

Food Sensitivity Reported by Patients with Asthma and Hay Fever

A Relationship between Food Sensitivity and Birch Pollen-Allergy and between Food Sensitivity and Acetylsalicylic Acid Intolerance

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Among adult patients with bronchial asthma and/or allergic rhinitis undergoing allergological investigation with skin test, nasal provocation test and RAST, 1129 answered a questionnaire regarding food sensitivity (FS). 276 (24%) of the patients reported some kind of allergic symptoms on eating or handling various foods, of which hazel nut, apple and shell fish were the most often named. Females reported FS more often than males.

A correlation was found between birch pollen allergy and FS with nuts, apple, peach, cherry, pear, plum, carrot and new potato. The higher the degree of birch pollen allergy, according to skin test, RAST or provocation test, the higher the frequency of FS.

A correlation was found too between acetylsalicylic acid intolerance and FS with some foods, e.g. nuts, strawberry, almond, green pepper, hip, chocolate, egg, cabbage, milk and wine.

The connection between birch pollen allergy and FS is probably explained by the structural relationship between birch pollen allergen and some allergens of the foodstuffs, whereas the high incidence of FS in acetylsalicylic acid-intolerant patients is probably explained by additives in foods as well as salicylates or benzoates naturally occurring in some food.

Key words: acetylsalicylic acid intolerance; birch pollen allergy; drug allergy; food allergy; pollen-related food allergy.

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Hay fever patients often complain of intolerance symptoms from ingestion of various nuts and fruits. Juhlin-Dannfelt (9) observed that such complaints were mainly found in patients with springtime hay fever, e.g. patients sensitive to pollen from deciduous trees, of which birch is the most important in Sweden. Belin (4) has demonstrated *in vitro* evidence for cross-sensitivity between birch pollen (BP) and hazelnut allergen. Clinical details concerning

the relation between BP allergy and food sensitivity (FS) have, however, not so far been published.

207 patients undergoing immunotherapy with pollen allergens in our department in 1972 were questioned about FS. 72% of patients treated with BP reported FS whereas only 7% of patients with other types of pollen allergy—mainly grass pollen allergy—had observed FS (Eriksson, not published).

The aim of the present study was to

elaborate further the relation between FS and various forms of other allergies in an adult allergic population.

PATIENTS AND METHODS

Patients. All patients (1376), mainly adults with bronchial asthma and/or rhinitis referred to our out-patient clinic for allergological investigation during 1973, were asked to fill in a questionnaire regarding FS and allergic symptoms from acetylsalicylic acid (ASA) compounds. A total of 1129 patients (521 males and 608 females) with an average age of 33 years (range 10–78) completed the questionnaire. Patients who answered "yes" to the question "Have you ever noticed allergic symptoms from nuts, berries, fruits, vegetables or other foods?" were asked to fill in a second questionnaire where more than 70 different foods were specially mentioned. They were asked to fill in the types of symptoms elicited according to the column headings of Table 1.

Skin tests with different inhalant allergens were performed as earlier described (5). In most cases intracutaneous tests with 10^{-3} w/v allergen extracts were used. When a strong reaction was expected according to patient history, a scratch test with 10^{-2} w/v extract was performed initially. Reactions were graded according to the recommendations of the Standardization Committee of the Northern Society of Allergology (1). Thus a wheal reaction of the same size as that of the positive histamine reference was recorded as three plus (+++). Reactions between the size of the negative phosphate-saline reference and that of the histamine reference were recorded as one or two plus (+, ++). Patients with skin test reactions of strength $\geq +$ were in this study defined as allergic to the allergen used.

Nasal provocation tests with pollen allergens, performed as earlier described (5), were done in a smaller number of patients. Allergen

concentrations from 10^{-3} to 10^{-1} were used for this purpose.

Radioallergosorbent test (Phadebas RAST®) was used in some patients for determination of specific IgE antibodies against pollen allergens in the serum. The analyses were performed according to the manufacturer's recommendation with a minor modification as earlier described (5).

Statistical method. Chi-square test was used for the statistical analyses.

RESULTS

Symptoms from various food allergens

Of the 1129 patients, 276 (24.4%) reported some kind of allergic symptoms on eating or handling various foodstuffs, of which hazelnut was the most common, followed by apple, shell fish, Brazil nut, orange and strawberry (Tables 1 and 2). Usually only fresh fruits, not cooked or tinned, caused allergic symptoms. Oral pruritus was the symptom most frequently observed. Other complaints were rhinitis, wheezing, conjunctivitis, skin or abdominal symptoms. The type of symptom elicited varied to some extent from one allergen to another; thus skin manifestations were the most common symptom from shell fish, citrus fruit, strawberry, egg and chocolate while rhinitis or wheezing was the trouble most often elicited by scraping or peeling new potatoes (Table 1).

Females observed FS in 29.2%, significantly ($P < 0.001$) more often than men (18.9%). This sex difference was especially pronounced with shell fish and some fruits such as peach, apple, grape and strawberry while no sex difference was noted regarding egg and cheese.

Patients with a combination of asthma, allergic rhinitis and eczema more often reported FS than patients with only one or two diagnoses (Table 3).

Table 1

Incidence and clinical manifestations of food sensitivity with foods eliciting symptoms in more than 2% of 1129 patients

Allergen	Incidence of food sensitivity %	Symptoms elicited by food (no. of patients)							
		Rhinitis	Wheezing	Conjunctivitis	Skin symptoms	Oral pruritus	Abdominal symptoms	Other symptoms	More than one symptom
Hazelnut	10.3	—	7	2	11	58	2	2	33
Apple	7.7	1	5	—	12	36	6	1	26
Shellfish	6.0	3	8	3	18	9	5	5	17
Walnut	5.4	—	7	1	5	27	—	1	20
Brazil nut	4.4	—	5	—	6	20	1	1	17
Orange	4.3	—	5	3	23	2	3	2	11
Strawberry	4.2	1	3	2	22	7	1	—	12
Peach	3.8	—	2	—	8	15	1	—	15
Cheese	3.0	4	1	—	9	6	2	1	11
Pear	3.0	1	—	—	6	14	1	—	12
Plum	3.0	1	1	—	4	16	—	—	12
Egg	2.8	—	2	2	13	5	3	—	7
Almond	2.7	—	2	1	1	15	1	1	9
Peanut	2.7	—	4	—	4	9	4	1	9
Carrot	2.5	—	—	1	3	16	1	—	8
Chocolate	2.3	1	2	1	13	2	1	—	6
Tomato	2.3	—	1	—	5	13	—	1	6
Grape	2.3	1	5	1	5	5	2	2	5
Wine	2.2	3	3	—	6	1	2	2	8
Fish	2.1	—	6	1	4	2	2	—	9

Table 2

Food eliciting symptoms in less than 2% of 1129 patients

Incidence of food sensitivity	Food
1.1–2%	Hip, mandarin, lemon, green pepper, banana, new potato, green peas, onion, cabbage, spices, beer
0.5–1.0%	Apricot, grape-fruit, pineapple, black currant, French plum, cucumber, beans, parsley, rhubarb, fig, honey, milk
<0.5%	Red currant, gooseberry, raspberry, blackberry, cloudberry, wild strawberry, date, melon, mountain cranberry, parsnip, common beets, horse-radish, artichoke, Swedish turnip, yellow peas, spinach, dill, lettuce, celery, meat

Table 3.

Incidence of food sensitivity with regard to diagnosis

	Diagnosis					
	A	R	A+R	A+R+E	A+E	R+E
Food sensitivity, %	13.9	15.7	31.3	53.8	25.0	28.0

A=Asthma, R=Rhinitis, E=Eczema

Younger patients reported FS more often than older ones. On the other hand, patients with long-standing histories of allergic rhinitis had noticed FS more often than patients with short histories. About 70% of the patients reported that the allergic rhinitis preceded the manifestations of FS whereas 30% of the patients noticed FS before symptoms of inhalant allergy.

Correlation between food sensitivity and various inhalant allergies

A significant correlation was found between the incidence of FS and positive skin test with BP ($P<0.001$). Of patients with FS, 44% had

positive BP reaction compared with 23% of patients without food complaints. Of 257 patients with positive BP skin test, 40% reported FS, a figure which is significantly higher ($P<0.001$) than that for other patient groups (Table 4).

The most common food allergen eliciting symptoms in BP allergic patients was hazelnut, which caused complaints in 27% of the BP allergic patient group. Other common allergens are listed in Fig. 1, which clearly shows the higher occurrence of sensitivity for nuts, apple, peach, cherry, pear, plum, carrot and fresh potato in patients with BP allergy compared with patients with grass pollen allergy. The figures of FS with some other

Table 4

Incidence of food sensitivity in patients with various types of inhalant allergy according to skin testing

Patient group	n	Food sensitivity, %
Birch pollen allergics ^a	257	39.7
Grass pollen allergics ^b	336	19.6
Compositae pollen allergics ^c	179	20.7
Animal dander allergics ^c	467	22.0
No inhalant allergy	285	15.8

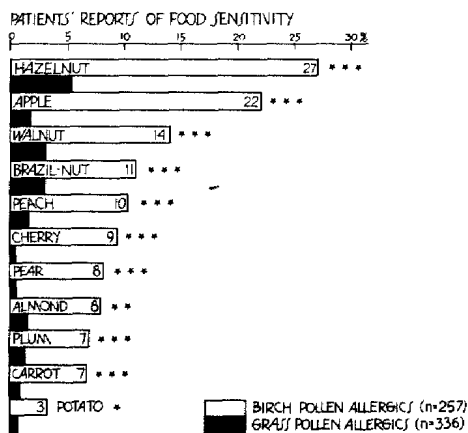
^aGrass pollen-allergic patients excluded.^bBirch pollen- and compositae pollen-allergic patients excluded.^cBirch pollen-allergic patients excluded.

Fig. 1. Birch pollen-related foods. A comparison between the incidence of food sensitivity in birch pollen-allergic patients and in grass pollen-allergic patients. The figures indicate per cent. * $P<0.05$ ** $P<0.01$ *** $P<0.001$.

foods too, e.g. strawberry, peanut, fish, cheese, tomato, mandarin and banana, were higher for BP allergics than for grass pollen allergics, the difference, however, was not statistically significant. Many BP-allergic patients observed FS with several of the nuts and fruits, mean 6. The most common symptom elicited on eating the BP-related products was itching in the mouth.

With some of the fruits (pear, plum, cherry, peach) the skin and the pulp of the fruit caused symptoms equally often. With others (apple) the skin gave rise to complaints more often than the pulp, whereas with potato only the skin seemed to be allergenic.

The distribution of FS for the various products in patients allergic against compositae pollen or animal dander was roughly

the same as that of the grass pollen allergic group.

Distribution of food sensitivity by intensity of birch pollen allergy

The higher the skin sensitivity with BP allergen, the higher the incidence of FS. Of patients with only a weak intracutaneous test reaction (+ or ++ at allergen concentration 10^{-5}), 21% reported FS while patients with the strongest BP skin reactions reported FS in 78%. With other pollen allergens no clear-cut tendency towards higher FS incidence with stronger skin reactions could be seen (Table 5). Similar results were obtained when FS was related to the strength of the RAST reaction with BP allergen; the higher the RAST class, the higher the incidence of FS (Table 6).

Table 5

Incidence of food sensitivity in relation to skin sensitivity with pollen allergens

Pollen allergen used in skin test	n	Incidence of food sensitivity, %							
		Results of intracutaneous test						Scratch test	
		neg.	10 ⁻⁵		10 ⁻⁴	10 ⁻⁵	10 ⁻²		
			+ / + +	+++			+ / + + +	++++	> + + + +
Birch	1110	19	21	31	37	43	57	36	78
Timothy ^a	816	10	22	50	17	33	19	10	50
Marguerite ^a	821	18	19	0	16	11	50	25	50

Figures calculated from $n < 10$ are indicated by italics.

Figures in column headings indicate allergen concentrations.

^a Patients with birch pollen allergy are omitted.

Table 6

Incidence of food sensitivity in relation to RAST results with pollen allergens

Pollen allergen used in RAST	n	Incidence of food sensitivity, %				
		RAST class				
		0	1	2	3	4
Birch	134	24	29	41	71	75
Timothy ^a	70	14	43	10	27	33
Marguerite ^a	70	27	36	17	25	50

Figures calculated from $n < 10$ are indicated by italics.

^a Patients with birch pollen allergy are omitted.

Provocation tests with BP allergen were performed on 134 patients. 33% of patients with only a slight reaction at the highest allergen concentration (10^{-1}) and 57% of those with strong reactions to the same concentration reported FS. All four patients reacting at an allergen concentration of 10^{-3} had observed FS.

Correlation between food sensitivity and acetylsalicylic acid intolerance

Fifty-five of the 1129 patients (4.9%) reported symptoms of ASA intolerance. Of these patients, 22 (41%) had observed FS, while only 24% of 1066 patients with no ASA intolerance history noticed such symptoms. The difference is statistically significant ($P < 0.01$). With some allergens, the difference between ASA-intolerant and ASA-tolerant patients was pronounced (Table 7), whereas no significant difference between the two groups of patients was seen with other allergens such as apple, pear, plum, cherry, peach, shellfish and cheese.

Wheezing was the symptom most often elicited in ASA-intolerant patients by several of the foodstuffs, such as nuts, almond and mountain cranberry. Strawberry more often caused skin reactions and oral pruritus, whereas abdominal complaints were often elicited by green pepper, cabbage, rhubarb and onion in these patients.

DISCUSSION

Since skin testing is reliable only with a few of the available food allergens, diagnosis of food allergy has to a large extent to depend on the patient's history—in some cases supplemented by elimination and oral provocation (6). When a questionnaire is used for diagnosis, food allergens causing immediate reactions will mainly be discovered. Allergies for common foods eaten frequently and causing chronic symptoms, will hardly be revealed. The majority of the patients in this study did not have chronic allergic symptoms and the figures found for

Table 7

Incidence of food sensitivity with ASA-related foodstuffs in ASA-intolerant patients and ASA-tolerant patients.

Incidence of food sensitivity	ASA intolerants <i>n</i> = 55	ASA tolerants <i>n</i> = 1066
10.1 – 20.0%	Hazelnut 18.2*, strawberry*** Brazil nut 14.5***, walnut 12.7***	—
5.1 – 10.0%	Almond 9.7***, peanut**, green pepper 9.1**, hip**, chocolate*, egg*, milk***, cabbage***, wine 7.4***, cucumber 5.8**, carrot**, new potato**, grape***, onion***, mountain cranberry 5.6***, parsley 5.5***	Hazelnut 9.7 walnut 5.1
1.0 – 5.0%	beans 3.8***, rhubarb**, yellow peas 3.7**	Brazil nut 3.9, strawberry 3.6 peanut, egg 2.4, almond, carrot, 2.3, chocolate 2.1, grape 2.0, hip 1.5

The figures indicate percentages.

ASA = acetylsalicylic acid.

* $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$

the relative relations between various foodstuffs should be satisfactorily reliable although under- as well as over-reporting cannot be avoided.

The prevalence of FS in our population—consisting mainly of adult patients with asthma and/or allergic rhinitis as main complaint—was found to be 25%. The most common allergens noted were nuts, shellfish, strawberry and some fruits. Textbooks of allergy state milk, egg and cereals as well as fish and spices as the most common food allergens (6). Speer (11) studying 250 food allergic patients, children and adults, in a private practice, found milk to be the most common allergen, followed by chocolate, citrus fruits, legumes, corn, egg and tomato. One explanation for discrepancies between various investigations is the age of the population studied. The present study covers mainly adults. It is well known that the fish, egg and milk allergy of childhood often disappears when the child grows up. Differences in food habits among various populations also play a part.

In the present study the most important factor influencing the figures for FS was, however, the presence of BP allergy. FS was observed much more often in BP-allergic patients than in patients with other types of pollen allergy or in patients without any inhalant allergy and the incidence of FS was higher in patients with a high degree BP allergy than in those with a low degree allergy. The allergens causing FS in BP-allergic patients more often than in others were nuts, apple, peach, cherry, pear, almond, plum, carrot and new potato. The observations made by Juhlin-Dannfelt (9) were thus corroborated with the exception of his claim that pea-sensitivity was BP related. Hannuksela & Lahti (7) recently published interesting investigations with similar results. Using a modified scratch test they found positive reactions with parsnip, apple, potato, carrot, celery, parsley, onion, tomato and swede much more frequently in patients allergic to BP than in patients without BP allergy. The low figures in that study as well

as in the present one for patients' report of FS with some of these foodstuffs (parsnip, swede) might depend on the fact that patients seldom handle or eat these substances uncooked. The authors found that cooking and even freezing destroyed the allergenic properties of the fruits and vegetables they tested. This is in concordance with the observations of the present study, that most of the allergenic fruits did not elicit symptoms when eaten tinned or cooked.

The connection between FS with some foodstuffs and BP allergy is probably explained by structural relationship between BP allergen and some allergens of the foodstuffs. It has been shown by Belin (4) that part of the major allergen in BP also occurs in hazelnut while another part of the BP allergen is not present in hazelnut extracts.

The occurrence of BP-related FS can be used as an aid in the diagnosis of pollen allergy; a patient with hay fever in springtime who reports allergic symptoms from hazelnut, apple, etc, obviously can be regarded as BP-allergic. On the other hand, the absence of FS does not exclude the possibility of BP allergy.

The fruits and nuts eliciting symptoms in BP-allergic patients botanically belong to the families of *Betulaceae* (hazelnut), *Juglandaceae* (walnut) or *Rosaceae* (apple, pear, almond, plum, cherry, peach). Most of the vegetables that, according to the findings of Hannuksela & Lahti (7) are BP-related, belong to the *Umbelliferae* family (carrot, parsnip, parsley and celery) or the *Solanaceae* family (potato, tomato). These findings are in agreement with those of Vaughan (12), who, applying a genetic classification to food allergens, found evidence of similarity among allergens of different members of food groups but found little evidence of crossed reactions with the commoner pollens belonging to the respective families.

Another type of pollen-related FS has been described by Anderson et al. (3). They found that 6% of the ragweed-allergic patients had a FS caused by melons or bananas, while no

such FS was reported among non-ragweed-allergics. Among their 90 patients with melon- or banana-induced FS, 86 had a characteristic itching in the roof of the mouth, palate or the throat on ingesting the relevant food. Similar symptoms were the most frequent complaints of the BP-allergic patients of the present study as well as of the patients of Hannuksela & Lahti (7). It seems that oral pruritus is a rather specific symptom of pollen-related FS; other types of symptom were much more common with shellfish, citrus fruits, cheese, egg and other non-pollen-related products. Furthermore, patients with ASA intolerance often observed asthma from products that in BP-allergics more often induced oral pruritus.

The relationship between ASA intolerance and FS demonstrated in this study largely agrees with the findings of Rosenhall (10) who among patients with positive oral challenges with ASA, sodium benzoate or tartrazine found a high incidence of intolerance to various alcoholic beverages, mountain cranberries and strawberries, but also to soft drinks, coffee, tea, cheese, apples, bananas, citrus fruits and shellfish, products that in the present study were not found to cause FS more often in ASA intolerant patients than in others. The disagreements might be explained by differences in interview technique.

It is probable that additives in food, as well as salicylates or benzoates naturally occurring in some foodstuffs, explain the high incidence of FS with certain products in ASA-intolerant patients and that this FS is not mediated by immunological mechanisms (2, 10).

Diet regimens have been presented for patients with ASA intolerance (8,10). The findings of the present study suggest that nuts and some fruits and vegetables should be included in the list of dangerous products. Patients with BP allergy should be informed about the possibility of reactions

with the nuts and fruits listed in Fig. 1. It should be noted, however, that boiled or tinned fruits and vegetables will usually be tolerated.

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