of the disease by itching, clinical course as in periods of remission or if constantly present in the last year and the extent of the eczema lesions measured by the rule of nines. Therefore severity ranged from 0-9.

Methodology

The role of the research nurse in the methodology of the study was to recruit relevant families (those having a child with eczema), complete an extensive questionnaire, take a blood sample and perform SPTs on each family member. The blood samples were taken for DNA (genetic studies) and total and spIgE

to egg white, house-dust mites and grass.

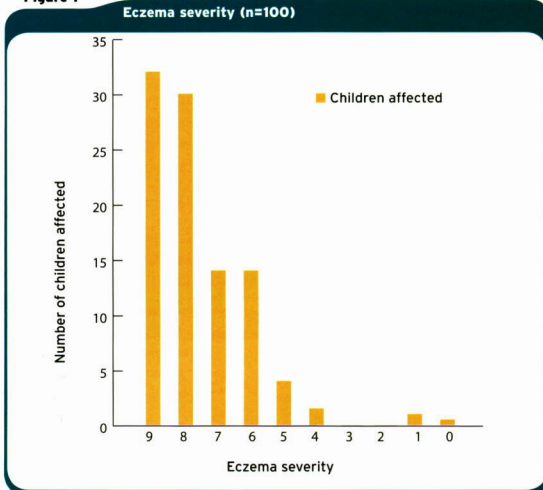
The questionnaire included a detailed history of any known allergies and how these affected the child. Effects on the children included obvious immediate allergic response with symptoms such as nausea/vomiting (with ingested allergens), urticaria and/or angio-oedema occurring within one hour of exposure. SPTs (with abstinence from antihistamines for 48 hours prior to the tests) were performed on all the families using the following allergens: house-dust mites (dermatophagoides pteronyssinus), timothy grass (phleum pratense), cat (felix domesticus), mould (cladosporium herbarium), egg white and positive and negative controls. A positive reaction was recorded if the wheal size was 3mm or above and larger than or equal to the size of the positive control.

For the purpose of this study we included the first 100 families who participated in all the tests. This was compared with a control group of children who had no history of eczema, asthma or hayfever. The age range of the affected child, through whom the family qualified for the study, was from two to 15 years with matched controls. (The term "proband" is used to refer to the affected child – meaning the person serving as the starting point for investigation of the family.)

Results

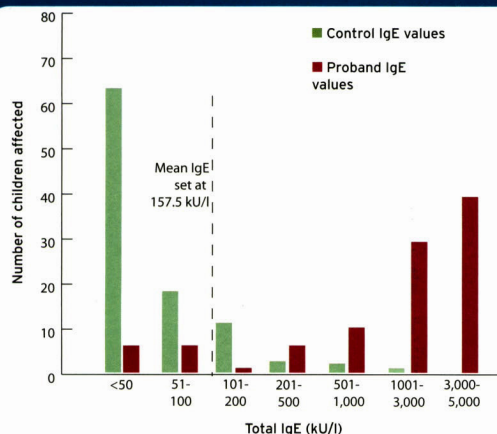
Severity: Severity was scored as follows: mild (3-4); moderate (5-7) and severe (8-9). The atopic dermatitis severity levels of the proband group of children were mostly severe at levels 8 and 9 (61 per cent) across the full spectrum of ages

Figure 1



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Figure 2 Total IgE values: comparison of controls and affected children



(Figure 1).

Total IgE: The values for total IgE were set by the laboratory for this group of children at 4.22 – 6124.18 with a mean of 157.5 kU/l. The results showed an overwhelming trend of elevated total IgE in the proband group compared with the controls. Sixty eight per cent of the probands were above 1000 kU/l. By comparison 1 per cent of control subjects showed a high total IgE (above 1000 kU/l). This is illustrated in Figure 2.

Specific allergens

The results of the tests for grass, house-dust mite and egg white are recorded in Tables 1 to 3 and divided into age groups, under five years and five to 16 years. Specific IgE (SpIgE) was recorded as follows: positive (Class 1 to 3) and strongly positive (Class 4 to 6) (Riches and Sheldon 1994).

Grass pollen: History of grass allergy was seen in each age group with predominance in the older age group. In both age groups, SpIgE was the strongest indicator (65 children in class 4-6), over and above the number with a history of grass allergy (50) and positive SPT

(44) (Table 1). The control group showed a small number of positive results with no known history of allergy to grass.

House-dust mite: No specific history was recorded to house-dust mite. Children in the older age group showed significantly more reactions to the skin prick test and strong positive IgEs. A greater number of children had spIgE results compared with SPTs. There were a small number of children with positive results in the control group (Table 2).

Egg white: The response to the food allergen is reversed. A greater percentage of children in the 'under five' age group had a history of egg white allergy, positive SPT and positive spIgE (class 1 to 3). The IgE highly positive (class 4-6) is markedly low in comparison with the other results. The control group showed no positive skin test results. Not all the control group of children had IgE measured for egg white.

Statistics to highlight sensitivity and specificity of the skin prick tests and IgE associated with the history of allergy were carried out on the grass and egg white (Table 4). A history of grass allergy correlated with the SPT for both sensitivity and specificity but showed this to be a poor indicator for allergy. The history compared with spIgE results was slightly better at 71 per cent specificity, suggesting if a choice between the tests is possible there would be a greater reliability in the spIgE test.

Similar results were obtained in the egg white group although the specificities were better. Again, spIgE showed greater sensitivity and specificity than the SPT. However, these test groups are relatively small. Carrying out both tests seems to provide for greater reliability of confirming the diagnosis of a specific allergy.

Discussion

A detailed literature search indicated that there has been some work already performed in this area of allergy diagnosis with children, including those with eczema/atopic dermatitis. Our study was larger than any previous studies with children who have severe disease and therefore we believe the results are clinically significant. The specialist nurse has been able to contribute to the diagnosis of allergy by careful history taking, listening to families and carrying out SPTs and spIgE tests while offering supportive holistic care.

In our experience, and as Niggemann *et al* (2000) reported, families are not always able to identify a

Table 1 Responses to grass

	Children with eczema – all	Under five (n=13)	Age five – 16 (n=87)	Controls (n=100)
History	50	4 (31 per cent)	46 (53 per cent)	0
SPTs	44 (≥3mm)	5 (38 per cent)	39 (44 per cent)	4 (≥3mm)
SpIgE (class 4-6)	65	7 (54 per cent)	58 (66 per cent)	2
SpIgE (class 1-3)	22	2 (19 per cent)	20 (23 per cent)	10

Table 2

Responses to house-dust mite SPT in children with eczema (and controls)

	Children with eczema – all	Under five (n=13)	Age five – 16 (n=87)	Controls (n=100)
History	–	–	–	–
SPTs	44 (≥3mm)	2 (15 per cent)	39 (44 per cent)	2 (≥ 3mm)
SpIgE (class 4-6)	71	6 (46 per cent)	65 (75 per cent)	2
SpIgE (class 1-3)	17	4 (31 per cent)	13 (15 per cent)	10

Table 3

Responses to egg white SPT in children with eczema (and controls)

	Children with eczema – all	Under five (n=13)	Age five – 16 (n=87)	Controls (n=100)
History	26	5 (38 per cent)	21 (24 per cent)	0
SPTs	15 (≥3mm)	3 (23 per cent)	39 (44 per cent)	0
SpIgE (class 4-6)	20	1 (8 per cent)	65 (75 per cent)	0 (only 20 tested)
SpIgE (class 1-3)	45	11 (85 per cent)	13 (15 per cent)	0

history of a specific allergy. Some were suspicious of a particular allergy and other families were concerned about why the eczema was continuing to flare. It is therefore important to try and identify any trigger factor, especially specific allergies relevant to that child. The converse is also true in that some families report allergy symptoms and this is not confirmed by any testing. Establishing which test or tests should be performed is not conclusive from the literature.

The total IgE measurements were consistent with expectations (Moffatt *et al* 2006). IgE was higher in children with the greater severity of eczema. The implication is that this group of children will display more allergic symptoms, thus there is a need to identify individual allergens. Past studies have suggested the measurement of total IgE is useful for the prediction of allergy but if it is not possible to identify the specific allergens then this test is of limited value to individuals.

Examination of the specific allergen results showed a high incidence of reactions to inhaled allergens especially in the over five-year-old group. In the example of grass, the incidence of a high spIgE titre was more frequent than a positive SPT. This would suggest it is the more sensitive test. However, although spIgE is more reliable than the SPT, it does have limitations.

There was no recorded history to HDM in any of the children; however, conclusions can still be drawn from the data which again showed a significantly higher percentage of children with a high spIgE titre compared with the SPT. The SPTs were all carried out by the same researcher (HG) providing consistency of technique and less chance of erroneous results. Based on the example of grass it is suggested the spIgE may be a more reliable test. In both control groups there was evidence of a small number of children with positive tests which would be expected from a normal population group.

The egg white study showed a different picture, with regard to age range. The history, SPT and positive spIgE were all higher in incidence in the children under five. The numbers were notably small. Statistically although only 20 children showed a high spIgE titre, specificity was high compared with all other tests. This means that almost all children with an egg allergy will be identified from this test. The egg white SPTs were not statistically significant although the specificity was higher in the SPTs and spIgE tests than in the inhaled allergens, suggesting there may be more accuracy in testing for ingested allergens (food allergy).

For all allergens, it is possible that the SPT was impeded by inadequate excretion time of antihistamines as these were only stopped for 48 hours prior to the test. The high total IgE status of this group of patients would suggest that there may be other allergens that are relevant in these children.

Much of the literature focuses on skin patch tests as a means of identifying late allergic reactions particularly in children with eczema/atopic dermatitis. These may be difficult to perform in this group of children who have extensive eczema; however, it is

Table 4

Sensitivity and specificity of history and tests

Allergen	Sensitivity	Specificity
Grass SPT	61 per cent	55 per cent
Grass IgE (class 4-6)	65 per cent	71 per cent
Egg white SPT	47 per cent	78 per cent
Egg white IgE (class 4-6)	60 per cent	82 per cent

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not known if the children who present with sensitivity to egg and negative SPT may have a delayed reaction to the allergen. Performing patch tests in this group of children is likely to have given further valuable information.

Conclusions and recommendations

This study highlights the importance of allergy in children with eczema and the need to try to identify which allergens are relevant. Sixty eight per cent of the children with moderate to severe eczema had a high total IgE, indicating that these children are more likely to have allergic reactions to a variety of allergens. The history is not always accurate or present but if positive it is a helpful aid in providing an indicator of allergy. Investigations, such as total and sIgE and SPTs will give greater reliability in confirming the presence or absence of a specific allergy.

Egg allergy was seen more frequently in the under five-year-olds. Inhaled allergens (HDM and grass) were seen more frequently in the over five-year-olds, but neither the sIgE or SPT alone were shown to give a clear indication of specific allergy. If limited tests are able to be performed, the sIgE is suggested as the test of choice, especially in infants, as it is easier as a routine investigation to take a blood test than perform SPTs. A negative sIgE result is likely to exclude an allergy. A high sIgE titre is strongly suggestive but

the level of titre can vary with time; alone it provides an indicator of allergy but not a specific diagnosis. SPTs have the advantage of measuring the wheal and repeat SPTs allow for more accurate monitoring of the allergic reaction. Many children with certain allergies, such as cows' milk, develop tolerance to these allergens as they get older (David 2006). For more details, studies with skin patch tests are important to exclude a late phase reaction (atopy patch test) and any positive contact dermatitis reactions.

It is well recognised that nurse specialists play an integral part in managing children with eczema. As well as supporting the families and giving advice on skin care it is also important for the nurse specialists to help identify what may be aggravating the child's eczema and whether there is any history of allergic reactions. They can also have a role in allergy testing and with the planned increase in allergy units being established in the UK, this is an area for further expansion and training of nurses who have an interest in this field of medicine. **PN**

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