

Food Hypersensitivity in Patients with Pollen Allergy

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Six hundred patients with pollen allergy answered a questionnaire about food hypersensitivity. Hypersensitivity to various nuts, fruits and roots was reported more often by patients with birch pollen allergy (70%) than by patients without birch pollen allergy (19%). The stronger the skin test reaction to birch pollen, the higher was the incidence of food hypersensitivity. A negative correlation was found between grass pollen allergy and food hypersensitivity.

In the diagnosis of springtime hayfever, the presence of hypersensitivity to nuts, fruits and roots supports a diagnosis of birch pollen allergy.

Key words: apple; birch allergy; food hypersensitivity; lectins; nuts; oral pruritus; pollen allergy; stone fruits.

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Food can evoke hypersensitivity symptoms such as diarrhoea, urticaria, rhino-conjunctivitis and asthma. IgE-mediated allergy is usually diagnosed by means of skin tests with relevant allergen extracts. However, food hypersensitivity cannot always be accurately diagnosed by this method as relevant allergen extracts are lacking. For screening purposes anamnestic information from questionnaires therefore seems to be more suitable.

In Sweden, 25% of adult patients referred for allergy investigation report some foodstuff sensitivity (11). Nuts, apple, shellfish, oranges and strawberries were the most frequently reported causes of hypersensitivity symptoms. In a study of food-intolerant Swedish children, egg, fish, citrus fruits, chocolate and tomatoes were the most common offenders (9).

Patients with springtime hayfever often complain of itching and tingling in the lips, tongue and throat, as well as of sneezing, after eating apples or hazelnuts (13). Hannuksela & Lahti (12) found that people allergic to birch pollen (BP) had positive skin reactions to fresh ex-

tracts of some fruits and vegetables. Furthermore, hypersensitivity to hazelnuts, apples, walnuts, Brazil nuts, peaches, cherries, pears, almonds, plums, carrots and potatoes has been shown to correlate to BP-allergy (11).

The purpose of this study was to analyse the relationship between various types of pollen allergy and food hypersensitivity.

PATIENTS AND METHODS

Patients with documented pollen allergy were asked to fill in a questionnaire regarding their tolerance to various foodstuffs. The questionnaire was answered by 600 patients (305 males and 295 females) with an average age of 26 years (range 3-75). The numbers of individuals in the various age groups are given in Fig. 1.

The patients were asked whether they had noticed symptoms like itching, cutaneous eruptions, oedema, nasal or ocular irritation, difficulty in breathing, cough or digestive problems after handling or eating any of 40 foodstuffs (see Table 2). For each foodstuff one

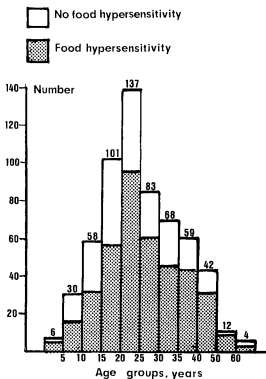


Fig. 1. Food hypersensitivity in various age groups. The figures at the top of the columns indicate numbers of patients.

of the following alternatives was to be filled in: "yes", "no", or "I do not know". If the answer was "yes", they were also to describe the symptoms experienced. Additional questions to be answered were whether fresh fruit or tinned fruit elicited symptoms, and for how long the patients had suffered from hayfever.

Skin tests. The patients were prick tested with a number of allergens, including BP extracts (*Betula verrucosa*) and, in most cases, pollen extract from a number of other deciduous trees as well. They were also tested with different grass pollens (*Phleum pratense*, *Alopecurus pratensis*) and mugwort (*Artemisia vulgaris*). We employed biologically standardized, glycerinated allergen extracts prepared at the Allergy Laboratory, Sahlgren Hospital, Gothenburg. The reactions were graded according to the recommendations of the Standardization Committee of the Nordic Society of Allergology (1). A wheal of the same area as the positive histamine reference was recorded as three plus (+++), a reaction of half the size was recorded as two plus (++), and a reaction less than (++) but still positive in relation to the negative reference (Coca's solution) was recorded as one plus (+).

The radioallergosorbent test (Phadebas RAST[®]) was used in some of the children instead of skin testing. The activity was expressed in RAST-classes 0–4.

Pollen allergy diagnosis

When judging whether there was a relevant allergy or not to the different pollens, the following criteria were used:

Non-allergic: Negative skin test or RAST-class 0, and no history indicating allergy.

Allergic: Skin test $\geq$ (+++), or RAST-class 2–4.

Doubtful: Skin test reaction (+/++) or RAST-class 1.

Table 1
Relationship between reported food hypersensitivity and birch pollen allergy

	Incidence (%) of food hypersensitivity in patients with			Difference between groups
	Birch pollen allergy (n = 380)	Doubtful birch pollen allergy (n = 117)	No birch pollen allergy (n = 103)	
Any food	77	52	36	*
Hypersensitivity to birch pollen-related food (see Table 2)	70	41	19	*

* $P < 0.001$.

Statistics

For statistical analyses Pitman's non-parametric permutation test was used (8). When correlation between food sensitivity and pollen allergy other than BP-allergy was analysed, the background variable BP allergy was taken into account by using the following non-parametric partial correlation test: the patients were divided into subgroups according to the strength of their skin test reaction to birch pollen. Within each subgroup Pitman's test variable was calculated. The results from the different groups were then pooled in a summarizing test (17).

RESULTS

Of the 600 patients, 380 had a convincing BP allergy and 117 a doubtful BP allergy. 290 patients were allergic to grass pollen and 143 to mugwort.

Table 2

Reported hypersensitivity to various foodstuffs in patients allergic to birch pollen and patients without birch pollen allergy

a) Foodstuffs with obvious relationship to birch pollen allergy:

	Incidence (%) of hypersensitivity in		
	Patients with birch pollen allergy (n = 380)	Patients without birch pollen allergy (n = 103)	Difference between groups
Hazelnuts	53	7	***
Apples	47	6	***
Peaches	34	5	***
Cherries	29	3	***
Almonds	27	3	***
Walnuts	26	6	***
Pears	26	4	***
Carrots	23	3	***
Plums	21	6	***
Potato peel	20	4	***
Brazil nuts	20	4	***
Peanuts	14	4	***
Dessert almonds	11	3	***
Apricots	8	1	***
Cocomuts	6	1	***

b) Foodstuffs with possible relationship to birch pollen allergy:

Tomatoes	18	2	**
Oranges	12	7	*
Grapes	5	4	*
Hips	4	2	*
Wild strawberries	3	2	*
Chinese gooseberries (Kiwi)	3	1	*
Melons	3	2	*
Beer	3	3	**
Parsley	3	1	*
Swedes	2	2	***
Celery	2	0	*
Avocado	1	0	**

c) Foodstuffs without statistically significant relationship to birch pollen allergy:

Strawberries	13	7	ns
Peas	11	5	ns
Shell-fish	10	11	ns
Figs	7	3	ns
Bananas	6	4	ns
Egg	6	6	ns
Wine	6	5	ns
Fish	6	3	ns
Cheese	5	5	ns
Onions	4	9	ns
Milk	2	3	ns
Parsnips	1	2	ns
Bread	1	1	ns

ns = not significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

The statistical significance of differences between groups is derived from analysis of the answers from all the patients, thus including those who could not clearly state "yes" or "no". The incidence of "I do not know"-answers in the groups thus affects the significance.

Food hypersensitivity was reported by 390 patients (65%) and was much more common in patients with BP allergy than in others (Table 1). For some foods, such as nuts, fruits and roots, the difference in incidence of hypersensitivity between patients with BP allergy and those allergic to other pollens was obvious (Table 2a). For some berries and fruits the difference was less clear (Table 2b), and for some foodstuffs no difference was noted (Table 2c). The foodstuffs listed in Table 2a will henceforth be referred to as BP-related foodstuffs (BPRF). The various BPRF elicited symptoms in fresh condition but were usually tolerated when tinned.

Table 3
Incidence of birch pollen allergy in relation to the number of birch pollen-related foodstuffs to which hypersensitivity was reported

	Number of birch pollen-related foodstuffs to which hypersensitivity was reported							
	0	1	2	3	4	5	6	≥ 7
No. of patients	266	59	41	32	37	29	34	102
Incidence of birch pollen allergy (%) [*]	68.7	86.0	82.5	93.5	97.2	96.4	94.1	99.9**

^{*} In these figures, patients with prick-test reaction ≥ + or RAST-class ≥ 1 to birch pollen allergen are included.

^{**} The only non-birch pollen allergic patient with hypersensitivity to more than 6 birch pollen related foodstuffs had an acetylsalicylic acid intolerance.

The greater the number of BPRF a patient stated that he did not tolerate, the higher was the probability that the patient was allergic to BP, and the figure approached 100% with four or more BPRF (Table 3). Of the 14 patients not allergic to BP, who reported symptoms from two or more BPRF, eight also complained of hypersensitivity symptoms from foodstuffs which are not related to BP allergy. Oral pruritus, which was commonly elicited by BPRF in patients allergic to BP, was reported by only seven of the 14 patients who were not allergic to BP.

There was a positive correlation between the size of the skin reaction to BP extract and the incidence of hypersensitivity to BPRF (Fig. 2).

A strong correlation was found between the prick test reaction to BP and hypersensitivity to alder (*Alnus glutinosa*), hazel (*Corylus avellana*), aspen (*Populus tremula*), linden (*Tilia cordata*), sallow (*Salix caprea*), oak (*Quercus robur*), bog-myrtle (*Myrica gale*), beech (*Fagus sylvatica*) and elm (*Ulmus glabra*) ($P < 0.01$), while no correlation was found between BP and grass, and only a weak correlation ($P < 0.05$) between BP and mugwort (*Artemisia vulgaris*).

A positive correlation was also found between hypersensitivity to some of the BPRF and prick test reactions to some other deciduous trees (Table 4). Patients who were allergic to both BP and these other deciduous trees more often reported food hypersensitivity than patients

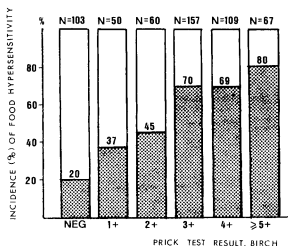


Fig. 2. Hypersensitivity to birch pollen related foodstuffs in relation to the strength of the prick test reaction to birch pollen allergen.

Table 4

Correlation between prick test reactions to some deciduous trees and hypersensitivity to some foods

	Alder <i>n</i> = 492	Hazel <i>n</i> = 486	Aspen <i>n</i> = 391	Bog-myrtle <i>n</i> = 318	Oak <i>n</i> = 313
Hazelnuts	***	**	*	*	ns
Walnuts	*	*	ns	ns	ns
Brazil nuts	ns	*	ns	ns	ns
Almonds	**	ns	ns	ns	ns
Apples	***	***	*	**	ns
Pears	*	***	ns	*	ns
Plums	**	ns	ns	ns	ns
Cherries	**	**	ns	ns	ns
Peaches	**	**	ns	*	ns
Apricots	ns	*	ns	ns	ns
Carrots	***	***	***	***	***
Potatoes	**	ns	ns	**	**
Bananas	ns	ns	*	*	**

ns = not significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Table 5

Hypersensitivity to birch pollen-related foodstuffs in relation to the strength of the prick test reaction to grass pollen allergen extracts

	Prick test reaction to grass pollen					
	neg	1+	2+	3+	4+	≥ 5+
No. of patients	134	69	91	156	73	24
Incidence of food hypersensitivity (%)	77	63	69	51	49	40

Significance of negative correlation: $P < 0.001$. The degree of concomitant birch pollen allergy was taken into account in the statistical analyses (see Methods).

Table 6

Relationship between type of symptoms and type of foods causing hypersensitivity reactions

	Incidence (%) of symptoms in patients with hypersensitivity to	
	Birch pollen-related foodstuffs only (<i>n</i> = 255)	Other foodstuffs (<i>n</i> = 33)
Oral pruritus	78	24
Rhino-conjunctivitis	41	21
Urticaria	17	24
Asthma	11	21
Eczema	11	9
Gastrointestinal symptoms	8	30

with BP allergy alone. A negative correlation was found between hypersensitivity to BPRF and prick test reactions to grass pollen allergens (Table 5).

Oral pruritus was the symptom that was most often provoked by BPRF. The next common symptom was irritation of the nose and eyes, while urticaria or asthma was less common. Other foodstuffs elicited rhino-conjunctivitis, urticaria and asthma just as often as oral pruritus (Table 6).

Food hypersensitivity was more common among women than among men. Two hundred and thirty of the females (78%) and 160 of the males (53%) reported food hypersensitivity ($P < 0.001$). The sex difference was observed

with both BPRF and other foods. The prevalence of food hypersensitivity was the same in all age groups (Fig. 1). As regards individual foodstuffs, a significant difference between the age groups was found only for egg, which elicited hypersensitivity symptoms more often among younger patients ($P < 0.001$). The duration of the pollen allergy did not correlate to the presence of food hypersensitivity.

DISCUSSION

For precise diagnosis of food allergy, only a few allergen extracts (e.g. cod, peas, nuts, eggs and peanuts) can be used in skin test and RAST (2). Hypersensitivity to some fruits, vegetables and roots can be detected by the scratch chamber test, using raw, fresh or deep-frozen edible products (12, 14). According to some authors a reliable diagnosis can only be obtained by double-blind provocation with foodstuffs given orally in capsules (18). Such a procedure is inconvenient for diagnosing food allergy even in a single patient, and impossible to use for studying the incidence of food hypersensitivity in large groups of patients. In this study, we therefore based the diagnosis of food hypersensitivity on the answers to the questionnaires. This method will mainly give information on reactions occurring close to food intake and gives little information on late responses. Although the diagnosis is not very precise, it is not likely that the error differs between people allergic to BP and those allergic to other pollens. The main purpose of this study was to evaluate the relationship between pollen allergies and hypersensitivity to certain food.

In this study we have found various nuts and fruits to be the most often reported causes of food hypersensitivity. The kind of food most commonly eliciting hypersensitivity reactions varies considerably in different reports, however. Speer (20) found milk to be the most common food allergen, followed by chocolate, citrus fruits, legumes, corn, egg and tomato. In another study, egg, fish and milk dominated, followed by shellfish, legumes, cereals and cocoa, while fruit, vegetables and nuts were at

the bottom of the list, eliciting symptoms in very low frequency (10). In children food hypersensitivity has been proved by provocation only for peanuts and other nuts, milk, egg, soya, chocolate, legumes, citrus fruits and apple (7, 19). Patient selection, diet and socioeconomic factors in various countries must influence the prevalence of food hypersensitivity found in different investigations.

As in earlier investigations (11, 12), hypersensitivity to apple, nuts, stone fruits and roots was more common among the patients with BP allergy than among others. Food hypersensitivity was found only in 20% of patients who were allergic to grass and mugwort, but in 70% of those allergic to BP. A correlation could also be established between hypersensitivity to some of the BPRF and some tree pollen allergies besides BP allergy.

Oral pruritus was the symptom most often elicited by BPRF, while other symptoms were as common as oral pruritus in patients allergic to other foods. Patients with ragweed allergy often are hypersensitive to melon and banana, with oral pruritus as the most common complaint (4). This symptom seems to be specific for pollen-related food hypersensitivity. The reason for this might be that the allergenic factor is destroyed by enzymes in the mouth and therefore only gives rise to local reactions.

An inverse correlation was found between grass pollen allergy and hypersensitivity to BPRF. We cannot see any obvious explanation for this unexpected finding. One might speculate on genetic interactions; genes promoting the development of grass pollen allergy might prevent hypersensitivity to BPRF.

Food hypersensitivity is generally considered to occur in children. In this study, however, the same incidence of hypersensitivity to BPRF was found in all age groups. Only for egg, a foodstuff without relation to BP allergy, was the incidence higher among the younger patients.

It has been assumed that immunological cross reactivity between BP and certain food allergen exists. Thus, Belin (5) and Andersen & Løwenstein (3) have demonstrated partial immunological identity between BP and hazelnut. Lahti & Hannuksela (14) have suggested that the most

important allergens in fresh apple and carrot are enzymes. Studies in Finland, employing RAST inhibition technique, indicate that apple and BP crossreact (6, 15). On the other hand Andersen & Löwenstein, using the crossed-line immunoelectrophoresis technique, could not demonstrate a partial immunological identity between BP and extracts and fresh peel from apple and potato (3).

There are thus contradictory findings concerning the question whether cross reactivity or other mechanisms are involved in BPRF hypersensitivity. It has been suggested that lectins (i.e. plant proteins which can react with certain polysaccharides in glucoprotein) could react with the carbohydrate chain in IgE and thereby give rise to hypersensitivity symptoms (3). The hypothesis that lectins are involved in BP-related food hypersensitivity is supported by the finding that BP RAST in sera from patients with known BP allergy can be inhibited by pretreatment of the sera, not only with apple and potato allergen, but also with Con A (16). It is, however, difficult to explain the clustering of food hypersensitivity and BP allergy with a non-immunologic lectin reaction since this would imply that lectins should react only with BP-specific IgE.

Whatever the mechanisms are in BPRF hypersensitivity, knowledge of this food hypersensitivity is of clinical importance. In the diagnosis of springtime hayfever, the presence of symptoms of hypersensitivity to these nuts, fruits and roots supports a diagnosis of BP allergy. The probability of BP allergy is close to 100% when the patient reports symptoms from several of these foodstuffs. Patients with this kind of hypersensitivity should be informed that they would probably tolerate the foodstuffs when boiled or tinned.

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