

Allergy to Apple, Carrot and Potato in Children with Birch Pollen Allergy

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Skin sensitivity to apple, carrot and potato, clinically related to birch pollinosis was investigated. Different skin test techniques using fresh fruit were compared. A simple prick test (SPT) technique with a lancet piercing the apple peel just before pricking the skin was shown to be the most practical and to give reproducible results. The allergenic activity in apple was found to be heat labile and deteriorated during storage at room temperature. Apple, carrot, potato, hazelnut and birch reactivity was transferable in Prausnitz-Küstner test like IgE antibodies. SPT reactivity to fresh material from apple, carrot and potato was investigated in 174 children of whom 128 suffered from pollen allergy. Positive SPT results were obtained almost exclusively in children who were SPT positive to a birch pollen extract. Children who noticed clinical symptoms when eating apple, raw carrot or potato were found to have a significantly larger SPT reaction than children with a negative history.

Key words: apple allergy; birch pollen allergy; carrot allergy; potato allergy; Prausnitz-Küstner test; skin test techniques.

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Already in 1948 Juhlin-Dannfeldt reported that birch pollen allergic patients often had a concomitant clinical sensitivity to nuts and fruits, with oral pruritus as the main symptom (8). This association between a specific pollen allergy and reactions to foods, mainly hazelnut, fresh apple, raw carrot and potato, has gained new interest lately. The association between birch pollen allergy and these food reactions has been confirmed and an increased incidence has been reported with increasing severity of the birch pollen allergy (6).

A partial identity has been demonstrated between birch pollen and hazelnut allergens using crossed line immunoelectrophoresis (2, 4) and RAST inhibition (9). With the former technique no partial identity was found between a birch pollen extract and fresh peel from apple and potato (2). On the other hand, positive apple RAST reactions could be totally inhibited by birch pollen extract (9). Löwenstein & Eriksson could inhibit birch pollen RAST but not CRIE with foods and concanavalin A (10).

Skin tests with fresh foods are generally regarded to be unreliable but Hannuksela & Lahti (7) have shown a scratch chamber test using fresh apple, raw carrot and potato to give clinically relevant reactions and Andersen & Löwenstein (2) found positive skin tests not only with freeze-dried extracts but also by pricking the skin through apple and potato peel placed on the skin.

The aim of the present study was to develop a simple skin test technique for routine diagnosis of allergy to apple, carrot and potato in children, to investigate by the Prausnitz-Küstner test the nature of these skin reactions and to study their clinical relevance.

MATERIAL AND METHODS

In the experimental part of the study all tests were performed by the authors on medical students or colleagues.

In the clinical part of the study 174 children (age 4-18, mean 12 years) were tested. Almost

all of the children, from pre-school ages and older, visiting for the first time the outpatient allergy clinic at the Department of Paediatrics during a period in 1980–1981 were included ($n = 99$). In addition, 75 children undergoing immunotherapy for pollen allergy ($n = 70$) or insect allergy ($n = 5$) were tested.

Fifty-two of the children suffered from birch pollen allergy (group B) and 48 additional children from birch pollen allergy combined with grass and/or mugwort pollen allergy (group B+G/M). Twenty-six children were allergic only to grass and/or mugwort (G/M) and 48 children had other kinds of allergy or asthma or rhinitis without any detectable allergy (group C).

The diagnoses of birch and grass pollen allergy were based on typical histories, positive skin prick tests and in many cases also a positive RAST. Mugwort allergy sometimes demanded a nasal or conjunctival provocation test to be confirmed. The diagnosis of clinical sensitivity to apple, carrot or potato was based only on the history.

Skin test techniques

Skin prick tests were performed with a lancet according to the method described by Pepys (12). Two perpendicular diameters of the wheals were recorded and their mean calculated. Wheals of at least 2 mm diameter were regarded as positive. In the experimental studies skin prick tests were usually performed in duplicate or triplicate. In the clinical part they were performed by an experienced nurse as single prick tests on the forearm together with the screening test panel of eight allergens representing the most common airborne allergens, and with histamine chloride 1 mg/ml.

In the experiments designed to evaluate different skin test techniques using fresh apple (Fig. 1) the following applications of allergen were chosen: a lancet was pricked into the apple and immediately thereafter into the skin (prick + prick); the skin was pricked and a piece of apple was firmly taped to this place (prick + taped fruit); the skin was pricked and a piece of apple was rubbed on this place (prick + rubbed

SKIN TESTS WITH FRESH APPLE

Technique					
Prick+prick					A
					B
Prick+taped fruit					A
					B
Prick+rubbed fruit					A
					B
Rubbed fruit+prick					A
					B
Scratch+taped fruit					A
					B
Histamine 1mg/ml					A
					B
Negative control					A+B

Fig. 1. Original results of skin prick tests obtained with fresh apple in two birch/apple sensitive subjects A and B. For explanation of techniques see "Methods".

fruit); the skin was rubbed with apple and immediately thereafter pricked (rubbed fruit + prick); the skin was scratched about 2 mm with a lancet and a piece of apple was applied (scratch + taped fruit).

In the Prausnitz-Küstner serum transfer test HBsAg-negative serum from one birch pollen allergic donor was used. This donor had the birch pollen allergy associated sensitivities to nuts and raw apples, carrots and potatoes. He was also skin prick test positive to these foods. In each of two recipients 30 portions of 0.2 ml serum were injected into the skin of the back. Challenge was performed by prick + prick tests (see above) after 4 and 24 h on sites of serum injection and after 24 h on non-sensitized skin. Both non-heated and heated (56°, 30 min) serum was used. The tests were performed in duplicate on reversed sites of the back.

The Students' *t* test was used in the statistical calculations.

RESULTS

Experimental studies

Skin test techniques. Pricking the fruit just before pricking the skin seemed to fulfill the demands of a simple test with good reproducibility and well outlined wheals without too much pseudopodia (Fig. 1). As similar results were obtained with the carrot and potato this prick test technique was used in the following experiments.

Allergen variability. Five different apple brands (Transparent Blanche, Gravensteiner, Democrate, Granny Smith and Golden Delicious) gave very similar wheal sizes in prick tests performed in triplicates on the forearm of one apple allergic adult. No difference was found when apple near to the peel and near to the core were compared.

Allergen stability. The clinical observation that apple allergic patients often tolerate apple cake or apple sauce made us interested in the storage and heat stability of the apple allergen(s). Two apple allergic students were skin prick tested with fresh apple and apple slices stored at room temperature and heated to 175°C re-

spectively. In student A a decreasing wheal size was seen with increasing storage time and no reaction at all with the heated apple (Table 1). In student B the reactions were much larger with pseudopodia but the same tendency was found although the heated apple still gave moderately positive skin reactions.

Prausnitz-Küstner test results. In recipient A positive reactions were obtained with all five allergens but only in the sites sensitized for 24 h with non-heated serum (Table 2). Recipient B was found to be skin test positive to the allergens used although he had no clinical symptoms when exposed to the allergens. In spite of that a tendency for stronger reactions was seen in the skin sites sensitized for 24 h with non-heated serum (Table 2). The transferred skin reactivity thus behaved like IgE antibodies.

Clinical study

Apple. Ninety per cent of the tested birch pollen allergic children (groups B and B + G/M) were skin prick test positive to fresh apple with an average wheal size of 150% of that obtained with the histamine control, 1 mg/ml (Fig. 2, Table 3). This means that the mean wheal dia-

Table 1

The stability of apple allergens at different temperature and storage time. The mean diameter of the individual wheals and their mean are given in mm

Temp.	Storage time (hours)	Subject A	Subject B
20°	0	4.0	7.75
		3.5	8.25
		3.25	9.5
		3.6	8.5
20°	3	3.5	8.25
		3.75	7.0
		2.75	7.0
		3.3	7.4
20°	12	2.25	8.25
		2.25	7.0
		2.50	8.5
		2.3	7.9
175°	0.5	—	3.9
		—	3.25
		—	4.0
		—	3.7

Table 2

The results of Prausnitz-Küstner passive transfer test in two recipients using serum from one birch/fruit sensitive donor. The mean wheal diameters of duplicate tests are given in mm

Interval sensitization-challenge	4 h		24 h					
Serum	Non-heated				Heated		No serum	
Subject	A	B	A	B	A	B	A	B
<i>Allergen</i>								
Birch	neg.	1.5	3.8	5.0	neg.	1.8	neg.	2.3
Hazelnut	neg.	4.0	4.8	6.3	neg.	2.5	neg.	3.3
Apple	neg.	4.8	4.3	4.5	1.5	3.0	neg.	1.8
Carrot	neg.	neg.	2.5	5.0	neg.	2.0	neg.	3.3
Potato	neg.	1.8	4.0	6.3	1.8	4.0	neg.	3.8

Table 3

The mean wheal diameter in skin prick tests expressed as per cent of the mean diameter obtained with histamine 1 mg/ml

	Apple	Carrot	Potato
<i>Group</i>			
B	152	154	164
B + G/M	146	149	154
G/M	92	113	103
C	84	85	132
<i>B + B + G/M</i>			
History pos.	160	191	208
History neg.	130	127	157

meter was about 6 mm. Forty-six per cent of the children with grass and/or mugwort allergy (group G/M) and 17% of the controls (group C) had a positive apple skin test. The mean wheal size was significantly smaller ($P < 0.05$ and $P = 0.05$ respectively) than that obtained in the birch pollen allergic children. Furthermore, about 70% of the apple test positive children in the G/M and C groups had a positive skin prick test with the birch pollen extract without any history indicating birch pollen allergy.

Sixty-three per cent of the birch pollen allergic children reported clinical symptoms when eating apple. They were all apple skin test positive with a larger mean wheal size than those birch pollen allergic children who were apple skin test positive but tolerated apple ($P < 0.05$).

Only one patient each in groups G/M and C reported symptoms when eating apple and they were both skin prick test positive to the birch pollen extract and to fresh apple.

Carrot. The skin prick tests to raw carrot yielded 85–90% positive reactions in the birch pollen allergic children and 50% and 25% respectively in the G/M and C groups (Fig. 2). Sixty-five per cent of the carrot skin test positive children in the latter groups were skin test positive to the birch pollen extract as well, although they lacked clinical symptoms during the birch pollen season. The wheal size in groups B and B + G/M was significantly larger than that in the C group ($P < 0.05$) but not larger than that in the G/M group (Table 3).

Clinical allergy to raw carrot was noted only in carrot skin test positive children. Forty-two per cent of the carrot skin test positive children in group B and 35% in group B + G/M reported such symptoms (Fig. 2). They had a significantly larger carrot skin test wheal than the children of the same groups who tolerated carrot ($P < 0.001$).

Potato. The skin test reactions to raw potato were rather similar to those of fresh apple and raw carrot although very few patients reported symptoms on contact with raw potato (Fig. 2). Between 80 and 85% of the birch pollen allergic children were skin test positive to raw

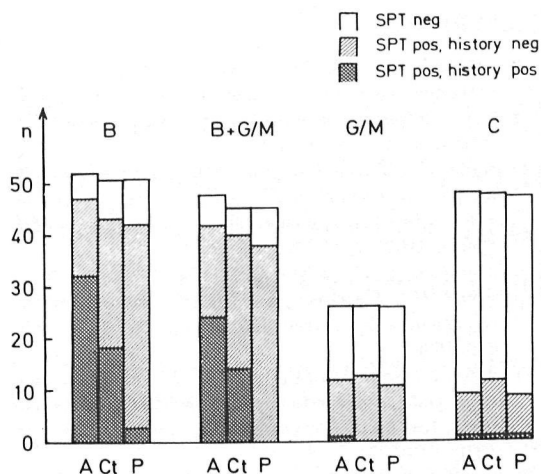


Fig. 2. The results of skin prick tests with fresh apple (A), carrot (Ct) and potato (P) and their relation to the clinical history in 174 children.

potato compared with 42% and 19% respectively in the G/M and C groups. The birch pollen allergic children had a significantly larger wheal than the children in the G/M group ($P < 0.05$). The majority of the potato skin test positive children in the groups G/M and C were also skin test positive to the birch pollen extract.

Only four children reported clinical symptoms on contact with raw potato. They had a significantly larger mean wheal size than the potato skin prick test positive children in the same groups without notable clinical symptoms ($P < 0.02$).

DISCUSSION

Our results confirm the association between birch pollen allergy and reactivity to apple, carrot and potato previously described mainly in adults (6, 7, 8). No conclusion regarding the true incidence of these food reactions in birch pollen allergic children can be drawn as all patients were referred to us and the material thus selected.

Positive skin reactions to the foods were found in all children reporting clinical symp-

toms and they had significantly larger wheals than those skin test positive children who tolerated the foods. The fact that a few weakly positive food skin tests were found in birch pollen skin test negative children may be ascribed to the low cut-off limit for a positive skin test with the fresh foods.

The use of fresh foods for skin testing has practical advantages but involves a risk of eliciting falsely positive reactions. The simple prick test technique with the fresh foods used in this study on a routine basis seemed to give at least as reliable results as the scratch chamber test used by Hannuksela & Lahti (7) and the prick test technique used by Andersen & Löwenstein (2).

A much higher percentage of skin test positive children had clinical allergy to apple than to raw carrot or potato although the skin test wheals with the foods were of the same size. Assuming that the size of the wheals reflect only IgE antibody activity, which was indicated by the Prausnitz-Küstner serum transfer tests, the difference in the incidence of clinically manifest allergy may seem peculiar. One explanation may be that the allergens in the raw carrot and potato are less readily available to the sensitized cells in the mucous membranes. Another explanation may be that other local factors influence the reactivity of the mast cell system in the mucous membranes. Children eat more apples than raw carrots and potatoes and they rarely peel raw potatoes. The greater exposure to apples may have induced such local factors in the mucosa. The occurrence of positive skin tests without clinical symptoms would thus reflect latent allergy rather than non-specific reactions.

The P-K test results are in agreement with the concept that these birch-related food sensitivities are allergies of type I according to Coombs & Gell (5). This has already been suggested by Lahti et al. (9), who could couple apple seed proteins to activated paper discs and subsequently show an IgE specific uptake with serum from patients with clinical sensitivity to apple.

Furthermore, the results exclude the presence in the test serum of IgG antibodies with skin sensitizing properties (11).

Why these food allergies are coupled to birch pollen allergy is still unclear. RAST inhibition studies (9) but not crossed line immunoelectrophoresis (2) indicate common allergens between birch pollen and apple. Why botanically so unrelated foods such as apple, carrot and potato should share allergens remains unexplained. A similar association has been reported between ragweed pollinosis and clinical sensitivity to melon and banana (3). Furthermore, a mutual inhibition of the IgE antibody uptake in RAST has been demonstrated between proteases, wheat and rye flour and grass and birch pollens (1). Aalberse and coworkers (1) suggest that the common finding of non-immune binding of IgE in extracts of some vegetables may be caused by a carbohydrate side chain in glycoproteins which are found in many plants. In their experience, this glycoprotein activity was heat stable and did not seem to give any clinical reactions. This is not in agreement with the present study in which the activity in apple, carrot and potato did give clinical symptoms of the immediate type and seemed to be heat labile.

We conclude that there is a strong association between birch pollen allergy and clinical reactivity to fresh apple, raw carrot and potato. This allergy is mediated by IgE antibodies and can easily be diagnosed by a simple prick test technique using fresh material. The poor reputation assigned to skin tests using fresh material has been restored for these foods. Whether the use of skin prick tests can be extended to other foods remains to be seen.

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