

Assessing the value of skin prick tests

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Summary

Skin test materials vary in their potency and specificity. Although 3 mm reactions are often regarded as diagnostic of a type 1 allergy, a study based on 100 allergy clinic patients with food intolerance showed that thirteen out of fifteen patients with a 3 mm reaction to common inhalant allergens had no RAST-detectable allergen-specific IgE.

Three millimetre reactions were significant for milk and egg extracts. Food intolerance was clinically demonstrable in six out of seven patients giving a 4 mm skin reaction and in ten out of thirteen with a 3 mm reaction. There was, however, a 'clinically false positive' reaction of 3 mm or more in 3.8% of allergy clinic patients for milk and 2.8% for egg.

In fifteen out of nineteen patients with a clinical diagnosis of fish allergy, the diagnosis was supported by a skin test reaction of 5 mm or more. However, seven patients with no history of intolerance to fish gave a 4 mm reaction to the same extract. Reactions of less than 5 mm were thus unhelpful clinically.

Introduction

Skin prick tests for the diagnosis of atopic allergy are simple to perform, provide useful information at the 1–3 mm reaction level (Stenius *et al.*, 1971; Bock *et al.*, 1978) and are usually preferred to intradermal tests (Reddy *et al.*, 1978; Cavanaugh *et al.*, 1977). Since skin-pricks have shown a 77% agreement with bronchial and nasal provocation tests (Eriksson, 1977a), it has been suggested that if the results of history, skin-prick and the radioallergosorbent test (RAST) technique are combined, provocation testing can often be avoided (Eriksson, 1977b and c). Nevertheless the skin-prick test can suffer from poor standardization of allergen extracts both as to concentration (Foucard *et al.*, 1972) and composition (Zelevnick *et al.*, 1977). Furthermore, the size of the

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skin reaction in patients with known allergies can be shown to vary with the concentration of the test material (Henocq, Brighton & Topping 1979). Until these problems are resolved, opinion as to what constitutes a diagnostically positive test will continue to vary.

The purpose of the present study was to assess both the sensitivity and the specificity of the skin prick response to allergenic extracts by comparison with clinical evidence of allergy and, in the case of common inhalant allergens, by comparison with IgE RAST results. In order to assess a variety of allergens, we studied 100 patients with food intolerance, of whom sixty-four also had asthma or eczema and a further twelve had rhinorrhoea. Their skin test results were compared with groups of allergy clinic patients who had no history of food intolerance.

Methods

Skin tests and laboratory investigations

Skin prick tests for inhalant and food allergens were carried out on the volar aspect of both forearms by an experienced technician, using commercially available allergen extracts (Bencard Ltd, Brentford, Middlesex) and saline and histamine controls. None of the subjects had received anti-histamines for at least 24 hr before testing. Measurements of specific IgE against allergenic extracts of meadow fescue, *Dermatophagoides pteronyssinus* and cat epithelium were carried out by Phadebas RAST (Pharmacia GB Ltd, Hounslow, Middlesex) using a modification of the manufacturer's technique (John & Merrett, 1979) on sera from the same patients. Graded on a 0–4 scale, scores of 1 or more were regarded as probably (grade 1) or strongly positive.

Our Allergy Clinic routine skin tests included milk and egg, and for these the results of 500 consecutive tests were analysed. Subsequently, routine skin tests against extracts of mixed nuts and fish were introduced and 200 of these tests were also analysed.

Results

Skin tests and RAST for inhaled allergens

When the total number of 3 mm skin reactions to grass pollen, *D. pteronyssinus* and cat was compared with the number of corresponding positive RASTs (Table 1), it was apparent that only two out of fifteen skin test reactions agreed with the RAST result but a significantly closer correlation ($P < 0.02$) was seen for 4 mm skin reactions (fifteen out of twenty-five) and also for 5–6 mm reactions (twenty-three out of twenty-nine— $P < 0.001$). It therefore appeared that 4 mm provided a threshold which corresponded approximately to that of the RAST method. Charted in this way, there appeared to be a close correlation between the size of the skin reaction to each of these antigens and the grade of the RAST result (Fig. 1).

Sixty-two patients had both a positive skin test by these criteria and a corresponding positive RAST to at least one inhaled allergen. Fifty-five had an associated asthma, eczema or rhinorrhoea. The remaining seven had strongly positive results to grass pollens (five) and/or *D. pteronyssinus* (three) but had no corresponding symptoms. Of thirty-one patients with totally negative tests, three had rhinorrhoea of uncertain origin but the remaining twenty-eight had no clinical evidence of allergy to grass pollen, dust mite or cat. Fourteen patients in this group nevertheless had respiratory symptoms or eczema provoked by foods, perfume (in one) or the scent of flowers (one).

Table 1. Comparison between skin test* and RAST for inhaled allergens

Size of skin reaction (mm)	Total number	Number with +ve RAST	Percentage of skin tests confirmed by RAST
3	15	2	13.3
4	25	15	60
5-6	29	23	79.3

* Grass pollen, *D. pteronyssinus* and cat

Among the sixty-two patients who had positive tests to at least one inhalant, there were some discrepant results for individual allergens (see Fig. 1). In addition, there were seven patients whose only abnormal result was a single positive skin test (in six) or RAST (in one). Four of these had asthma, eczema or rhinorrhoea but three had no symptoms to correspond to their weakly positive tests.

The 100 patients who were the subject of this study had been diagnosed on clinical grounds as having specific food intolerance, confirmed by a recurrence of symptoms on challenge with the suspect food on at least two occasions a week or more apart. The diagnosis was confirmed subsequently by skin tests or RAST in fifty-one (Lessof *et al.*, 1979). Reactions were also seen when these patients were skin tested with foods to

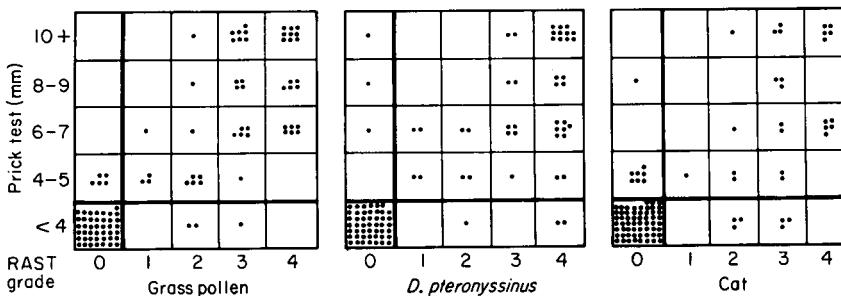


Fig. 1. Correlation between skin prick tests and RAST results in 100 allergy clinic patients tested against three common inhalant allergens.

which they had not previously been proved to be sensitive, although in some the diagnosis had been suspected (see Table 2). Three asthmatic patients with 4 mm reactions to milk improved after milk exclusion. Having relapsed on re-challenge and improved again without milk, they were accepted as having a specific milk allergy, with a skin test which was consistent with this diagnosis. The same conclusion was reached in three out of four patients with 3 mm reactions to milk. Of those with 4 mm reactions to egg (four cases) three had clinical intolerance, and 3 mm reactions (nine cases) identified seven who were clinically intolerant.

The clinical significance of a 3-4 mm reaction to milk or egg appeared to contrast with the results for mixed nuts or fish, which showed a poor correlation below the 5 mm level. Three to four millimetre reactions to nuts occurred in seven patients but there was clinical intolerance in only three of these. Eleven patients showed 3-4 mm reactions to fish though all firmly denied fish-induced symptoms.

Table 2. Results of additional skin tests† in 100 patients with food intolerance

	Size of skin reaction (mm)	Number with reactions	Number with* clinical intolerance
Milk	4	3	3 (1)
	3	4	3
Egg	4	4	3 (2)
	3	9	7 (3)
Nut	4	2	1 (1)
	3	5	2
Fish	4	7	0
	3	4	0

* Number with positive RAST in brackets.

† Excluding foods to which there was a proven intolerance.

Skin test reactions to foods were also analysed in a consecutive series of allergy clinic patients. Among 500 patients who had no clinical evidence of food intolerance there were nineteen (3·8%) who gave skin reactions to milk of 3 mm (thirteen), 4 mm (two) or 5 mm (four). For whole egg the comparable figures were seven reacting at 3 mm, three at 4 mm and four at 5 mm (fourteen in all, i.e. 2·8%). In the case of nuts, five out of 200 symptomless patients had 3 mm reactions, one reached 4 mm and three reached 5 mm (totalling nine, i.e. 4·5%). For fish, the corresponding figures were nine, five and one (totalling fifteen, i.e. 7·5%). There was no evidence as to whether these positive reactions were non-specific or whether they indicated low degrees of allergic sensitization.

Among the less frequently used skin test materials, chicken extract correctly identified three out of four allergic patients by 5 mm weals but added three 'clinical false positives'. Both orange and strawberry correctly identified one out of two allergic patients, but pork, tomato and chocolate extracts gave unreliable results.

Discussion

For the diagnosis of type I allergy in a hospital clinic, skin prick testing is simple, cheap and rapid; it may also detect non-IgE and delayed reactions. Even in the absence of symptoms and in the face of a negative challenge test, a repeatedly positive skin test may nevertheless be significant, for example after successful immunotherapy, and in patients in whom a positive test precedes the development of hay fever (Hagy & Settignano, 1972) or who have recovered spontaneously from their allergy. Such positive tests can be shown to be associated with the presence of specific IgE in the serum, as in seven of our patients who denied all respiratory symptoms. If confirmed by more than one method, a positive skin prick reaction may thus indicate a sensitization which, for one reason or another, is not accompanied by clinical allergy in a particular target organ. By this criterion, a 4 mm reaction to grass pollen, *D. pteronyssinus* or cat was a highly significant finding in our patients irrespective of the clinical diagnosis, since it

correlated with the RAST result in 92% of grass pollen, 89% of *D. pteronyssinus* and 84% of cat allergen tests. There was also a good correlation with the clinical history, both for positive and negative results, except for three patients whose weakly positive prick tests were unsupported either by the clinical history or by RAST and a further seven (see above) who had IgE antibody but no clinical sensitivity.

The extracts used for these comparisons between skin tests and RAST were not identical in each case but the test methods had similar sensitivities. Among the 300 comparisons which were made (for the three inhalant allergens) twenty significant weals were associated with negative RAST results, but fourteen insignificant skin tests were obtained with positive RAST results (Fig. 1). It should be accepted that these two techniques measured different parameters—one quantifies skin sensitivity to mediators and possibly non-IgE mediated skin sensitization, while the other measures circulating IgE.

The extracts used in this study contained a mixture of allergens. Other results might have been obtained with different concentrations or different extracts. However, because of the multiplicity of allergens involved even in apparently simple reactions to bee venom (King *et al.*, 1976; Paull *et al.*, 1977), cat epithelium (Stokes & Turner, 1975) and ragweed (King, Norman & Lichtenstein, 1967), attempts to develop pure allergen preparations for diagnostic tests may at this stage be misguided. Until standardization by allergen content becomes a feasible proposition, allergy test materials can only be evaluated in clinical terms by means of challenge tests, clinical correlations, histamine release studies, and a comparison between such methods as skin prick tests and RAST.

With the materials used in this study, 3 mm reactions to milk and egg provided diagnostic help in previously uncertain cases of allergy to these foods and compared favourably with accepted confidence limits for other diagnostic tests in the number of 'clinical false positives' reported. Other food preparations gave more 'false positive' results, emphasizing the need for better standardization of test materials—or else the need for a better appreciation of the significance of non-clinical degrees of sensitization. The diagnostic value of fish and nut extracts was nevertheless satisfactory at the 5 mm level. Out of nineteen cases of known fish or shellfish allergy, the preparations in use gave a skin prick reaction of 5 mm or more in fifteen.

It may be concluded that, despite the continuing difficulty in providing purified allergens for diagnostic tests, a combined analysis of skin test reactions, clinical diagnosis and RAST can assist in the standardization of skin test preparations. It is suggested that where clinical diagnosis is the principal purpose, individual preparations should have their skin reaction range defined for groups of atopic and non-atopic subjects. If 3 mm is then to be regarded as a convenient threshold for an abnormal response, the dilution of different test materials may have to be adjusted accordingly.

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