

Original article

Epidemiology of food allergy/food intolerance in adults: associations with other manifestations of atopy

Background: Food allergy and food intolerance (FA/FI) are believed to be frequent medical problems; however, information from epidemiologic studies in adults is scarce. The objective was to determine the frequency of FA/FI and allergic sensitization to food in a large adult sample. Furthermore, the associations between FA/FI and other outcomes of atopy were studied.

Methods: Within a population-based, nested, case-control study, a standardized interview was performed to obtain detailed information on FA/FI and the history of atopic diseases. In addition, a skin prick test with 10 common food and nine aeroallergens was performed.

Results: Overall, 20.8% of the 1537 studied subjects (50.4% female, age median 50 years) reported FA/FI (women 27.5%, men 14.0%; OR 2.35, CI 1.80–3.08). Nuts, fruits, and milk most frequently led to adverse effects, and the sites of manifestation were oral (42.9%), skin (28.7%), gastrointestinal (13.0%), systemic (3.2%), and multiple (12.2%). One-quarter of the subjects (25.1%) were sensitized to at least one food allergen in the prick test, with hazelnut (17.8%), celery (14.6%), and peanut (11.1%) accounting for most of the positive reactions. The corresponding frequency estimates for the representative study base ($n=4178$) were 15.5% for reported adverse reactions and 16.8% for allergic sensitization. Relevant concomitant sensitization to food and aeroallergens was observed. Food-allergic subjects (positive history and sensitization to corresponding allergen) suffered significantly more often from urticaria, asthma, atopic eczema, and especially hay fever (73.1%) than controls (3.0%). Furthermore, hay fever was treated significantly more often in subjects who suffered from concomitant food allergy.

Conclusions: FA/FI in adults is frequently reported and associated with other manifestations of atopy. Hay fever in conjunction with FA/FI tends to be clinically more severe since therapeutic needs are enhanced.

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Food allergy/food intolerance is a common medical problem; however, epidemiologic data are scarce. Frequency estimates based on self-reported symptoms range from 4.9% (1) to 33% (2), and it is believed that FA/FI is more common early in life (3). In fact, children have been studied more often than adults so far (4, 5). There have been only two studies, which used DBPCFC in selected subgroups of the study population in order to estimate the prevalence in the general population (6, 7). According to their results, the prevalence was estimated to be as low as 1.4–2.4%, indicating an overestimation by questionnaire-based studies. From patient-based studies, it is known that food allergy in adults is often associated

with hay fever and that the spectrum of relevant food allergens is different from that in children (8–10). However, very little is known from population-based studies in adults on the frequency and characteristics of FA/FI, sensitization, and association with manifestations of atopy (11–13). Within an epidemiologic study, we determined quantitatively and qualitatively the frequency of FA/FI and the prevalence of allergic sensitization to 10 common food allergens. Furthermore, we sought to investigate the association of FA/FI and other manifestations of atopy and to examine the clinical relevance of that association by taking information on therapeutic needs into account.

Material and methods

Study design

We here report on a nested, case-control study, which was performed between September 1997 and December 1998, and in which cases were defined according to the history of FA/FI and sensitization to the corresponding allergy. Details of the sampling frame and study design are given in Fig. 1. The subjects were recruited from the third MONICA survey, which was conducted in Augsburg, Germany, during the years 1994 and 1995. The objective and protocol of the MONICA surveys were published earlier (14, 15). The study base of the MONICA surveys consisted of all registered residents aged 25–74 years of the city of Augsburg and two surrounding counties. A random, cross-sectional sample stratified for age and sex was studied in 1994/5 ($n=4356$). In the sera of these subjects, allergen-specific IgE antibodies to common aeroallergens (grass and birch pollen, house dust-mite, cat, and *Cladosporium*) were determined by fluorescence enzyme immunoassay technique (CAP-RAST, Pharmacia, Uppsala, Sweden). For this study, we aimed to recruit an enriched sample of 1600 subjects out of the 4178 individuals who had valid RAST results. Subjects were selected, stratified by age and sex, so as to provide 50% with and 50% without a positive RAST, and, furthermore, so that within these groups 50% had given a positive answer to one of the following questions of the MONICA questionnaire ("Have you had asthma attacks within the last 12 months?", "Do you have allergic rhinitis, e.g., hay fever?", "How much do you suffer from allergies/skin irritation?"; positive=moderate/severe). To account for an estimated response of 63%, a gross sample of 2539 subjects was approached. Finally, 1537 subjects participated (60.5%), of whom 50.2% exhibited a positive RAST result, and 53.9% of this group and 43.1% of those with negative RAST result reported symptoms of atopy. Written, informed consent was obtained from all participants prior to the beginning of the study.

Outcome assessment

Questionnaire. As part of the study protocol, a computer-assisted standardized interview was performed. Subjects were asked whether they had allergic reactions to food, and if so, the type of reaction was recorded in detail for 18 possible food allergens and allergen groups. The reported reactions were categorized according to the reaction site as oral (oral allergy syndrome defined as tingling, itching, or swelling of lips, palate, or throat), gastrointestinal (e.g., diarrhea or pain), skin (rash, wheals, itch, or redness), systemic (shortness of breath, asthma, or circulatory disorders), or multiple. Furthermore, the history and doctor's diagnosis of atopic diseases (hay fever, asthma, or atopic eczema) as well as urticaria and migraine, were recorded.

A conventional lancet skin prick test (SPT) was performed on the volar aspect of the forearm by the method of Pepys (16). A sample of common aeroallergens (grass, birch, rye, mugwort pollen, *Alternaria*, *Cladosporium*, cat, dog, and house dust-mite [*Dermatophagoides pteronyssinus*]), as well as the following food allergens, was tested: milk, egg, peanut, pork, mackerel, celery, hazelnut, wheat, soy, and crab. Saline and histamine were used as controls (ALK-Scherax, Hamburg, Germany), and results were read after 15 min. The tests were scored according to the mean wheal diameter by the method of Ring (17) and considered positive when the wheal diameter exceeded at least 2 mm. Results showing a positive reaction to saline or no reaction at all (including histamine) were excluded from further analysis.

Statistical analyses

Most descriptive results were given with sex stratification. Age-adjusted odds ratios and 95% confidence intervals were used as parameters of association and stability.

To analyze further associations of food allergy and atopic

diseases, we defined a group of food-allergic subjects as those who reported FA/FI to specific food and exhibited a positive SPT reaction to the corresponding allergen. The SPT reactions were attributed to the questionnaire data as follows:

Questionnaire	SPT
Milk (products)	Milk
Egg (products)	Egg
Flour (products)	Wheat
Fish/seafood	Mackerel/crab
Meat	Pork
Tomatoes	
Other vegetable	Celery
Citrus (fruits)	
Fruit I (peach etc.)	
Fruit II (apple etc.)	
Other fruit	
Peanut	Peanut
Nuts	Hazelnut
Soy	Soy
Herbs/spices	
Wine (sparkling)	
Sugar	
Additives	

To estimate population-based frequencies, we extrapolated the findings of this nested study ($n=1537$) to the representative study base of the MONICA survey ($n=4178$) by taking the weighted distribution of our selection criteria (RAST/symptoms) into account.

Results

Complete valid data were available from 1537 subjects (50.4% female, age median 50 years, 50.3% with aeroallergen-specific IgE antibodies). A history of FA/FI was given by 20.8%, and women (27.5%) reported significantly more often such reactions than men (14.0%) (OR 2.35 CI 1.80–3.08). The frequency of FA/FI to single food allergens and sex stratification is given in Table 1. Reactions were most frequently observed after the consumption of nuts, fruit, milk, wine, and vegetables. For 11 out of 18 allergens, women reported adverse reactions more frequently than men, and this was significant for citrus fruits. A total of 790 adverse reactions to 18 foods was recorded by the interview. The majority of these reactions could be classified as oral allergy syndrome (42.9%); 28.7% were attributable to skin reactions. Gastrointestinal symptoms accounted for 13.0%, and in 3.2% systemic symptoms (respiratory/cardiovascular) were reported. In the remaining 12.2%, more than one of these reaction types occurred simultaneously. Detailed information with respect to reaction site and allergen is given in Table 2. Fruits and nuts most frequently caused symptoms of the oral allergy syndrome, whereas milk, egg, and flour products were reported as the predominant trigger of gastrointestinal complaints. Skin reactions often occurred after the ingestion of citrus fruits, herbs, and wine. With respect to absolute numbers, systemic reactions were reported frequently in connection with the consumption of fruits and nuts.

One-quarter of the subjects (25.1%) exhibited at least

Table 1. Prevalence of reported adverse food reactions

	Overall <i>n</i> = 1537	%	Men <i>n</i> = 762	%	Women <i>n</i> = 775	%	General population estimates (<i>n</i> = 4178)
Milk (products)	43	2.8	16	2.1	27	3.5	1.8
Egg (products)	6	0.4	3	0.4	3	0.4	0.4
Flour (products)	13	0.8	3	0.4	10	1.3	0.7
Fish/seafood	22	1.4	8	1.4	14	1.8	1.0
Meat	9	0.6	3	0.4	6	0.8	0.5
Tomatoes	29	1.9	6	0.8	23	3.0	1.3
Other vegetable	39	2.5	14	1.8	25	3.2	1.7
Citrus (fruits)	90	5.9	15	2.0	75	9.7*	4.5
Fruit I (peach etc.)	89	5.8	23	3.0	66	8.5	3.7
Fruit II (apple etc.)	104	6.8	34	4.5	70	9.0	3.9
Other fruit	77	5.0	24	3.1	53	6.8	3.8
Peanut	33	2.1	9	1.2	24	3.1	1.3
Nuts	130	8.5	38	5.0	92	11.9	5.3
Soya	7	0.5	2	0.3	5	0.6	0.3
Herbs/spices	24	1.6	8	1.0	16	2.1	1.1
Wine (sparkling)	44	2.9	10	1.3	34	4.4	1.9
Sugar	11	0.7	4	0.5	7	0.9	0.5
Additives	20	1.3	5	0.7	15	1.9	0.7
Any	320	20.8	107	14.0	213	27.5	15.5

* Denotes effect estimate “women” vs “men” OR 3.33; CI 1.80–6.16.

one positive reaction in the skin test with 10 food allergens. Results with respect to single allergens and sex differences are displayed in Table 3. The highest prevalence of allergic sensitization was obtained with hazelnut, celery, and peanut allergen. Women exhibited a significantly higher frequency of reactions overall (27.5%), and in particular to celery (17.2%) and hazelnut (20.4%), than men (22.7%, 12.1%, and 15.2%, respectively).

One-third of the subjects (33.4%) were sensitized to only one food allergen. On average (median), reactions to two different food allergens were observed. More than 80% of those sensitized to soy, celery, or peanut also exhibited reactions to hazelnut, and 85.7% with positive SPT reaction to soy also showed a positive test to celery. With respect to all allergens, the most concomitant sensitizations were seen to hazelnut, celery, and peanut. Those who were sensitized to one

Table 2. Prevalence of reported adverse reactions to food by reaction site

<i>n</i>	Total <i>n</i>	Reaction site									
		Oral ¹		GI ²		Skin ³		Systemic ⁴		Multiple	
		%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>
Milk (products)	43	9	20.9	17	39.5	11	25.6	2	4.7	4	9.3
Egg (products)	6			4	66.7	2	33.3	–	–	–	–
Flour (products)	13			7	53.8	4	30.8	1	7.7	1	7.7
Fish/seafood	22	3	13.6	7	31.8	8	36.4	–	–	4	18.2
Meat	9			4	44.4	5	55.6	–	–	–	–
Tomatoes	29	10	34.5	1	3.4	13	44.8	–	–	5	17.2
Other vegetable	39	17	43.6	7	17.9	5	12.8	2	5.1	8	20.5
Citrus (fruits)	90	22	24.4	7	7.8	50	55.6	1	1.1	10	11.1
Fruit I (peach etc.)	89	56	62.9	4	4.5	14	15.7	4	4.5	11	12.4
Fruit II (apple etc.)	104	71	68.3	3	2.9	9	8.7	3	2.9	18	17.3
Other fruit	77	29	37.7	8	10.4	35	45.5	–	–	5	6.5
Peanut	33	10	30.3	6	18.2	13	39.4	1	3.0	3	9.1
Nuts	130	94	72.3	5	3.8	10	7.7	6	4.6	15	11.5
Soya	7	2	28.6	1	14.3	3	42.9	–	–	1	14.3
Herbs/spices	24	2	8.3	5	20.8	13	54.2	–	–	4	16.7
Wine (sparkling)	44	11	25.0	8	18.2	17	38.6	4	9.1	4	9.1
Sugar	11	1	9.1	3	27.3	5	45.5	1	9.1	1	9.1
Additives	20	2	10.0	6	30.0	10	50.0	–	–	2	10.0

¹ Oral allergy syndrome defined as tingling, itching, or swelling of lips, palate, or throat.

² Gastrointestinal problems, e.g., diarrhea or pain.

³ Skin rash, wheals, itch, or redness.

⁴ Shortness of breath, asthma, circulatory disorders.

Table 3. Prevalence of allergic sensitization to food allergens in prick test

	Overall <i>n</i> = 1537	%	Men <i>n</i> = 762	%	Women <i>n</i> = 775	%	General population estimates (<i>n</i> = 4178)
Milk	59	3.8	27	3.5	32	4.1	2.3
Egg	47	3.1	26	3.4	21	2.7	1.9
Peanut	170	11.1	78	10.2	92	11.9	6.8
Pork	53	3.4	26	3.4	27	3.5	2.0
Mackerel	45	2.9	21	2.8	24	3.1	1.8
Celery	225	14.6	92	12.1	133	17.2*	9.1
Hazelnut	274	17.8	116	15.2	158	20.4 ⁺	11.3
Wheat	59	3.8	28	3.7	31	4.0	2.8
Soya	42	2.7	20	2.6	22	2.8	1.7
Crab	41	2.7	21	2.8	20	2.6	1.9
Any	385	25.3	173	22.7	213	27.5 [#]	16.8

Effect estimates “women” vs “men”:

* OR 1.53 (1.15–2.06)

⁺ OR 1.45 (1.11–1.89)[#] OR 1.31 (1.04–1.65).

Table 4. Prevalence of concomitant sensitization to other food allergens

	Milk	Egg	Peanut	Pork	Mackerel	Celery	Hazelnut	Wheat	Soya	Crab
Milk	59 [#]	27 (57.4%)	28 (16.5%)	21 (39.6%)	25 (55.6%)	33 (14.7%)	37 (13.5%)	17 (28.8%)	15 (35.7%)	11 (26.8%)
Egg	27 (45.8%)	47	30 (17.6%)	23 (43.4%)	22 (48.9%)	28 (12.4%)	32 (11.7%)	20 (33.9%)	15 (35.7%)	15 (36.6%)
Peanut	28 (47.8%)	30 (63.8%)	170	38 (71.7%)	33 (73.3%)	130 (57.8%)	139 (50.7%)	32 (54.2%)	30 (71.4%)	19 (46.3%)
Pork	21 (35.6%)	23 (48.9%)	38 (22.5%)	53	30 (66.7%)	35 (15.6%)	38 (13.9%)	20 (33.9%)	18 (42.9%)	15 (36.6%)
Mackerel	25 (42.4%)	22 (46.8%)	33 (19.4%)	30 (56.6%)	45	35 (15.6%)	34 (12.4%)	21 (35.6%)	16 (38.1%)	16 (39.0%)
Celery	33 (55.4%)	28 (59.6%)	130 (76.5%)	35 (66.0%)	35 (77.8%)	225	182 (66.4%)	43 (72.9%)	36 (85.7%)	25 (61.0%)
Hazelnut	37 (62.7%)	32 (68.1%)	139 (81.8%)	38 (71.7%)	34 (75.6%)	182 (80.9%)	274	45 (76.3%)	36 (85.7%)	23 (56.1%)
Wheat	17 (28.8%)	20 (42.6%)	32 (18.8%)	20 (37.7%)	21 (46.7%)	43 (19.1%)	45 (16.4%)	59	23 (54.8%)	22 (53.7%)
Soya	15 (25.4%)	15 (31.9%)	30 (17.6%)	18 (34.0%)	16 (35.6%)	36 (16.0%)	36 (13.1%)	23 (39.0%)	42	18 (43.9%)
Crab	11 (18.6%)	15 (31.9%)	19 (11.2%)	15 (28.3%)	16 (35.6%)	25 (11.1%)	23 (8.4%)	22 (37.3%)	18 (42.9%)	41
Polyvalence*	3	5	2	4	6	2	2	3	4	4

* Number (median) of food allergens to which concomitant sensitization was present.

[#] Percentages per column refer to bold figures, which represent absolute positive reactions to allergens given in respective column heading.

Table 5. Prevalence of concomitant sensitization to food and aeroallergens in SPT

	Milk <i>n</i> = 59	Egg <i>n</i> = 47	Peanut <i>n</i> = 170	Pork <i>n</i> = 53	Mackerel <i>n</i> = 45	Celery <i>n</i> = 225	Hazelnut <i>n</i> = 274	Wheat <i>n</i> = 59	Soya <i>n</i> = 42	Crab <i>n</i> = 41
Grass pollen	44 (74.6%)	34 (72.3%)	112 (65.9%)	41 (77.4%)	39 (86.7%)	135 (60.0%)	159 (58.0%)	39 (66.1%)	28 (66.7%)	21 (51.2%)
Birch pollen	45 (76.3%)	36 (76.6%)	144 (84.7%)	45 (84.9%)	36 (80.0%)	189 (84.0%)	257 (93.8%)	41 (69.5%)	33 (78.6%)	21 (51.2%)
Rye pollen	47 (79.7%)	37 (78.7%)	136 (80.0%)	46 (86.8%)	39 (86.7%)	167 (74.2%)	211 (77.0%)	43 (72.9%)	34 (81.0%)	25 (61.0%)
Mugwort	43 (72.9%)	36 (76.6%)	105 (61.8%)	41 (77.4%)	37 (82.2%)	132 (58.7%)	149 (54.4%)	38 (64.4%)	33 (78.6%)	23 (56.1%)
<i>Alternaria</i>	37 (62.7%)	31 (66.0%)	66 (38.8%)	43 (81.1%)	36 (80.0%)	84 (37.7%)	92 (33.6%)	35 (59.3%)	27 (64.3%)	22 (53.1%)
<i>Cladosporium</i>	37 (62.7%)	30 (63.8%)	54 (31.8%)	33 (62.3%)	30 (66.7%)	65 (28.9%)	73 (26.6%)	29 (49.2%)	24 (57.1%)	18 (43.9%)
Cat	48 (81.4%)	36 (76.6%)	83 (48.8%)	43 (81.1%)	37 (82.2%)	104 (46.2%)	124 (45.3%)	33 (55.9%)	29 (69.0%)	21 (51.2%)
Dog	42 (71.2%)	36 (76.6%)	94 (55.3%)	46 (86.8%)	38 (84.4%)	121 (53.8%)	136 (49.6%)	39 (66.1%)	31 (73.8%)	27 (65.9%)
HDM (<i>D. pter.</i>)	43 (72.9%)	31 (66.0%)	68 (40.0%)	32 (60.4%)	30 (66.7%)	80 (35.6%)	99 (36.1%)	22 (37.3%)	21 (50.0%)	22 (53.7%)
Polyvalence*	8	8	5	8	8	4	4	7	7	4

* Number (median) of aeroallergens to which concomitant sensitization was present.

HDM: house-dust mite (*D. pteronyssinus*).

Table 6. Association of food allergy and atopic diseases (including urticaria and migraine)

	Overall				Men				Women			
	Food allergy				Food allergy				Food allergy			
	Yes*		No ⁺		Yes		No		Yes		No	
	n=119	%	n=602	%	n=37	%	n=317	%	n=82	%	n=285	%
Atopic eczema ^d	12	10.1	11	1.8	3	8.1	5	1.6	9	11.0	6	2.1
	OR ^β 5.19 (2.21–12.19)				OR 5.25 (1.19–23.04)				OR 4.50 (1.52–13.33)			
Hay fever ^d	87	73.1	18	3.0	26	70.3	6	1.9	61	74.4	12	4.2
	OR 87.67 (46.60–164.93)				OR 153.90 (47.56–498.0)				OR 60.94 (28.29–131.25)			
Asthma ^d	18	15.1	24	4.0	4	10.8	9	2.8	14	17.1	15	5.3
	OR 5.19 (2.64–10.17)				OR 4.62 (1.31–16.24)				OR 4.79 (2.11–10.88)			
Urticaria	13	10.9	10	1.7	2	5.4	2	0.6	11	13.4	8	2.8
	OR 7.11 (3.00–16.90)				OR 11.41 (1.52–85.67)				OR 4.80 (1.81–12.70)			
Migraine	18	15.1	56	9.3	—	—	12	3.8	18	22.0	44	15.4
	OR 1.73 (0.97–3.01)				n.d.				OR 1.61 (0.86–3.02)			

* Defined as subjects with history of FA/FI and positive SPT to corresponding food allergen.

⁺ Defined as subjects without history of FA/FI and without detectable allergen-specific IgE antibodies to common aeroallergens.

^β Denotes effect estimates “yes” vs “no”, all adjusted for age.

^d According to doctor's diagnosis.

of these three allergens exhibited, on average, only two additional positive SPT to food allergens. Subjects with a positive SPT to mackerel or egg were sensitized to six or five more food allergens, respectively (Table 4).

The concomitant sensitization of food and aeroallergens in the SPT is summarized in Table 5. Only 8% of food-sensitized subjects did not react to at least one of the tested aeroallergens. A strong association was observed for hazelnut- and celery-sensitized individuals, who showed concomitant sensitization to birch pollen in 93.8% and 84.0% of cases, respectively. Overall, a high rate of simultaneous sensitization to food allergens and birch or rye pollen was observed. The majority of those who showed reactions to mackerel or pork were also sensitized to most of the aeroallergens (Table 5).

For the analysis of food allergy and atopic diseases, a total of 119 (7.7%) subjects were identified, who

reported FA/FI to specific food and exhibited a positive SPT to the corresponding allergen. These subjects were compared to those without a history of FA/FI and without detectable allergen-specific IgE antibodies to aeroallergens. FA/FI was significantly associated, after adjustment for age, with a history of doctor's diagnosed atopic eczema, hay fever, or asthma, and also with a self-reported history of urticaria. A history of migraine was also positively, but not statistically significantly, associated with FA/FI. The strongest association was found with hay fever, which had been diagnosed in 73.1% of subjects with FA/FI. Similar significant and age-adjusted associations were observed in the groups of women and men, with urticaria and migraine being reported more frequently by women (5.2 vs 1.1%; 16.9 vs 3.4%) (Table 6).

To assess indirectly the severity of hay fever in food-

Table 7. Food allergy and hay fever (frequency and treatment)

	Overall				Men				Women			
	Food allergy				Food allergy				Food allergy			
	Yes*		No ⁺		Yes		No		Yes		No	
	n=119	%	n=344	%	n=37	%	n=198	%	n=82	%	n=146	%
History of hay fever	106	89.1	52	15.1	33	89.2	29	14.6	73	89.0	23	15.8
Therapy												
Local	88	83.0	31	59.6	28	84.8	18	62.1	60	82.2	13	56.5
	OR ^β 3.27 (1.53–7.00)				OR 3.79 (1.10–13.02)				OR 3.27 (1.15–9.30)			
Systemic (antiallergic drugs)	66	62.3	15	28.8	19	57.6	8	27.6	47	64.4	7	30.4
	OR 4.36 (2.08–9.13)				OR 4.07 (1.35–12.22)				OR 4.45 (1.54–12.84)			
Specific immunotherapy	42	39.6	8	15.4	13	39.4	5	17.2	29	39.7	3	13.0
	OR 3.47 (1.48–8.14)				OR 2.99 (0.91–9.86)				OR 4.56 (1.22–17.08)			
No treatment	9	8.5	17	32.7	4	12.1	9	31.0	5	6.8	8	34.8
	OR 0.18 (0.07–0.45)				OR 0.27 (0.07–1.05)				OR 0.14 (0.04–0.48)			

* Defined as subjects with history of FA/FI and positive prick test to corresponding food allergen.

⁺ Defined as subjects without history of FA/FI and with detectable allergen-specific IgE antibodies to common aeroallergens.

^β Denotes effect estimates “yes” vs “no”, all adjusted for age.

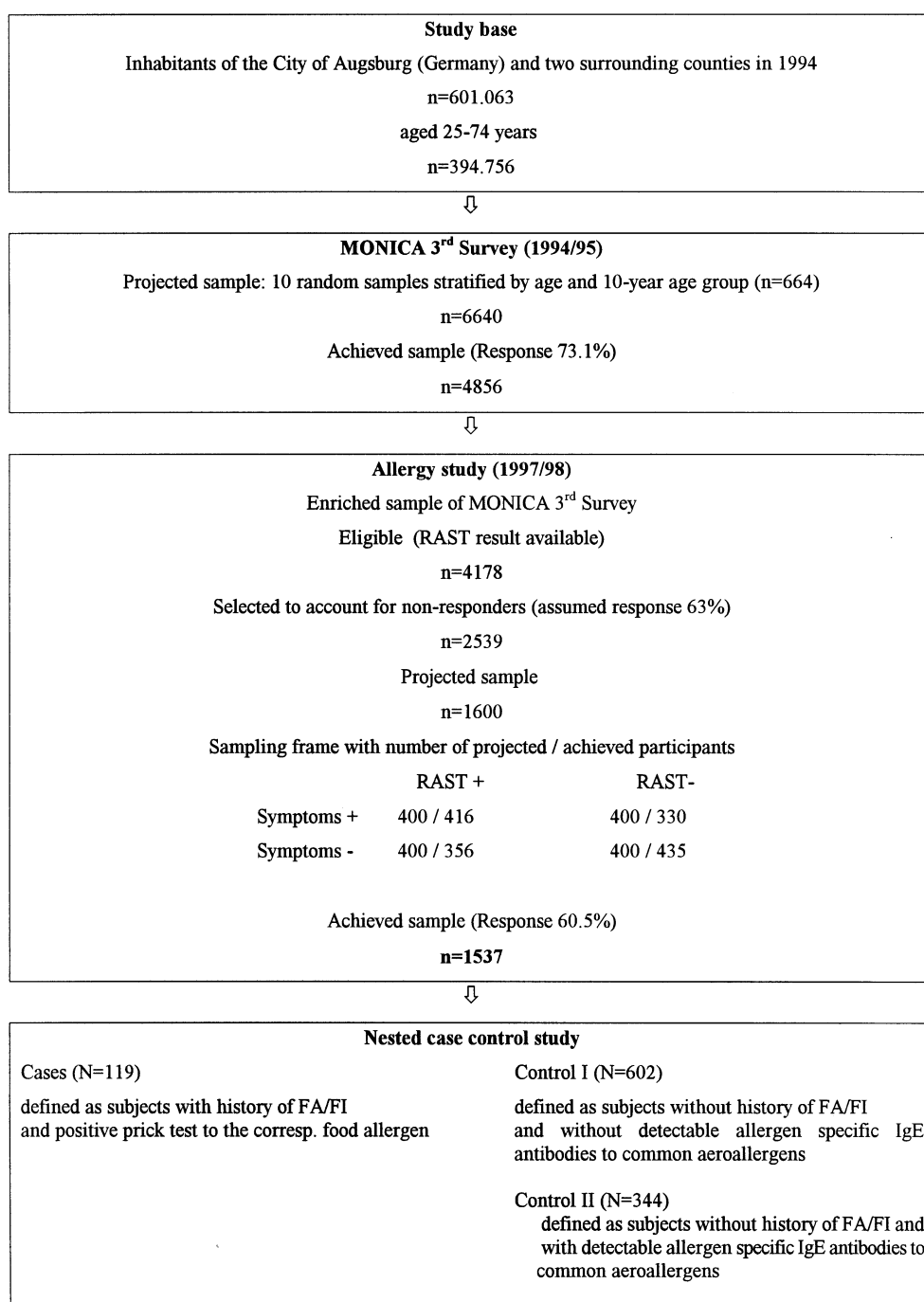


Figure 1. Study design and sampling frame.

allergic subjects, we compared these cases ($n = 106$, 89.1%) with individuals from the aeroallergen-sensitized group who reported hay fever, but not food allergy ($n = 52$, 15.1%). Subjects with hay fever and concomitant food allergy received significantly more often treatment in general, and in particular more local and systemic drug therapy, as well as specific immunotherapy, than individuals with hay fever alone. Details are given in Table 7.

In order to obtain population-based estimates on the

frequency of reported food allergy and sensitization, we extrapolated the findings of this study to the representative study base. Detailed results on that are given in Tables 1 and 3. By these calculations, the prevalence of reported FA/FI in the general population was estimated to be 15.5%, and we concluded that 16.8% of the general adult population were sensitized to at least one food allergen. The relative frequencies of adverse reactions or sensitization to single food allergens of these estimates corresponded to the findings in our selected sample.

Discussion

We here report population-based data on FA/FI, sensitization, and associations with other manifestations of atopy in adults. A major strength of the study lay in its population-based setting. Complex data on FA/FI, sensitization, and manifestations of atopy have been barely available so far.

One has to take into account, however, that according to the study design, subjects were selected from a representative study base by sensitization status and reported symptoms. This affects the generalizability of the derived absolute frequencies. Under the assumption that the prevalence of allergic sensitization to aeroallergens in representative adult populations reaches 30% (28.9% in Switzerland [18], 27.6% in Germany [19]), the effect of an overestimation might be moderate. Since the distribution of the selection criteria was known for the representative study base, we extrapolated our findings to this larger population. According to this calculation, 15.5% of the general adult population report FA/FI and 16.8% exhibit at least one positive reaction to food allergens in the SPT. According to literature data, these findings are well within the range of previous results. Estimates of the relative frequency of FA/FI, sensitization, and cross-reactivity, however, should not be influenced by that study design.

FA/FI was reported by 20.8% in our study, which is almost identical to the results of a large population-based study in the UK (19.9–20.4%) (6) and higher than the results of a Dutch study (12.4%) (7). Other studies revealed results varying between 4.9% (1) and 33% (2). In an earlier German population-based study of 910 adults, we found a reported frequency of food intolerance of 18.8% (20), and 25% of 1812 adults in a Swedish study gave a history of adverse reactions to food (12). This is in contrast to epidemiologic studies which investigated FA/FI in the population by DBPCFC (double-blind, placebo-controlled food challenge), and which revealed prevalence estimates between 1.4% and 2.4% (6, 7). The limitations of these studies arise from the small subsets which were tested ($n=73$ and 93); the selection process; the fact that in one study a standard battery of eight allergens were tested, allowing inferences only on these substances; and the type of reactions, which were to some extent only loosely related to FA/FI (headache, and behavioral and joint symptoms). One has to take into account, however, that data based on reported symptoms only will lead to a considerable overestimation of the prevalence of FA/FI. We therefore combined for further analysis the questionnaire information with the results of the SPT on the level of single allergens in order to achieve a more precisely defined group of subjects with FA/FI.

The predominance of the female sex, which was seen

in this study, is in accordance with most other observations (2, 6, 7, 21). The spectrum of relevant food allergens in adults differs from that in childhood, where milk and egg account for the majority of reactions. In our study, reactions to nuts, fruit, milk, wine, and vegetable were most frequently reported. Studies in patients revealed a predominance of similar allergens. A substantial percentage of food-sensitive subjects in our study reacted to peanut (10.3%), an allergen that accounts for even more reactions in countries where peanut consumption is more common. Different dietary habits may also explain the rather low reaction frequency to fish/seafood (6.9%) and soy (2.2%) in our population.

The vast majority of reactions occurred at the skin or mucosa (>70%). The given percentages of reactions at different organ systems from this population-based study add to the data that were derived from patient populations and in which more severe reactions were seen (8, 9).

One-quarter of the study population (25.1%) exhibited at least one positive reaction to the 10 food allergens in the skin test. There are hardly any comparable data from population-based studies in adults using the SPT with food allergens. In another representative adult sample, we found 7.1% sensitized to egg and 3.4% sensitized to milk in the SPT (20) compared to 3.1% and 3.8% in this study. In a nonatopic adult population from Singapore, 11.7% were found to be sensitized to at least one of 18 food allergens in the SPT (13). Specific IgE antibodies to at least one of six food allergens were exhibited in 8% of a Swedish adult population (12). Possibly, the absolute frequency of sensitization to food allergens was overestimated in our study due to sample selection.

Within the group of food allergens tested, we found a strong association of sensitization to soy and celery or hazelnut, as well as sensitization to celery or peanut and hazelnut. This clustering indicates cross-reactivity between food and pollen allergens causing food allergy in adults as a sequel to pollen sensitization. This is supported by the finding that over 70% of subjects with food allergy, as defined by history of FA/FI and sensitization, had a history of doctor-diagnosed hay fever. A strong and clinically relevant association of food and pollen sensitization is known from several patient-based studies (22, 23) and gave rise to descriptions of clinical entities such as the celery-carrot-mugwort-syndrome (24). Food allergy was also found to be significantly associated with other outcomes of atopy in this study, by which primarily the association with urticaria might reflect a clinical manifestation of food allergy itself. From patient populations, it was estimated that 65% of those with food allergy exhibit other clinical manifestations of atopy (8). Associations of food allergy or

sensitization with asthma and bronchial hyperresponsiveness were reported in a population-based study (12).

Furthermore, we could show that subjects suffering from hay fever and food allergy had a significantly higher need for therapy. This may indicate that hay fever in conjunction with food allergy tends to be clinically more severe.

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References

1. COHEN M, SPLANSKY G, GALLAGHER J, BERNSTEIN D, BERNSTEIN I. Epidemiologic survey and validation of adverse food reactions in adult populations [Abstract]. *J Allergy Clin Immunol* 1985;**75**:206.
2. BENDER A, MATTHEWS D. Adverse reactions to food. *Br J Nutr* 1981;**46**:403–407.
3. STROBEL S. Epidemiology of food sensitivity in childhood – with special reference to cow's milk allergy in infancy. In: BURR M, editor. *Epidemiology of clinical allergy*. Basel: Karger, 1993:119–130 (Monogr Allergy, vol. 31).
4. SAMPSON H. Epidemiology of food allergy. *Pediatr Allergy Immunol* 1996;**7 Suppl** 9:42–50.
5. ZEIGER R, HELLER S. The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomized study of combined maternal and infant food allergen avoidance. *J Allergy Clin Immunol* 1995;**95**:1179–1190.
6. YOUNG E, STONEHAM M, PETRUCKEVITCH A, BARTON J, RONA R. A population study of food intolerance. *Lancet* 1994;**343**:1127–1130.
7. JANSEN J, KARDINAAL A, HUIJBERS G, Vlieg-BERSTRA J, MARTENS B, OCKHUIZEN T. Prevalence of food allergy and intolerance in the adult Dutch population. *J Allergy Clin Immunol* 1994;**93**:446–456.
8. HOFER T, WÜTHRICH B. [Food allergy. II. Prevalence of organ manifestations of allergy-inducing food. A study on the basis of 173 cases, 1978–1982]. *Schweiz Med Wochenschr* 1985;**115**:1437–1442.
9. MÜHLEMANN R, WÜTHRICH B. [Food allergies 1983–1987]. *Schweiz Med Wochenschr* 1991;**121**:1696–1700.
10. RING J, VIELUF D. Adverse reactions to food. *Curr Probl Dermatol* 1991;**20**:187–202.
11. SICHERER S, MUÑOZ FURLONG A, BURKS A, SAMPSON H. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol* 1999;**103**:559–562.
12. BJÖRNSSON E, JANSON C, PLASCHKE P, NORRMAN E, SJÖBERG O. Prevalence of sensitization to food allergens in adult Swedes. *Ann Allergy Asthma Immunol* 1996;**77**:327–332.
13. CHNG H, TANG C, LEONG K. Healthy adults demonstrate less skin reactivity to commercial extracts of commonly ingested food than to *D. farinae*. *Asian Pac J Allergy Immunol* 1999;**17**:175–178.
14. BÖTHIG S. WHO MONICA Project: objectives and design. *Int J Epidemiol* 1989;**18**:29–37.
15. KEIL U, LIESE A, HENSE W, et al. Classical risk factors and their impact on incident non-fatal and fatal myocardial infarction and all-cause mortality in southern Germany. Results from the MONICA Augsburg cohort study 1984–1992. Monitoring trends and determinants in cardiovascular diseases. *Eur Heart J* 1998;**19**:1197–1207.
16. PEPYS J. Skin testing. *Br J Hosp Med* 1975;**14**:412–417.
17. RING J. *Angewandte Allergologie*. 2nd ed. München: MMV, 1988.
18. WÜTHRICH B, SCHINDLER C, LEUENBERGER P, ACKERMANN-LIEBRICH U. Prevalence of atopy and pollinosis in the adult population of Switzerland (SAPALDIA Study). *Int Arch Allergy Immunol* 1995;**106**:149–156.
19. SCHÄFER T, NIENHAUS A, HAUPT G, et al. Befunde der Hautuntersuchung und allergologischen Diagnostik. In: BAGS Hamberg, editor. *Epidemiologisches Untersuchungsprogramm Bille-Siedlung*. Frankfurt am Main: Peter Lang Verlag, 1997:158–194.
20. SCHÄFER T, RING J. Epidemiology of adverse food reactions due to allergy or other forms of hypersensitivity. In: EISENBRAND G, AULEPP H, DAYAN A, editors. *Food allergies and intolerances*. DFG Symposium. Weinheim: VCH Verlag, 1996:40–54.
21. BURR M, MERRETT T. Food intolerance: a community survey. *Br J Nutr* 1983;**49**:217–219.
22. DREBORG S. Food allergy in pollen-sensitive patients. *Ann Allergy* 1988;**61**:41–46.
23. ERIKSSON N, FORMGREN H, SVENONIUS E. Food hypersensitivity in patients with pollen allergy. *Allergy* 1982;**37**:437–442.
24. WÜTHRICH B, DIETSCHI R. [The celery-carrot-mugwort-condiment syndrome: skin test and RAST results]. *Schweiz Med Wochenschr* 1985;**115**:258–264.