

Self-Reported Food Hypersensitivity in Sweden, Denmark, Estonia, Lithuania, and Russia

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Summary: Aim: The main aim of the study was to describe the differences between some Northern countries regarding what foods, according to the patients, elicit hypersensitivity symptoms.

Methods: At the participating clinics, patients with a history of food hypersensitivity (n = 1139) were asked to fill in a questionnaire in which 86 different foodstuffs were listed. Skin-prick tests (SPT) were performed with common inhalant allergens.

Results: The foods that were reported as eliciting symptoms differed between countries. In Russia, Estonia, and Lithuania; citrus fruits, chocolate, honey, apple, hazelnut, strawberry, fish, tomato, egg, and milk were most often reported as causes of hypersensitivity. In Sweden and Denmark; birch pollen (BP) related foods, such as nuts, apple, pear, kiwi, stone fruits, and carrot were the most common causes. In all countries, children, more often than adults, had symptoms of allergic reaction to citrus fruits, tomato, strawberry, milk, egg, and fish. Most patients (95%) reported hypersensitivity to several foodstuffs (median: eight foods). The most common symptoms were oral allergy syndrome and urticaria. Severe symptoms were most common with fish, shellfish, nuts, and milk. Slight symptoms were most common with rice, coriander, poppy seed, lingonberry, corn, caraway, red currant, and fig. Earlier well-known correlations, such as that between BP sensitization and some fruits and vegetables, as well as that between mugwort and some spices, were corroborated. Positive correlations were found between self-reported hypersensitivity to crustaceans and SPT with horse. A negative correlation was seen between hypersensitivity to crustaceans and SPT with BP.

Conclusions: The foodstuffs that often are reported to cause food hypersensitivity, differ between Sweden/Denmark on one side and the Baltic States and Russia on the other. BP-related foods dominate in Scandinavia, whereas some mugwort-related foods are of more importance in Russia and the Baltic States.

Keywords: allergy, East Europe, cross-reactions, epidemiology, food allergy, food hypersensitivity, Northern countries, questionnaire

Introduction

The frequency of hypersensitivity to various foods varies across regions and it may also vary with time depending on changes in eating habits [1-3]. Documentation of the different patterns of food hypersensitivity in different populations is of importance in the selection of relevant ingredients for food product labeling in different countries [3].

The true frequency of hypersensitivity to various foods is difficult to establish. A rather good estimation can be based on double-blind placebo-controlled food challenges (DBPCFC) [4]. Such tests are very time-consuming and for practical reasons they can only be

carried out with a limited number of foods. Atopic sensitization can be shown by skin prick tests (SPT) or in vitro IgE-tests. Ranking lists of foods causing hypersensitivity based on the results of such tests are, however, not very accurate, since many false-positive test results are found, when compared to DBPCFC [5]. Furthermore, food allergy, diagnosed by SPT or IgE-tests, is not synonymous with food hypersensitivity [6]. For evaluation of the prevalence of hypersensitivity to a large number of foods in a large number of patients, the use of an inquiry is a more realistic method, although the history, like SPT and IgE-tests, has a relatively low diagnostic precision [4]. The present study aimed at finding out which foods are of clinical importance in

some Northern countries: Sweden, Denmark, Estonia, Lithuania, and Russia. Some results from the study regarding social consequences of food hypersensitivity have been reported earlier [7].

Patients and Methods

Patients and Questionnaires

At 17 participating clinics in 15 cities, all patients referred for allergy testing (regardless of whether they were referred for inhalant allergy or food allergy) were asked "Do you get hypersensitivity symptoms from any food stuff?" Those who answered "Yes" to the question were asked to fill in a questionnaire in which 86 foods were listed. The participants could choose one of the following alternatives for each food: "I get slight symptoms," "I get moderate symptoms," "I get severe symptoms," "I don't know, I have not eaten this food." Furthermore, patients were asked to state which symptoms they got from their food hypersensitivity. The questionnaire was translated into Swedish, Danish, Estonian, Lithuanian, and Russia by native allergists.

A total of 1139 patients (393 males and 746 females) reported some kind of food hypersensitivity and agreed to participate in the study (Table 1). The patients' mean age was 29 years (range 1-84 years). There were 56

children 1-7 years of age, 175 individuals 8-15 years, and 908 adult patients \geq 16 years.

Skin Prick Tests (SPTs)

SPTs were performed at 13 clinics on 685 patients with Soluprick 10 HEP allergens (ALK Abello, Hörsholm, Denmark) of birch, timothy, mugwort, *Dermatophagoides pteronyssinus* (DP), cat, dog, and horse.

SPT was performed on the volar sides of the forearms in accordance with International recommendations [8]. Histamine HCl 10 g/l was used as a positive reference. The reactions were recorded in accordance with the recommendations of the Standardization Committee of the Northern Society of Allergology [9]. A wheal reaction of the same size as that of a histamine reference thus was recorded as three plus (3+) and a reaction half the size of the reference was recorded as two plus (2+). Reactions \geq 2+ were regarded as positive.

The work with patients started in November 1997 and finished in May 2000.

Statistics

The chi² test and Mann-Witney U-test were used for comparisons between groups. Multivariate logistic regression analysis was used when taking several independent variables into account. Values of $p < 0.05$ were considered. All tests used were two-tailed.

Table 1. Age and sex of patients at 15 cities participating in the study

	Age 1-7 years	Age 8-15 years	Age > 15 years	Females	Males	Total
Vladivostok (R)	8	16	34	29	29	58
Novosibirsk (R)		1	52	33	20	53
Kostroma* (R)	10	9	20	17	22	39
Tartu (E)		14	33	26	21	47
Tallinn (E)	4	6	99	97	12	109
Vilnius* (L)	7	24	96	81	46	127
Klaipeda (L)	2	6	45	39	14	53
Shiauliai (L)	18	34	6	28	30	58
Umeå* (S)	7	59	57	74	49	123
Uppsala (S)		5	2	3	4	7
Göteborg (S)			78	51	27	78
Halmstad (S)			78	54	24	78
Lund (S)			149	102	47	149
Borås (S)			60	42	18	60
Aarhus (D)		1	99	70	30	100
Total	56	175	908	746	393	1139

R = Russia, E = Estonia, L = Lithuania, S = Sweden, D = Denmark.

* Two clinics from these cities participated.

Table 2. Self-reported food hypersensitivity in five countries. The figures indicate percentages. The foodstuffs are ranked according to the column Total

	Russia (n = 150)	Estonia (n= 156)	Lithuania (n = 238)	Sweden (n = 495)	Denmark (n = 100)	Total (n = 1139)
Hazelnut	32	28	30	60	64	46
Apple	38	40	25	56	50	45
Orange	47	55	45	24	31	36
Chocolate	38	44	48	21	17	32
Kiwi	9.3	30	14	46	40	32
Walnut	26	21	17	39	46	31
Strawberry	43	38	21	31	26	31
Tomato	29	31	21	32	30	29
Peach	19	24	16	40	28	29
Pear	11	25	16	38	33	28
Peanut	20	25	16	36	28	27
Carrot	25	22	21	32	28	27
Almond	6.7	14	8.0	42	43	27
Honey	47	49	31	7.7	5.0	23
Nectarine	5.3	18	8.0	36	27	23
Lemon	33	32	32	14	14	23
Milk	23	24	29	20	14	22
Grapefruit	27	28	28	15	19	21
Egg	21	25	35	15	8.0	21
Plum	6.7	12	8.0	34	19	21
Wine	24	19	15	18	36	20
Fish	39	26	22	12	11	19
Cherry	6.7	16	11	29	18	19
Additive	21	27	21	14	20	19
Potato	13	22	13	19	26	18
Pineapple	21	23	15	16	24	18
Apricot	15	19	9.2	24	8.0	18
Grape	13	26	14	18	19	18
Sunflower seed	38	16	17	11	14	17
Pistachio nut	7.3	12	10	22	25	17
Pea	11	11	16	17	28	16
Raspberry	35	21	12	11	14	16
Paprika	8.7	19	11	18	16	15
Shrimp	8.7	12	4.6	22	20	15
Cocoa	13	14	31	9.9	5.0	15
Brazil nut	4.7	6.4	2.5	25	21	15
Cheese	14	12	9.2	17	14	14
Banana	12	17	7.6	18	12	14
Coconut	4.0	13	11	15	17	13
Coffee	22	21	16	7.5	4.0	13
Melon	11	15	5.0	15	15	12
Crab	21	8.3	6.3	14	11	12
Beer	9.3	11	12	11	19	12
Chicken	23	7.1	17	7.1	6.0	11
Bean	5.3	8.3	12	12	12	11
Cashew nut	1.3	3.8	2.5	19	11	10
Crawfish	3.3	7.7	4.2	16	9.0	10
Wheat	6.7	10	11	9.9	11	9.9
Redcurrant	13	15	8.0	7.5	6.0	9.2
Avocado	0.0	7.1	2.5	15	11	9.0
Other spices	5.3	9.0	7.1	9.5	15	8.9

	Russia (n = 150)	Estonia (n = 156)	Lithuania (n = 238)	Sweden (n = 495)	Denmark (n = 100)	Total (n = 1139)
Mango	4.7	11	6.7	11	6.0	8.7
Lobster	5.3	7.7	2.1	12	12	8.3
Soy	4.0	4.5	5.5	13	5.0	8.3
Mustard	8.7	11	11	7.1	4.0	8.3
Onion	3.3	7.1	10	9.3	7.0	8.2
Garlic	2.7	14	11	7.3	6.0	8.2
Rose hip	6.0	12	7.1	9.1	3.0	8.1
Corn	10	7.7	9.2	6.9	7.0	7.9
Blackcurrant	10	15	6.3	6.7	4.0	7.9
Blackberry	8.0	9.0	5.9	7.9	10	7.8
Celery	5.3	4.5	8.4	7.3	14	7.5
Camomile	11	12	11	3.8	6.0	7.5
Mushroom	10	9.6	7.6	5.9	7.0	7.4
Pepper	6.7	13	9.2	5.3	5.0	7.3
Nutmeg	0.7	7.7	4.6	9.3	10	7.0
Poppy seed	1.3	4.5	5.5	10	4.0	6.8
Fig	3.3	5.1	2.9	10	6.0	6.7
Parsley	6.0	8.3	5.0	6.1	10	6.5
Sesame seed	1.3	2.6	2.1	10	9.0	6.2
Clam	17	4.5	1.3	6.3	5.0	6.2
Cowberry	4.7	8.3	7.6	6.5	0.0	6.1
Curry	0.7	1.9	1.7	9.9	8.0	5.7
Pork	3.3	7.7	9.2	4.0	6.0	5.7
Beef	3.3	5.8	5.9	4.2	11	5.3
Date	4.0	7.1	2.5	6.3	6.0	5.3
Lentil	0.0	3.2	2.5	7.1	4.0	4.4
Rice	4.0	3.2	4.6	4.4	3.0	4.1
Gluten	2.0	1.9	2.1	6.1	4.0	4.0
Chestnut	2.0	1.3	1.3	4.6	6.0	3.2
Caraway	1.3	6.4	3.8	2.4	4.0	3.2
Anise	0.7	5.8	3.4	2.8	4.0	3.2
Oyster	3.3	5.1	2.1	3.2	2.0	3.2
Fennel	0.7	1.3	1.3	3.6	5.0	2.5
Coriander	1.3	3.2	1.3	1.6	1.0	1.7
Snail	2.7	1.9	1.3	0.8	2.0	1.4

Ethics

The Ethics Committees in the participating centers approved the study.

Results

As far as some of the foodstuffs are concerned, many patients answered "I don't know, I have never eaten this foodstuff." Fewer than 50% of the patients had tried chestnut, snail, oyster, brazil nut, cashew nut, and clam; more than 90% did know if they tolerated chocolate, strawberry, apple, and orange.

Ranking Lists

Hazelnut, apple, orange, kiwi, walnut, chocolate, and

strawberry were the foods most often reported to elicit symptoms (Table 2). Among patients from Sweden and Denmark, nuts, apple, pear, kiwi, stone fruits, tomato, and carrot were the most common foods. In the Baltic states and in Russia, citrus fruits, chocolate, honey, strawberry, fish, tomato, egg, milk, and sunflower seed were at the top of the ranking list (Figure 1). The items at the top of the list were similar when only the patients reporting severe symptoms were included (Table 3).

Age Differences

In children, hypersensitivity to citrus fruits, tomato, milk, egg, strawberry, and some other foodstuffs was more common than in adults, whereas apple, nuts and stone fruits were less common as offending foods (Figure 2).

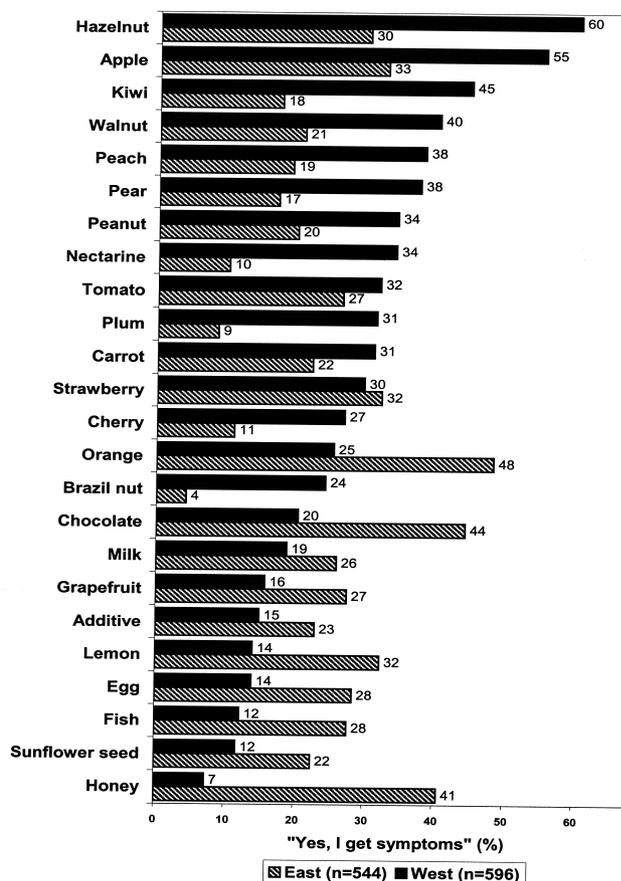


Figure 1. Foodstuffs most often eliciting symptoms in the East (Estonia, Lithuania, and Russia) and in the West (Sweden and Denmark)

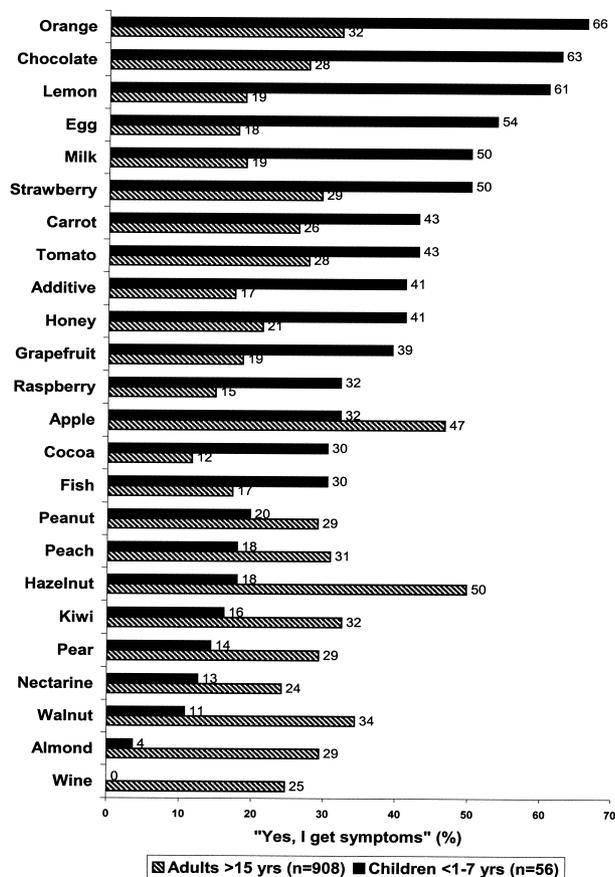


Figure 2. Foodstuffs most often eliciting symptoms in children and in adult patients

Number of Foods Reported to Produce Symptoms

Most of the patients reported hypersensitivity to several foodstuffs (median 8) and 467 patients (41.0%) regarded 10 or more foodstuffs as offenders. Females reported more foodstuffs (median 10) than men (median 7). Forty-nine patients (4.3%) named only one foodstuff (Table 4).

Symptoms

Urticaria was the symptom most often reported by children and oral allergy syndrome (itching or swelling of lips, mouth, or throat) was reported most often by adult patients (Figure 3). Patients from Sweden and Denmark more often reported thorax pain, gastrointestinal and oral symptoms as well as anaphylaxis, whereas those from the Eastern clinics more often reported urticaria (Figure 4).

Severity of Symptoms

Slight symptoms were most common (40%), whereas moderate symptoms were stated in 33% of the reactions, and severe symptoms in 27% of the 13994 hypersensitivity reactions reported.

The relationship severe symptoms/slight symptoms was highest for fish, shellfish, Brazil nut, milk, and hazelnut, and lowest for rice, coriander, cowberry, corn, red currant, date, parsley, and coffee.

Correlations Between Self-Reported Food Hypersensitivity and SPT with Inhalant Allergens

The earlier well-known correlation between SPT with birch pollen (BP) and hypersensitivity to BP related foods, such as apple, pear, nuts, and stone fruits [10] was confirmed (Table 5). Among patients with an isolated BP sensitization, 96% of the patients reported symptoms from one or several of the BP-related foods. Among those without BP allergy the figure was 68% ($p < 0.001$).

Table 3. Foodstuffs most often eliciting severe symptoms in Eastern countries (Estonia, Lithuania, and Russia) and in Western countries (Sweden and Denmark). Figures indicate individuals reporting severe symptoms elicited by respective allergen (%)

Rank Foodstuff in East	Frequency in East (n = 544)	Rank Foodstuff in West	Frequency in West (n = 596)		
1	Fish	14	1	Hazelnut	28
2	Honey	14	2	Apple	21
3	Orange	12	3	Walnut	17
4	Chocolate	9.4	4	Peanut	15
5	Lemon	9.2	5	Kiwi	14
6	Strawberry	9.1	6	Peach	14
7	Grapefruit	7.9	7	Pear	13
8	Hazelnut	6.7	8	Almond	12
9	Milk	6.6	9	Brazil nut	11
10	Egg	6.6	10	Carrot	11
11	Apple	6.1	11	Nectarine	11
12	Additive	6.1	12	Milk	10
13	Raspberry	5.5	13	Cherry	10
14	Carrot	4.9	14	Pistachio nut	9.0
15	Tomato	4.7	15	Strawberry	8.5
16	Crab	4.7	16	Potato	7.5
17	Peanut	4.5	17	Cheese	7.5
18	Sunflower seed	4.2	18	Tomato	7.0
19	Walnut	4.0	19	Shrimp	7.0
20	Kiwi	3.9	20	Crawfish	6.8

The correlation between SPT with mugwort and hypersensitivity to foods known to be mugwort pollen related (11) was rather poor. Only with celery, parsley, honey, sunflower seed, and carrot was there a significant correlation to SPT with mugwort (Table 6). In order to take into account the influence of a concomitant BP allergy multivariate logistic regression was used. It was found that symptoms from carrot were influenced only by a sensitization to BP, whereas symptoms from celery were only related to mugwort sensitization.

Positive correlations were found between self-reported hypersensitivity to crustaceans and SPT results with house dust mites, as well as with horse allergen. Among patients having positive SPT with DP, 41% reported hypersensitivity to crustaceans, whereas 27% of those with negative DP-tests reported such a hypersensitivity ($p < 0.01$). Of patients with positive SPT with horse, 38% reported a crustacean hypersensitivity, vs. 27% of the horse-negative patients ($p < 0.05$).

A negative correlation was found between hypersensitivity to crustaceans and SPT with BP. Only 23% of patients having a positive SPT with BP reported a hypersensitivity to crustaceans vs. 39% of those showing a negative SPT with BP ($p < 0.001$).

When multivariate logistic regression was used, with the SPT results with BP, DP, and horse included in the equation, it was found that the positive relationship between SPT with horse and hypersensitivity to crustaceans, and the negative relationship between SPT with BP and report of crustacean hypersensitivity, was independent of the SPT with DP.

Discussion

Our study shows that among patients referred to allergy clinics and having a self-reported food hypersensitivity there are differences between the Scandinavian countries of Sweden and Denmark and Russia, Estonia, and Lithuania regarding which foodstuffs patients consider to be the offending ones. In Russia, Estonia, and Lithuania, hypersensitivity to citrus fruits, chocolate, honey, apple, hazelnut, strawberry, fish, tomato, egg, and milk were reported most often. In Sweden and Denmark, birch pollen related foods, such as nuts, apple, pear, kiwi, stone fruits (plum, cherry, peach, etc.), and carrot were most common.

Differences between countries could reflect differences in eating habits, genetic differences, different

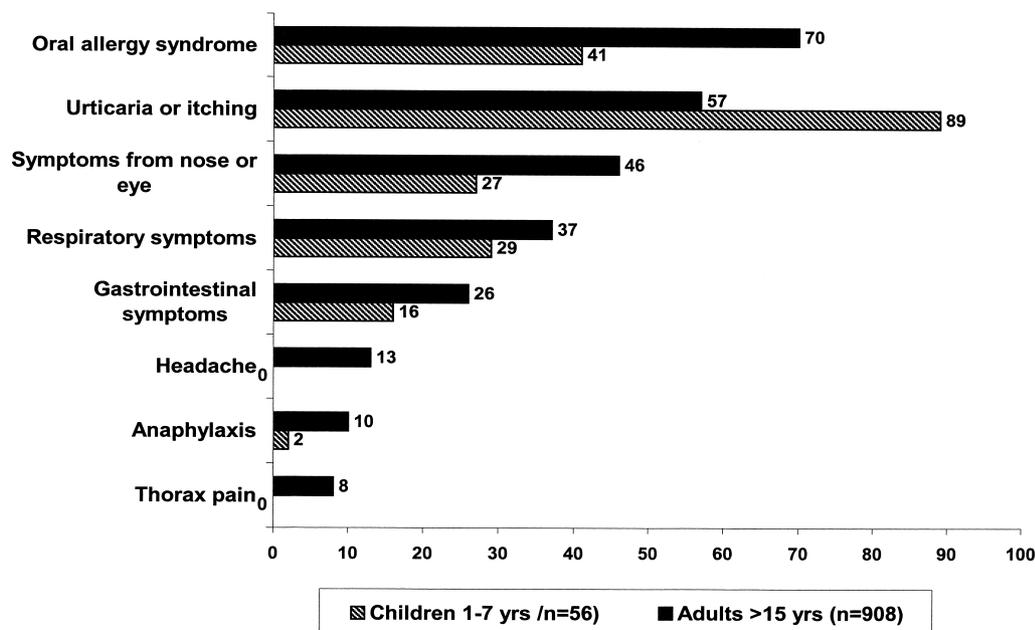


Figure 3. Symptoms reported by children and adult patients

amounts of inhalant cross-reacting allergens, or the perception of what is meant by "hypersensitivity to food" in the questionnaires. Another possibility is an influence of the general difference in atopy between Western and Eastern countries in Europe [12]. Different intestinal flora might impart a tolerance for some foods in the developing former socialistic countries compared to Scandinavia.

It should be noted that self-reported hypersensitivity includes reactions other than those mediated by IgE. There seems to be more self-reported food hypersensitivity depending on IgE-mediated reactions in Scandinavia and more with nonallergic mechanisms (e.g., citrus fruits and chocolate) in the Eastern countries.

The items at the top of the list in Scandinavia were similar to those of a Swedish study conducted in 1973 [10], with one exception: kiwi is now eliciting symptoms much more often. This difference obviously is the result of changing eating habits as more and more exotic fruits are introduced in Northern countries. Earlier epidemiological studies on food hypersensitivity are not available from the Baltic states and Russia.

A high frequency of hypersensitivity to honey and sunflower seed, foodstuffs that are related to mugwort pollen [13, 14], was reported in the Eastern countries. This finding could depend on a prevalence of mugwort allergy higher in these countries than in Scandinavia [15]. Eating habits could also be a factor of importance, since large amounts of honey are consumed in the Eastern countries, partly because there is a common belief that honey brings health. The foodstuffs most often causing symptoms in Scandinavia are mainly the BP related ones [10], reflecting a high incidence of BP

allergy in Scandinavian countries [15, 16]. A recently published population study from Germany also found nuts and fruits to be most common there [17]. There are other studies showing differences between countries, possibly depending in part on differences in the predominant pollen allergy. Thus, in Northern Italy BP allergy is common, and at the top of the ranking list in that region are found apple, nuts, and stone fruits, as in Sweden [18], whereas in Switzerland, where mugwort pollen allergy is more common, allergy to celery, carrot, and spices is frequently found [19]. Examples of the influence of food habits on food hypersensitivity are the high prevalence of sesame sensitization in Israel [20] and peanut sensitization in the USA [5].

Hypersensitivity to chocolate was commonly reported from the Eastern countries. Such a hypersensitivity tops the ranking list of some other studies, in which the patients' opinion of hypersensitivity had been asked for [2, 21, 22]. These reactions are probably not mediated mainly by IgE.

In children, foodstuffs of animal origin (egg, milk, and fish), as well as foods that probably elicit symptoms because of nonallergic mechanisms (citrus fruits, chocolate, strawberry, and tomato), were regarded as offending foods more frequently than in adults. These findings are in accordance with other reports on food hypersensitivity in children [4, 23].

We found a correlation between hypersensitivity to crustaceans and SPT with DP, which is in accordance with an earlier clinical study from the same countries [24]. The cross-reactions between mites, insects, and crustaceans, demonstrated *in vitro*, have been shown to depend on tropomyosin [25]. We have no explanation

Table 4. Foodstuffs eliciting symptoms in forty-nine patients reporting hypersensitivity against one food only

Foodstuff	No. of patients	Oral allergy syndrome (OAS)	Thorax pain	Gastro intestinal symptoms	Urticaria or itching	Nose eye symptoms	Respiratory symptoms	Headache	Anaphylaxis
Fish	9			5	7	1	3	1	
Apple	5				2	3			1
Egg	4	3		1		1		1	
Honey	4	1		1	2				1
Kiwi	4	4					1		
Shrimp	4	1			4				
Tomato	3				3	2			
Potato	3	1	1	1					
Milk	3			1					
Carrot	2	2				1			
Peanut	2				2				
Hazelnut	2	2				1			
Celery	2	2			2	2	1		1
Pineapple	1				1				
Orange	1			1					
Soy	1								
Crab	1	1							
Crawfish	1	1			1	1	1		1
Clam	1		1	1			1		1
Wine	1				1				
Additive	1	1	1			1	1		
Sunflower seed	1			1					
Total	49	21	3	6	22	13	6	1	5

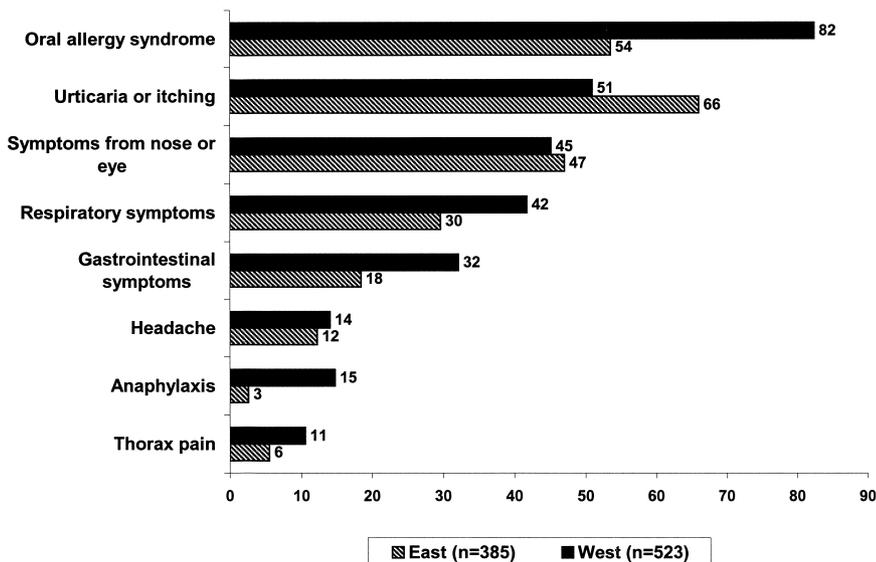


Figure 4. Symptoms reported by adult patients in the East (Estonia, Lithuania, and Russia) and in the West (Sweden and Denmark)

for our finding of a correlation between hypersensitivity to crustaceans and SPT with horse, a relationship not earlier reported.

Self-reported food hypersensitivity via questionnaires is, of course, not synonymous with true food hypersensitivity. All diagnostic methods regarding food hypersensitivity have limitations. IgE-tests and SPT cannot be used for diagnosis of nonallergic hypersensitivity and these tests give many positive reactions in spite of negative DBPCFC [5], as well as negative reactions in spite of positive challenges [5, 26]. Although DBPCFC is regarded as "the gold standard," there can be problems. If a co-factor, for instance, exercise, is necessary in addition to the food in order to elicit symptoms, then a DBPCFC will give a false-negative result. In the present study, a questionnaire was used for the patients' reports of hypersensitivity to 86 different foodstuffs. Although false-negative as well as false-positive answers may be obtained, when a patient's history is used for diagnosis [4] a rather good estimation

of the ranking lists of foods eliciting symptoms in different populations will be obtained. Furthermore, with some foods, such as hazelnut and apple, a good correlation has been shown between the case history and the result of DBPCFC [27].

To conclude, in a questionnaire-based study on self-reported food hypersensitivity in Northern countries, differences were found between Eastern countries (Russia, Estonia, and Lithuania) and Western (Sweden and Denmark), probably mainly reflecting differences in pollen sensitization (birch pollen related food in the West, mugwort pollen related food in the East) and food habits.

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Table 5. Self-reported hypersensitivity to foodstuffs with relationship to birch pollen sensitization

Foodstuff	STP BP - (n = 237)	SPT BP + (n = 407)	Sign.
Hazelnut	3	70	***
Apple	30	69	***
Peach	16	49	***
Almond	23	48	***
Kiwi	30	48	***
Pear	16	48	***
Walnut	27	45	***
Carrot	12	42	***
Nectarine	15	41	***
Plum	15	37	***
Peanut ¹⁾	25	36	**
Cherry	8.0	35	***
Potato	7.9	32	***
Apricot	9.3	29	***
Brazil nut	15	25	***
Pistachio nut ¹⁾	16	24	***
Cashew ¹⁾	11	18	***
Coconut ¹⁾	12	17	**
Nutmeg ¹⁾	5.5	10	*
Chestnut	2.5	5.9	**
Any birch-pollen-related food-stuff	69	93	***

¹⁾ No significant difference when only patients with a mono-birch pollen sensitization were included in the calculation.
* p < 0.05, ** p < 0.01, *** p < 0.001; - = negative, + = positive.

Table 6. Self-reported hypersensitivity to foodstuffs with relationship to mugwort pollen sensitization (%)

Foodstuff	SPT mugwort negative (n = 465)	SPT mugwort positive (n = 172)	Significance
Carrot ¹⁾	29	39	*
Sunflower seed	15	33	***
Honey	11	23	***
Celery	6.1	21	***
Parsley	5.4	13	***
«Other spices»	9.2	16	*
Any mugwort-pollen-related food-stuff	47	71	***

¹⁾ No significant difference when only patients with a mono-mugwort pollen sensitization were included in the calculation. With other mugwort related foodstuffs (anise, caraway, coriander, curry, fennel, garlic, paprika sweet, wild camomile) there were no significant difference between patients with negative and patients with positive SPT with mugwort.

* p < 0.05, ** p < 0.01, *** p < 0.001

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