

Short communication

Correlations between skin prick tests using commercial extracts and fresh foods, specific IgE, and food challenges

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The skin prick test is the most widely used test for detecting IgE-mediated food hypersensitivity. Our study aimed to define firstly the correlations between results obtained with prick tests using commercial extracts and fresh foods, and secondly the correlations between these results and those obtained with labial and/or oral challenge. We compared the wheal diameters read at 15 min with commercial extracts and fresh foods, for four foods, in 430 children with suspected food allergy. For cow's milk, wheal diameters were larger with commercial extracts, but the difference was not significant. Conversely, wheal diameters were significantly larger with fresh foods for the other food allergens. Skin prick tests were positive in 40% of cases with commercial extracts and in 81.3% with fresh foods. The overall concordance between a positive prick test and positive challenge was 58.8% with commercial extracts and 91.7% with fresh foods. These results indicate that fresh foods may be more effective for detecting the sensitivity to food allergens. Fresh foods should be used for primary testing for egg, peanut, and cow's milk sensitivity.

Key words: challenge; commercial extract; correlation; food allergy; fresh food; sensitivity; skin prick test; specificity.

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The skin prick test (SPT) is the most widely used test for detecting IgE-mediated food hypersensitivity. This technique is simple; rapid; associated with less discomfort, compatible with testing more allergens per session, and less apt to give rise to systemic reactions than other tests; and inexpensive (1–4). If the SPT are positive, further investigation can be carried out by measurement of specific serum IgE and by oral challenge, which is the cornerstone of the diagnosis of food allergy (5–8). The quality of the allergen extracts used in SPT influences the results. Some food allergens rapidly lose their antigenic properties and the corresponding extracts sometimes have no allergenic activity (9, 10). Our study aimed to define the correlations between the results obtained with SPT using commercial extracts and using fresh foods, and also to define any correlations with food challenge.

Material and methods

Subjects

The study group comprised 430 children (136 girls and 294 boys; average age, 4.2 years; range 2 months to 20 years) who were admitted to the day hospital from December 1993 to December 1995. All of these patients had a history of immediate hypersensitivity to foods. The control subjects comprised 2189 children, who suffered from atopic dermatitis, bronchial asthma, urticaria, or edema, but these patients had negative SPT whatever the commercial and/or fresh foods used.

Commercial SPT

SPT were done with Stallergènes (France) extracts (1 : 10 w/v). We tested egg yolk, egg white, peanut, and cow's milk (casein, lactalbumin, and whole

milk). CSPT were done on the volar side of the forearm with a lancet from Dome Hollister-Stier, Slough, UK (1-mm tip) by placing a drop of extract on the skin and pricking through the drop. The CSPT results were assessed by relating wheal area to that induced by histamine, 10 mg/ml histamine base, and/or codeine 9% if histamine was negative. We excluded a dermographic reaction with a negative control solution: 50% glycerosaline solution. Only wheals half the average of the positive control or more, and equal to or larger than 3 mm were considered positive.

Fresh SPT

Fresh SPT were done by the prick+prick technique (11). The fresh foods were bought locally, frozen as 1-cm³ cubes, and then thawed at room temperature on the day of the test. Foods with a hard consistency, such as peanut, were ground, diluted in buffered saline at 1/3 w/v, or 500 mg of food to 1.5 ml of saline. The same foods were tested as by CSPT, except cow's milk. Only whole milk was tested by FFSPT. The results of FFSPT were calculated by the same method as the CSPT.

We compared the diameter of the wheal obtained with commercial extracts and with fresh foods for the four foods.

Specific IgE

Most patients were tested by ELISA specific IgE (DPC-Behring Diagnostic, France) for these food allergens. Only results of 1.50 IU/ml or more (> class 1) were taken as positive.

Challenge tests

We carried out labial challenge by the technique described by Moneret-Vautrin (12). Positivity was rated on a scale of 1–5: 1) smoothing of the lower lip, 2) erythema below the lip, 3) contigus urticaria of the cheek and chin, 4) edema of the cheek associated with rhinitis and watering of the eyes, and 5) systemic reaction associated with pruritus of regions affected by eczema, and coughing. A negative labial challenge test was followed by a single-blind oral challenge. Positivity criteria were the appearance of systemic, respiratory, cutaneous, or digestive manifestations (vomiting, diarrhea). Labial challenge were done in 85% of cases.

The diagnostic accuracy of SPT and specific IgE is based on the results of food challenges. Food allergy was diagnosed on the basis of positive skin tests, associated with the presence of specific IgE (greater than 1.50 IU/ml) and with positive labial and/or oral challenge.

Data analysis

Fisher's test or the chi-square test was used for statistical analysis.

We calculated sensitivity, specificity, positive predictive accuracy (PPA), and negative predictive accuracy (NPA) by the method of Goldman (13).

Results

All patients had positive SPT either with commercial extracts or with fresh foods, or both. SPT were positive with commercial extracts in 40% of cases (172 positive results of 430 patients tested) and with fresh foods in 81.3% (350 positive results of 430 patients tested): $P < 0.001$ (chi-square test). Specific IgE was done in 351 patients (81.6%), and positivity was noted in 70.6% of cases (248 positive results). Labial and/or oral food challenges were carried out in 209 children (48.6%), and were positive in 81.3% of cases (170 positive results).

The overall correlation between SPT (equal to or larger than 3 mm) and positive challenges was 52% with commercial extracts, and 80% with fresh foods (this difference was significant). We also observed that challenges in 40.5% of negative commercial SPT were positive, and only 7.4% were positive for negative fresh SPT. This demonstrated that a negative fresh SPT could exclude food sensitization. Conversely, food allergy was detected in half the cases when commercial extracts were used (Table 1).

The correlations between specific IgE, SPT using commercial extracts and fresh foods, and both are presented in Table 1.

When compared with the commercial extracts, more positive challenge tests were obtained when using both fresh SPT and specific IgE. On the other hand, fewer positive challenge tests were noticed when both negative fresh SPT and specific IgE were used. There was a significant statistical difference (Table 2).

Wheal diameter was larger with commercial cow's milk extract, but the difference was not significant. Conversely, wheal diameter was significantly larger with fresh food for the other food allergens (Table 3).

Sensitivity was excellent with fresh foods for egg white and peanut. Specificity appeared to be higher with fresh foods for cow's milk (Table 3).

The positive predictive accuracy was higher with commercial extracts, except for cow's milk. The negative predictive accuracy was higher with fresh foods for egg white, peanut, and cow's milk (Table 3).

Table 1. Correlations between positive challenges, negative challenges, SPT with commercial or fresh extracts, and specific IgE results with individual foods

	Positive challenges (n)						Negative challenges (n)					
	SPT > 3 mm			SPT < 3 mm			SPT > 3 mm			SPT < 3 mm		
	CE	FF	P	CE	FF	P	CE	FF	P	CE	FF	P IgE (%)
Overall results (%)	58.8	91.7	<0.001	40.5	7.4	<0.001						
Egg white	26	53		26	0		5	10		9	1	79
Peanut	22	52		41	11		78	17		62	78	60.7
Cow's milk	9	9		14	14		16	0		7	10	55

SPT: skin prick test; CE: commercial extract; FF: fresh food; P (chi-square test).

Table 2. Correlations between food challenge and both positive or negative SPT/specific IgE

	SPT and IgE both positive (%) with positive food challenge			SPT and IgE negative (%) with positive food challenge		
	CE	FF	P	CE	FF	P
Egg white	43	79.3	0.005	1.8	0	
Egg yolk	15.8	52.9	<0.001	0.5	0	
Peanut	47.3	70.5	<0.001	3	0.5	
Cow's milk	47.1	35.2		0	0	

SPT: skin prick test; CE: commercial extract; FF: fresh food; P (chi-square test).

In other words, we observed more false-positive SPT with fresh foods and more false-negatives with commercial extracts.

Discussion

Blackley first introduced the technique of skin tests in 1873 in the form of scarifications. The SPT was described by Lewis and Grant in 1924 and modified by Pepys in 1972 (10). SPT with an allergen seek specific antibodies (mainly of the IgE type) to this allergen on cutaneous mast cells. Fresh food

extracts give a stronger, more sensitive response than commercial extracts. Results are also better correlated with positive challenges, the cornerstone of the diagnosis of food allergy. The age of the child must be taken into account. The papule is smaller in children aged under 3 years. Its size then increases up to the age of 20 years, with no difference between the sexes (4, 14). The use of other methods (intradermal reaction, scratch tests) is limited in the child because of their painful nature and the possibility of a systemic reaction. Various needles are available: the type and make used must be specified in all studies (15). Nelson et al. (16) compared the diameter of the wheal obtained with five different commercial SPT devices. They obtained 99% specificity with a 2-mm wheal, using a prick lancet (Dome Allergy Products). Lastly, the size of the papule must be compared with the sizes of the positive and negative controls (17).

The quality of the extracts used, which has improved over the last 15 years, affects the results. Other factors must also be taken into consideration, such as operator technique and histologic qualities of the skin (vasculature, number of H₁-receptors, number of mast cells, and dermal thickness) (18). Some food allergens are destroyed in a few minutes by oxidation, making standardization

Table 3. Correlations between results obtained with commercial extracts and fresh foods

	Egg white		Egg yolk		Peanut		Cow's milk	
	CE	FF	CE	FF	CE	FF	CE	FF
No. of tests		128		75		119		22
Mean wheal	2.7*	5.3*	1.1*	5.4*	3.7	5.9	6	3.6
Positive SPT (%)	45	96*	18	76*	50.4	79.8*	68	54.5
No. of challenges		70		9		65		17
Sensitivity (%)	56	100	16	60	66	90	73	66
Specificity (%)	80	10	0	33	69	30	50	100
PPA (%)	93	87	100	66	91	86	91	100
NPA (%)	28	100	37	33	30	40	20	28

SPT: skin prick test; CE: commercial extract; FF: fresh food; PPA: positive predictive accuracy; NPA: negative predictive accuracy; *P < 0.001.

difficult. Ortolani et al., Rosen et al., and Norgaard et al. have demonstrated the superiority of SPT with fresh foods (19–21).

With regard to eggs and cow's milk, Norgaard et al. compared SPT with fresh foods and commercial allergen extract in 17 adults suspected of type I egg and/or milk allergy (21). The sensitivity of commercial SPT was 0.75, and none of the tests showed concordance with the double-blind, placebo-controlled food challenge (DBPCFC). With fresh foods, the overall sensitivity of SPT was 1.00 and showed concordance with the DBPCFC ($P < 0.05$). Thus, skin test sensitivity and concordance with oral challenge are improved when fresh foods are used. Our own results match the data described above. The exception of cow's milk arises from the fact that commercial extracts allow testing not only of whole milk but also of the different milk proteins (casein, α -lactalbumin, and β -lactoglobulin), which is not possible with fresh milk.

With regard to peanut, when compared with CSPT or RAST, for a group study of 100 adults with history of oral allergy syndrome, Ortolani et al. (19) showed better sensitivity with fresh SPT for foods such as carrot, celery, cherry, apple, and potato. But the sensitivity was better with commercial extract for foods such as peanut, almond, banana, and pea. The low sensitivity of CSPT may be due to a loss of allergenicity during extract preparation. Conversely, our study showed a better sensitivity with ground peanut.

Rosen et al. (20) confirmed the superiority of fresh extracts in a study of 22 patients including nine children, of whom 14 had presented an anaphylactic reaction and eight an oral syndrome after intake of foods other than fruit or vegetables. In fact, all these patients had positive SPT with fresh foods but negative SPT with commercial extracts of peanut, fish, shellfish, other mollusks, egg, and milk.

In an earlier study, we observed 86% concordance between SPT and oral challenge in a series of 105 children with suspected food allergy. With fresh foods, the concordance increased to 91.7% (22). Most authors agree that correlation is better when fresh foods are used (19–21, 23–25).

In conclusion, these results suggest that fresh food extracts are more effective in detecting sensitization. Thus, in the first instance, it would seem advisable to use fresh foods for SPT with egg, peanut, and probably cow's milk. Our study will be continued with other foods. The method and the extract used have considerable influence, and should be clearly detailed in all epidemiologic investigations in order to obtain good reproducibility and to assess the positivity limit.

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