

Heredity of food allergies in an unselected child population: An epidemiological survey from Finland

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The heredity of food allergies (FA) has not previously been addressed in a large unselected child population. Our target population comprised all children born from April 2001 to March 2006 resident in one province of South-East Finland (*n c.* 6000), as identified from the national population register. In a questionnaire survey conducted in 2005–2006, data were obtained on allergic manifestations (FA symptoms, atopic rash, allergic asthma, hay fever/pollen allergy, or animal allergy) in the biologic parents of 3800 children (64% of the total). Concurrently with the survey but independently of it, results of specific immunoglobulin E antibodies (sIgE), skin prick tests (SPT), and open food challenges (OFC) in the offspring were collected from patient records throughout the province. Up to the age of 4 yr, the incidences of any positive FA test, a positive SPT or sIgE for food items, and a positive OFC in these children were threefold higher if both parents reported having an allergic manifestation and twofold higher if either mother or father had such a manifestation when compared with children whose parents did not report any of these conditions. The estimated risk of any positive FA test increased by a factor of 1.3 (95% CI 1.2–1.4) for each additional allergic manifestation in the parents. Positive FA tests in the offspring were relatively strongly associated with the reports of allergic phenotypes and the number of these phenotypes in their biologic parents.

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The hereditary nature of asthma (1–6), hay fever (1, 6, 7), and atopic dermatitis (1, 8) has been documented in population surveys. According to twin studies, 70% of atopic manifestations are attributable to hereditary factors (9). Because a close association exists between atopic diseases and food allergies (FA), all these conditions are thought to share common risk factors, including hereditary ones (10).

Even though FA is often the first manifestation of allergy in early childhood (11), few population-based studies have focused on its heredity (10). Chinese pre-school children with a family history of adverse reactions to food had a higher prevalence of parent-reported adverse

reactions to food than those without such a family history (12). A few studies provide evidence for the heritability of peanut allergy (13, 14), higher frequencies of certain HLA types have been found among patients with nut allergy, and particular genetic polymorphisms are more common among patients with either nut or any FA than in other patients (15–20).

In conjunction with the South Karelian Allergy Research Project (SKARP) (21), a population-based survey on the occurrence of FA and its risk factors among children aged 0–4 yr in Finland, results of all FA tests performed on the target population were collected and linked with the questionnaire data. The present paper

describes the occurrence of positive results of FA tests among the offspring in relation to allergic manifestations among their biologic parents.

Methods

Population

The target population comprised *c.* 6000 children born between April 1, 2001, and March 31, 2006, who were resident in the province of South Karelia in South-East Finland at the time of the questionnaire survey (21). The subjects were identified and their demographic details obtained from the Finnish Population Registry (<http://www.vaestorekisterikeskus.fi>).

Ethics and permissions

The protocol was reviewed by the Ethical Committee of the Northern Ostrobothnia Hospital District, and a notification of data collection was sent to the Data Protection Ombudsman. The allergy test data were collected from the patient records with the permission of the Finnish Ministry of Social Affairs and Health. All eleven health care centers in the region gave their approval for cooperation. None of the authors provided any medical care for the population.

Data collection

Details of the study design and data collection have been reported elsewhere (21). Briefly, we conducted a questionnaire survey in close cooperation with local child health clinics during 2005–2006, when the children were 0- to 4- yr-old. Parents of 3899 children returned the questionnaire, the overall response rate being 66%. The questionnaires are available at <http://ke-lo.oulu.fi/tutkimus/EKAT/>.

The results of all FA tests performed on the target children (including non-respondents in the questionnaire survey) were collected from the patient and laboratory records of all the hospitals, health care centers, private clinics, and laboratories in the province. All the FA tests had been ordered by a physician and had been performed from August 2001 to September 2006; the results being collected concurrently with the administration of questionnaire survey but independently of it. We estimated from parental reports that our test data covered at least 90% of all children tested for suspected allergy in the area and that the test data failed to cover *c.* 1% of the children who had only been tested elsewhere. The test data included the referring

practice, dates, and results of the tests and the child's unique personal identity code (PIC).

Measurements and classification

Outcomes. The outcomes were the first positive test results for (i) milk, (ii) egg, (iii) essential food items including milk, egg, and cereals (wheat, barley, rye, oat, maize, rice, or buckwheat), and (iv) any food item measured by (a) skin prick tests (SPT), (b) specific immunoglobulin E antibodies (sIgE) to food items, and (c) open food challenges (OFC). As SPTs and sIgEs indicate IgE-mediated immunologic responses (22), they were combined here into a single outcome (sIgE/SPT).

A mean of two orthogonal diameters of the urticarial weal equal to 3 mm, applied to both positive and negative controls, was taken as the cut point for a positive result in SPTs. The cut point for sIgEs was 0.35 kU/l (for RAST-CAP FEIA or Phadiatop Combi) in 98% of the tested subjects and 1.43 standardized units per milliliter (for Magic Lite) in the rest. The positive results of the OFCs in the patient records were based on the conclusion made by a pediatrician; therefore, they can be considered FAs as well.

Explanatory variables. The parents were asked in the questionnaire whether the child's biologic mother, biologic father, or both had ever been found to have asthma or any allergic or hypersensitive disease (atopic rash, animal dust allergy, hay fever or pollen allergy, asthma or FA). These allowed the following categories to be formed: (i) physician-diagnosed allergic disorder, (ii) self-perceived allergic disorder, (iii) no allergic disorder ever perceived, and (iv) unknown. The parent was classified as having 'allergic asthma' if he or she had physician-diagnosed asthma and a physician-diagnosed inhalant allergy (animal dust allergy or hay fever or pollen allergy). Based on the above, the following phenotypes were defined for the parents:

- A. FA symptoms (self-perceived or physician-diagnosed FA)
- B. Physician-diagnosed allergic manifestations other than FA (atopic rash, animal allergy, hay fever/pollen allergy, or allergic asthma)
- C. Any allergy (any of the above conditions)

'Atopic rash' and other 'allergic manifestations' were solely based on the parents' own reports of a diagnosis made by a physician, and no additional documentation of IgE-mediated sensitiza-

tion was available. The children were classified according to the parents' phenotype: (i) neither, (ii) only mother, (iii) only father, (iv) both parents, and (v) missing (complete data on both parents were required for phenotypes A and B). In the case of parental phenotype C: 'Any allergy', the children were classified according to phenotypes A and B if at least one manifestation of these allergies in either parent was mentioned. We also created a variable expressing the 'number of allergic manifestations' in both parents, given that complete data were available on both parents. This variable representing the severity of the parents' allergic disease was based on the consideration that an allergic predisposition may manifest itself in different organs with a multitude of symptoms and the more severe the predisposition is, the broader the spectrum of manifestations will be.

The birth order was classified as 'firstborn' and 'not firstborn'. Firstborn twins were both classified as firstborn.

Statistical methods

The cumulative incidences of a positive test result in FA tests by age were estimated by the Kaplan–Meier method, using the `survfit` function of the survival package in the R environment release 2.9.2 (<http://www.r-project.org/>). The 'event' in these analyses was the first positive result observed, the 'event age' of the positive test result was the child's age on the date of the event, and the 'risk time' began on the child's birthday and ended at the event age if any event occurred. Among children not experiencing the pertinent event during the follow-up, the risk time of the first positive test was deemed to have ended on the closing date of data collection (September 30, 2006). In the case of sIgE/SPT, the 'event' was the first positive result in either of these tests and the event age was the child's age at the date of its occurrence.

The incidence rates were further analyzed by the Cox proportional hazards model (with the `coxph` function in the R survival package), using the parental phenotypes and the number of allergic manifestations among the parents as explanatory factors. The total number of allergic manifestations among the parents was also used as a continuous variable. Gender and birth order were included as covariates in all the Cox models. The assumption of proportional hazards was assessed by inspecting the cloglog transforms of the cumulative proportions.

Results

Participants

Altogether, 5973 children in the intended population were identified and their demographic details obtained from the Population Registry. In the questionnaire survey, the parents of 53 children (1.5%) refused permission to perform the data linkage, and these children were excluded from all further analyses. The study population thus comprised 5920 eligible children of 4751 mothers. The parents of 3221 families returned the questionnaires on a total of 3899 participating children (participation rate 66%). Among the questionnaires returned, 3800 (97%) contained information on allergic conditions in the biologic parents, and 3170 (81%) were 'complete cases', i.e., the required data on each allergic manifestation were available for both parents. Twenty percent of the children whose parents had any allergy and 12% of the children with non-allergic parents had been tested for FA. Seventy-three percent of the participants with some information on parents' allergic manifestations belonged to families from which a single child was recruited to the survey, and 80% of the participants were the only participants from their families. In 49 families, multiple participants had been FA tested, and in 11 of these families, multiple participants had a positive FA test result. The overall relative rate (RR) of a positive sIgE/SPT was higher in boys than in girls (RR 1.5, 95% CI 1.1–2.0) and higher in the firstborn children than in the others (RR 1.5, 95% CI 1.1–1.9).

Any allergy in parents and FA test results in their offspring

The cumulative incidence of any positive FA test in the children by 4 yr of age was threefold higher if both biologic parents had an allergic manifestation and twofold higher if one parent had an allergy than if both parents were free of allergies (Table 1). The incidence of a positive sIgE/SPT for any food item followed the same pattern (Table 1, Fig. 1), as also did the separate incidences regarding essential food items, milk, and egg (data not shown).

Specific allergic manifestations in parents and FA test results in their offspring

Associations of a similar kind were repeated for each individual manifestation of allergy in the parents and FA test results in their offspring (Table 1). The prevalence of maternal asthma was 7.8% (with inhalation allergy 6.5%) and that of paternal asthma 5.9% (with inhalation allergy

Table 1. Numbers (N) of children participating in the questionnaire survey, the cumulative incidences (%) up to 4 yr of age and gender and birth order adjusted relative rates (RR) of a positive result in food allergy (FA) tests (during the follow-up) in relation to separate manifestations of allergy in the biologic parents. Numbers of cases (n) and 95% confidence intervals are shown in parentheses

	N	First positive FA test for any food item					
		Any FA test*		sIgE or SPT		OFC	
		% (n)	RR (95% CI)	% (n)	RR (95% CI)	% (n)	RR (95% CI)
FA symptoms							
None	2377	5.9 (131)	1	4.4 (95)	1	2.7 (59)	1
Mother only	626	12.3 (67)	2.0 (1.5–2.7)	10.1 (54)	2.3 (1.6–3.2)	7.1 (39)	2.6 (1.7–3.9)
Father only	298	12.5 (34)	2.2 (1.5–3.2)	10.0 (27)	2.4 (1.6–3.7)	4.9 (13)	1.8 (1.0–3.2)
Both	111	19.2 (17)	3.0 (1.8–5.0)	15.2 (13)	3.2 (1.8–5.6)	8.7 (9)	3.4 (1.7–6.8)
Missing	388	6.7 (24)	1.1 (0.7–1.7)	5.7 (20)	1.3 (0.8–2.1)	1.6 (6)	0.6 (0.3–1.4)
Animal allergy							
None	2349	5.9 (130)	1	4.7 (101)	1	2.6 (58)	1
Mother only	584	12.7 (62)	2.0 (1.5–2.7)	9.5 (45)	1.8 (1.3–2.6)	6.1 (33)	2.3 (1.5–3.6)
Father only	399	11.7 (42)	2.0 (1.4–2.8)	9.5 (34)	2.1 (1.4–3.1)	4.7 (16)	1.7 (1.0–2.9)
Both	109	17.0 (17)	2.9 (1.8–4.8)	11.2 (11)	2.4 (1.3–4.4)	10.8 (11)	4.1 (2.2–7.8)
Missing	359	6.5 (22)	1.1 (0.7–1.7)	5.3 (18)	1.1 (0.7–1.9)	2.6 (8)	0.9 (0.4–1.8)
Hay fever or pollen allergy							
None	2054	5.3 (102)	1	3.9 (75)	1	2.5 (49)	1
Mother only	712	12.1 (77)	2.3 (1.7–3.1)	8.9 (56)	2.3 (1.6–3.2)	6.3 (41)	2.5 (1.6–3.8)
Father only	541	11.2 (54)	2.1 (1.5–2.9)	9.3 (44)	2.3 (1.6–3.4)	4.1 (20)	1.6 (0.9–2.6)
Both	183	14.2 (22)	2.5 (1.6–3.9)	11.4 (17)	2.6 (1.5–4.4)	5.8 (10)	2.3 (1.2–4.5)
Missing	310	6.6 (18)	1.1 (0.7–1.9)	6.4 (17)	1.5 (0.9–2.5)	2.3 (6)	0.8 (0.3–1.8)
Atopic rash							
None	2473	6.2 (137)	1	4.8 (104)	1	2.6 (58)	1
Mother only	597	12.4 (68)	2.1 (1.6–2.8)	9.6 (51)	2.1 (1.5–2.9)	7.5 (43)	3.1 (2.1–4.6)
Father only	268	13.3 (34)	2.3 (1.6–3.4)	9.8 (25)	2.2 (1.4–3.5)	5.4 (14)	2.2 (1.2–4.0)
Both	82	18.9 (15)	3.4 (2.0–5.7)	17.0 (13)	3.8 (2.1–6.8)	6.9 (5)	2.6 (1.0–6.5)
Missing	380	5.3 (19)	0.9 (0.6–1.4)	4.4 (16)	1.0 (0.6–1.7)	1.9 (6)	0.7 (0.3–1.5)
Allergic asthma							
None	3039	7.7 (213)	1	5.9 (159)	1	3.8 (105)	1
Mother only	210	13.8 (27)	1.9 (1.3–2.9)	10.4 (20)	1.9 (1.2–3.0)	6.9 (14)	2.0 (1.1–3.5)
Father only	144	5.2 (7)	0.7 (0.3–1.4)	5.2 (7)	0.9 (0.4–1.9)	(0)	
Both	6	25.0 (1)	2.5 (0.3–17.5)	25.0 (1)	3.3 (0.5–23.7)	(0)	
Missing	401	7.0 (25)	0.9 (0.6–1.3)	6.2 (22)	1.0 (0.7–1.6)	1.8 (7)	0.5 (0.2–1.1)
Any allergy							
None	1502	4.0 (57)	1	3.0 (42)	1	2.0 (28)	1
Mother only	1093	9.4 (93)	2.4 (1.7–3.3)	7.0 (69)	2.3 (1.6–3.2)	4.9 (49)	2.5 (1.6–3.9)
Father only	693	9.1 (58)	2.3 (1.6–3.3)	7.2 (45)	2.4 (1.6–3.7)	3.1 (20)	1.6 (0.9–2.8)
Both	512	14.5 (65)	3.5 (2.4–5.0)	12.2 (53)	3.2 (1.8–5.6)	6.2 (29)	3.1 (1.8–5.1)
Missing	0						
Total	3800	7.9 (273)		6.2 (209)		3.6 (126)	

*Including specific immunoglobulin E antibodies (sIgE) for any food item, skin prick tests (SPT) for a food item and open food challenges (OFC).

4.6%). As allergic asthma was not very common among the parents, only a few children with positive FA tests were found among the offspring of asthmatic parents. The incidence of positive OFCs was higher in the case of each separate manifestation of maternal allergy alone than in the case of each paternal allergy alone (Table 1, Fig. 1), the finding being largely similar regarding essential food items, and milk in particular (data not shown).

Number of allergic manifestations in parents and positive FA tests in their offspring

The incidence of positive FA tests increased with the number of allergic manifestations

among the parents (Table 2 and Figs 1 and 2). The Cox analysis showed that the incidence of any positive FA test increased by a factor of 1.3 (95% CI 1.2–1.4) for each additional allergic manifestation, the corresponding increment being 1.3 (95% CI 1.2–1.4) for a positive test for milk, and 1.3 (95% CI 1.2–1.5) for a positive test for egg. The incidence of both a positive sIgE/SPT to a food item and a positive OFC was associated with the number of allergic manifestations in their parents (Fig. 2). The incidence of a positive OFC for milk increased by 1.3 (95% CI 1.2–1.5) and that of a positive sIgE/SPT by 1.3 (95% CI 1.2–1.4) for each additional allergy in the parents.

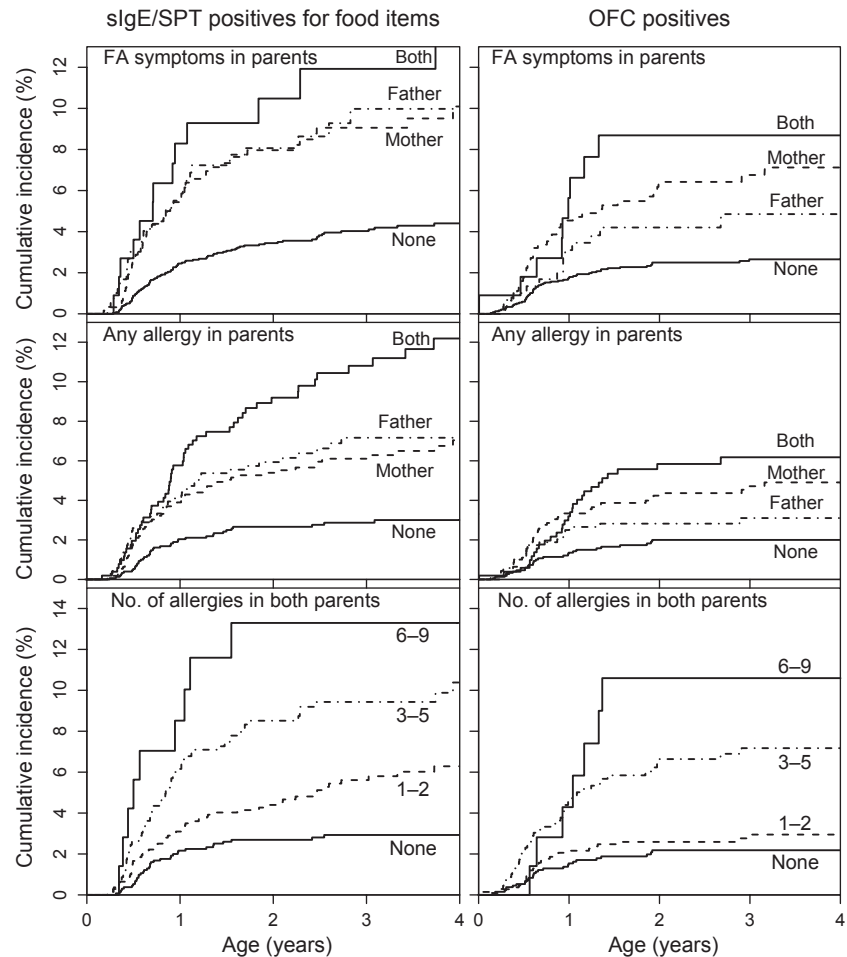


Fig. 1. Kaplan–Meier plots for the cumulative incidences of positive results in specific immunoglobulin E tests or skin prick tests for a food item and open food challenges in the children in relation to food allergy symptoms, any allergy, and number of allergic manifestations in both biologic parents.

Positive predictive values of FA tests

The positive predictive values of FA tests (PPV) were 45% (93/207) if the mother alone and 43% (58/135) if the father alone, 48% (65/135) if both parents had an allergic manifestation, and 33% (57/173) if neither of them had an allergic manifestation (Table 3). The occurrence of a positive result in any FA test was 50% higher in the children of one or two allergic parents than in children of non-allergic parents. The PPVs for SPTs and OFCs were higher for the offspring of non-allergic than allergic parents, but because of low numbers, this finding remained equivocal. The PPVs were also higher for sIgE, sIgE/SPT, and any test in the offspring of allergic than non-allergic parents.

Missing data

The cumulative incidences of positive FA tests were usually higher in children with missing data on their parents' allergies (310–630 children for various parental manifestations of allergy) than in the children of no allergies reported in their

parents (Tables 1 and 2). When non-respondents were included in the missing category, the incidence of positive FA tests for various parental manifestations of allergy was attenuated and came closer to the figures for the children with no allergies reported in their parents (data not shown).

Discussion

Principal findings

Our population-based survey provides evidence for a fairly strong association between parental allergies and positive FA tests in their offspring. The incidence of positive FA tests in the offspring was twofold higher if FA symptoms or any allergy had been reported in either parent, and threefold higher if these conditions had been reported in both parents when compared with the offspring of parents having no allergies. The risk of a child having a positive result in FA tests rose as a function of the number of allergic manifestations in the biologic parents.

Table 2. Numbers (N) of children participating in the questionnaire survey, cumulative incidences (%) up to 4 yr of age and gender and birth order adjusted relative rates (RR) of a positive result in food allergy (FA) tests (during the follow-up) in relation to the number of allergic manifestations in both biologic parents. The numbers of cases (n) and 95% confidence intervals are shown in parentheses

		First positive FA test for selected food items					
		Any FA test*		slgE or SPT		OFC	
Food item	N	% (n)	RR (95% CI)	% (n)	RR (95% CI)	% (n)	RR (95% CI)
No. of allergic manifestations							
Milk							
None	1321	2.8 (35)	1	1.8 (20)	1	1.9 (23)	1
1–2	1085	4.7 (44)	1.6 (1.0–2.4)	3.3 (30)	1.9 (1.1–3.3)	2.4 (24)	1.3 (0.7–2.3)
3–5	693	10.3 (63)	3.6 (2.3–5.4)	6.6 (39)	3.8 (2.2–6.5)	5.9 (37)	3.1 (1.8–5.2)
6–9	71	12.1 (8)	4.5 (2.1–9.8)	7.0 (5)	5.0 (1.9–13.2)	11.0 (7)	5.8 (2.5–13.5)
Missing	630	5.4 (31)	1.9 (1.2–3.0)	3.8 (22)	2.3 (1.3–4.3)	2.0 (12)	1.1 (0.5–2.2)
Total		5.3 (181)		3.5 (116)		2.9 (103)	
Egg							
None	1321	1.5 (19)	1	1.5 (19)	1	(0)	
1–2	1085	3.3 (33)	2.2 (1.2–3.8)	3.2 (32)	2.1 (1.2–3.7)	0.3 (2)	
3–5	693	5.5 (32)	3.3 (1.9–5.8)	5.5 (32)	3.3 (1.9–5.8)	(0)	
6–9	71	15.8 (9)	9.6 (4.3–21.2)	15.8 (9)	9.6 (4.3–21.2)	(0)	
Missing	630	4.3 (25)	2.8 (1.5–5.0)	4.3 (25)	2.8 (1.5–5.0)	(0)	
Total		3.5 (118)		3.4 (117)		0.1 (2)	
Essential food items†							
None	1321	4.0 (51)	1	2.8 (36)	1	2.0 (25)	1
1–2	1085	7.0 (68)	1.7 (1.2–2.4)	5.4 (53)	1.8 (1.2–2.8)	2.9 (29)	1.4 (0.8–2.4)
3–5	693	13.1 (81)	3.2 (2.2–4.5)	9.5 (58)	3.2 (2.1–4.8)	6.9 (43)	3.3 (2.0–5.5)
6–9	71	10.0 (11)	4.4 (2.3–8.4)	13.3 (9)	5.1 (2.5–10.6)	10.6 (7)	5.4 (2.3–12.4)
Missing	630	8.1 (46)	1.9 (1.3–2.8)	7.0 (39)	2.3 (1.5–3.6)	2.8 (16)	1.3 (0.7–2.5)
Total		7.4 (257)		5.7 (195)		3.4 (120)	
Any food item							
None	1321	4.1 (52)	1	2.9 (37)	1	2.2 (27)	1
1–2	1085	7.8 (75)	1.8 (1.3–2.6)	6.3 (59)	2.0 (1.3–3.0)	2.9 (30)	1.4 (0.8–2.3)
3–5	693	14.0 (87)	3.4 (2.4–4.7)	10.4 (64)	3.4 (2.3–5.2)	7.2 (45)	3.2 (2.0–5.2)
6–9	71	16.3 (11)	4.3 (2.2–8.2)	13.3 (9)	5.0 (2.4–10.3)	10.6 (7)	5.0 (2.2–11.4)
Missing	630	8.6 (48)	2.0 (1.3–2.9)	7.4 (40)	2.3 (1.5–3.6)	3.0 (17)	1.3 (0.7–2.4)
Total	3800	7.9 (273)		6.2 (209)		3.6 (126)	

*Including specific immunoglobulin E antibodies (slgE) for any food item, skin prick tests (SPT) for a food item and open food challenges (OFC).

†Including milk, egg, and cereals.

Strengths and weaknesses

The main strengths of the present study lie in the unique data, based on a large, unselected child population in a defined geographical area, nearly all FA tests performed on these children, and the possibility for individual linkage of these records with a questionnaire survey. As a result of the relatively high participation rate and comprehensive data collection procedure, the target area and its general child population were covered reasonably well.

The study design enabled an assessment of the selection bias inherent in any questionnaire survey. The incidence of positive FA tests in categories having missing data on the parents' allergies points to a missing-at-random process (23) rather than to selective response. The attenuation of the incidence figures in the categories with missing data and the non-respondents indicates a slight overrepresentation of allergic parents and cases among the participants.

Although the questions were designed in a way to reduce the possibility of information bias, such biases cannot be entirely ruled out. All the parents were informed about the organs where the symptoms might possibly emerge (21). Allergic parents may still perceive more sensitively the association between food items and any symptoms of their offspring, which might lead to over-reporting of food-related symptoms. The allergic symptoms (e.g., atopic eczema) may also have been observed by the nurses during the regular visits to the child health clinics. Based on the experience of the public health nurses and physicians in these clinics practically all children with food-associated symptoms, particularly those of essential food items, are identified and referred to FA tests. In Finland, all the FA tests are ordered by a physician and are either free of charge, when they are performed in the public health care sector, or partly reimbursed by the national sickness insurance when they are

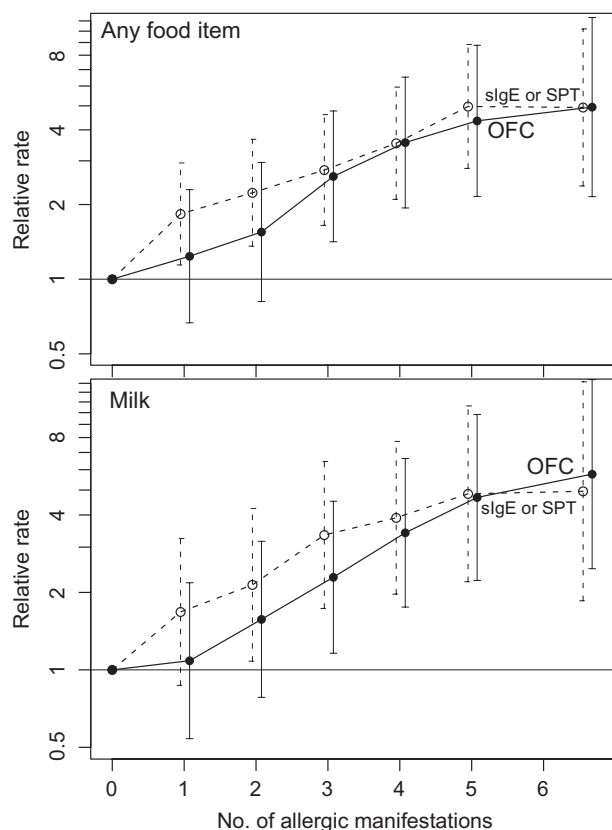


Fig. 2. Relative rates (RR) of the child's first positive results in allergy tests for any food item (upper plot) and for milk alone (lower plot) in relation to the number of allergic manifestations (food allergy symptoms, atopic rash, allergic asthma, pollen allergy, and/or animal allergy) in both biologic parents. Both plots show RR for open food challenges (solid lines) and specific immunoglobulin E antibodies or skin prick tests for a food item. Confidence intervals of the RR are shown by vertical lines.

performed in the private sector. Because neither SPTs nor sIgEs are painless tests and both SPTs and food challenges (with preceding elimination diet) and may cause systemic reactions (24–26), conducting these tests on symptomless children would be unethical and therefore unlikely. A higher PPV of FA tests among the offspring of allergic parents rather points to more careful selection of the children to FA tests than over-testing. Thus, the strong association between parents' allergies and positive FA tests can hardly be explained away solely by differential misclassification of the outcome.

The measurements of the FA tests in several laboratories with varying practices and procedures as well as different cut points probably caused non-differential misclassification of the outcome. All sIgEs with different cut points were included in the final test data. Results of CAP and Magic Lite methods of sIgE are highly correlated and have been used together (11).

Heterogeneity of our data in this regard has apparently been quite independent of parental allergies, and hence most likely caused attenuation of our RR estimates toward 1. Therefore, non-differential misclassification has at least partly counteracted with the biasing effect of any differential misclassification.

Although this study was based only on questionnaire data on allergic phenotypes in both biologic parents and FA test data on their offspring, it serves adequately as a first-stage descriptive survey, a *sine qua non* of genetic epidemiology (27). Although the FA testing of the children mostly occurred before our questionnaire survey, the parents' reports on their own physician-diagnosed allergies are likely to be an adequate source of data. The prevalences of parental asthma (non-allergic and allergic) agree well with figures found for the same age groups in another Finnish cohort (28). The parents were born between the 1950s and the 1980s, an era when FAs were rarely diagnosed in early childhood. On the other hand, pollen allergies were well known and diagnosed more commonly among these generations, even in childhood. We therefore assume that the parents' FAs are predominantly secondary food hypersensitivities related to pollen allergies, which are commonly found in adults, too (29).

A positive result in a FA test can be interpreted in terms of sensitization to food items rather than clinical FA. A positive sIgE/SPT alone without information on a history of FA symptoms indicates 'IgE-mediated sensitization to the food item' (22), while a positive OFC can be defined as a 'physician-diagnosed FA' (26). The occurrences of 'sensitization to food items' and 'physician-diagnosed FAs' should nevertheless be interpreted with caution, because they are subject to variations in testing practices and the selection of food items to be tested.

Comparison with other studies

The few previous studies on the heredity of FA have concentrated on specified food items, e.g., peanuts (13, 14), and nuts (15, 16). The widely varying frequencies of genetic polymorphisms and HLA types among patients with FA and their controls may also be indicative of a genetic background for FA (17–19). These previous findings are not yet convincing evidence for the inheritance of FA, however (10, 20). A slightly stronger association between a maternal than a paternal history of adverse reactions to food and children's adverse food reactions has recently been reported among Chinese pre-school

Table 3. Positive predictive values of food allergy–tested subjects (%) and relative rates (RR, based on Cox regression with 95% confidence intervals) according to parental allergies

	SPT		slgE		slgE/SPT		OFC		Any test	
	%	RR (95% CI)	%	RR (95% CI)	%	RR (95% CI)	%	RR (95% CI)	%	RR (95% CI)
Milk										
None	20	1	10	1	14	1	77	1	24	1
Mother only	23	1.15 (0.6–2.3)	19	1.95 (1.0–3.8)	22	1.62 (1.0–2.7)	65	0.68 (0.4–1.1)	34	1.47 (1.0–2.2)
Father only	18	0.93 (0.4–2.2)	17	1.75 (0.9–3.6)	21	1.55 (0.9–2.7)	69	0.85 (0.5–1.6)	30	1.34 (0.9–2.1)
Both	15	0.71 (0.3–1.6)	24	2.60 (1.3–5.1)	23	1.69 (1.0–3.0)	72	0.69 (0.4–1.2)	35	1.57 (1.0–2.4)
	19		17		20		70		31	
Essential food items										
None	36	1	18	1	26	1	81	1	35	1
Mother only	35	0.95 (0.6–1.6)	28	1.64 (1.0–2.7)	32	1.31 (0.9–1.9)	72	0.68 (0.4–1.1)	43	1.29 (0.9–1.8)
Father only	30	0.78 (0.4–1.5)	29	1.83 (1.1–3.1)	34	1.44 (0.9–2.2)	69	0.75 (0.4–1.4)	44	1.38 (1.0–2.0)
Both	33	0.84 (0.5–1.5)	36	2.18 (1.3–3.6)	39	1.63 (1.1–2.5)	72	0.63 (0.4–1.1)	48	1.44 (1.0–2.1)
	34		27		33		73		42	
Any food items										
None	39	1	16	1	24	1	82	1	33	1
Mother only	35	0.85 (0.5–1.4)	28	1.84 (1.1–3.0)	34	1.49 (1.0–2.2)	75	0.79 (0.5–1.3)	45	1.47 (1.1–2.0)
Father only	31	0.76 (0.4–1.4)	28	1.98 (1.1–3.4)	34	1.55 (1.0–2.4)	67	0.71 (0.4–1.3)	43	1.47 (1.0–2.1)
Both	38	0.89 (0.5–1.5)	33	2.29 (1.4–3.8)	40	1.80 (1.2–2.7)	67	0.58 (0.4–1.0)	48	1.58 (1.1–2.3)
	36		26		32		73		42	

SPT, skin prick test for a food item; slgE, specific immunoglobulin E antibodies for any food item; OFC, open food challenges.

children (12), and our results are in agreement with these findings, which can be explained by the closer immunologic contact with the mother than with the father during the gestational and breastfeeding periods. Our results are also in accordance with the previous finding according to which atopic mothers are more likely to report food-related problems in their child up to the age of 1 yr (30).

Implications of the findings

This Finnish cohort is the first unselected population ever in which the inheritance nature of ‘IgE-mediated sensitization to food items’ or ‘physician-diagnosed FA’ has been described, and the results suggest that the incidences of ‘sensitization to food items’ and ‘physician-diagnosed FA’ are highest in children whose biologic parents reportedly have an allergic phenotype. Thus, allergic phenotypes and the number of these among the biologic parents provide valuable a priori information for the physician when contemplating whether to continue with the testing process. Any diagnosis of FA diagnosis should still be based on adequate FA tests including the OFCs.

Unanswered questions and future research

Comparative surveys in different populations are desirable for achieving results that are applicable elsewhere. Further investigations should focus on potential causal mechanisms and interactions

between genes and the social and biologic environment to increase our population-based knowledge of the hereditary and environmental risk factors for FAs.

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Conflicts of interests

None declared.

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