

Incidence of parentally reported and clinically diagnosed food hypersensitivity in the first year of life

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Background: There are very few population-based studies investigating the incidence of food hypersensitivity during the first year of life.

Objective: To determine the incidence of parentally reported food hypersensitivity and objectively diagnosed food hypersensitivity during the first year of life.

Methods: A birth cohort was recruited ($n = 969$). At 3, 6, 9, and 12 months, information regarding feeding practices and reported symptoms of atopy were obtained. At 1 year, infants underwent a medical examination and skin prick testing to a battery of allergens. Symptomatic infants underwent food challenges.

Results: Adverse reactions to foods were reported by 132 (14.2%) parents at 3, 83 (9.1%) at 6, 49 (5.5%) at 9, and 65 (7.2%) at 12 months. Of the subjects, 1.0% (8/763) were sensitized to aeroallergens and 2.2% (17/763) to food allergens. Between 6 and 9 months and 9 and 12 months, 1.4% (14/969) and 2.8% (27/969) infants were diagnosed with food hypersensitivity on the basis of open food challenges and 0.9% (9/969) and 2.5% (24/969) on the basis of double-blind, placebo-controlled food challenges. Cumulative incidence of food hypersensitivity by 12 months was 4% (39/969; 95% CI, 2.9% to 5.5%) on the basis of open food challenges and 3.2% (31/969; 95% CI, 2.2% to 4.5%) on the basis of double-blind, placebo-controlled food challenges. **Conclusion:** Between 2.2% and 5.5% of infants have food hypersensitivity in the first year of life. The rate of parental perception of food hypersensitivity is higher than the prevalence of atopic sensitization to main food allergens or objectively assessed food hypersensitivity.

Clinical implications: In the first year of life, the rate of parentally perceived food hypersensitivity is considerably higher than objectively assessed food hypersensitivity. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Food hypersensitivity, infants, double-blind, placebo-controlled food challenge

Food hypersensitivity (FHS) is defined as an adverse reaction after food ingestion. FHS can be divided into either *food allergy* if immunologically mediated or *nonallergic food hypersensitivity*, previously referred to as *food intolerance*.¹ The gold standard in establishing food hypersensitivity is the double-blind, placebo-controlled food challenge (DBPCFC).² Research evidence suggests that the rates of objectively diagnosed FHS using DBPCFCs differ greatly from rates of self-reported FHS.³⁻⁵

Very few population-based studies have investigated the rate of food hypersensitivity or the rates of parentally reported FHS. Only 1 population-based study, conducted more than 25 years ago, has examined the incidence of parentally reported FHS and objectively diagnosed 8% of children (0-3 years) with FHS using food challenges.⁶ There are 4 population-based studies^{3,7-9} examining only the incidence of cow's milk FHS. Gerrard et al⁹ diagnosed 59 out of 787 (7.5%) consecutively born Canadian infants with cow's milk FHS on the basis of open food challenges (OFCs). A study conducted in Denmark⁸ established the incidence of cow's milk FHS at 2.2% at 1 year of age by means of food challenges in a cohort of 1749 infants. In another study conducted in the Netherlands,⁷ 1158 unselected newborn infants were followed from birth to 1 year of age. The calculated incidence rate for cow's milk FHS was 2.8%. More recently, Eggesbo et al¹⁰ established that by 2 years, the cumulative incidence of parentally reported adverse reactions to foods was 35%.

The purpose of this study was to establish the rates of objectively assessed food hypersensitivity in the first year of life and compare this with the rate of parentally reported FHS during this time. In addition, we determined the rates of sensitization to food allergens at 12 months of age.

METHODS

Design

A whole population birth cohort was established on the Isle of Wight to study the incidence of food hypersensitivity. Approval for

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Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge
 FHS: Food hypersensitivity
 OFC: Open food challenge
 SPT: Skin prick test

the study was obtained from the Isle of Wight, Portsmouth, and South East Hampshire Local Research Ethics Committee (Ref 09/01).

Participants

All pregnant mothers with an estimated delivery date of September 2001 to August 2002 were approached at antenatal clinics. After consent, information regarding family history of allergy (parental or sibling), parental smoking, socioeconomic status, and household pets was obtained.

At 3, 6, and 9 months, information regarding feeding practices, immunization status, and reported symptoms of atopy were obtained by using a standardized questionnaire administered by telephone. Two members of the research team screened this information, and subjects who reported an adverse reaction to a food were contacted. Infants with an indicative history were invited to attend the Allergy Centre, where a more detailed history was taken to ascertain which foods were implicated in producing the reported symptoms. In addition, they were skin prick tested to the suspected foods at whatever age they presented.

At the age of 1 year, all of the infants were invited to be reviewed at a clinic for a medical examination guided by a detailed questionnaire. The questionnaire covered symptoms of atopy (informed by International Study of Asthma and Allergies in Childhood [ISAAC] questions), feeding and weaning practices, immunization history, and environmental factors. All infants were approached to undergo skin prick testing to a standard battery of food (milk, egg, wheat, peanut, sesame, and cod fish), aeroallergens (house dust mite *Dermatophagoides pteronyssinus*, cat, and grass), and other allergens as identified by history. SPTs were conducted with commercial extracts of standard food and aeroallergens (Soluprick SQ allergens; ALK Allergologisk Laboratorium A/S, Horsholm, Denmark). The wheal was measured after transfer to paper from the skin with translucent tape. Measurement was undertaken in standard fashion, measuring the largest wheal diameter and the diameter orthogonal to it. The mean wheal diameter was calculated. Results were expressed as positive if mean diameter was 3 mm or more in the presence of a negative control and a positive histamine reaction after 15 minutes.

Infants were invited for a food challenge if they had never previously knowingly eaten a large amount of the food to which they had a positive SPT or if they had a previous adverse reaction to foods regardless of their SPT result. Food challenges were conducted with all foods except peanuts and sesame, because it is thought that infants should not be exposed to these foods in the first year of life (Sampson H, et al, Personal communication, May-July 2001). We aimed to perform all challenges after 6 weeks of exclusion diet, but each challenge with reported symptoms was assessed individually to ensure it was a true negative food challenge rather than the child outgrowing the FHS.

Challenges were performed following an algorithm. Procedures for both 1-day and 1-week challenges have been described previously.¹¹

All eligible infants underwent open challenges, and only those with a positive reaction were invited to participate in a DBPCFC. Those with a history of immediate symptoms were invited to the

TABLE I. Characteristics of recruited infants (n = 969)

Male sex	500 (51.6%)
First child	401 (41.4%)
Exposure to environmental tobacco smoke in the first year of life	421 (43.5%)
Reported history of allergic disease	
Family history of FHS	322 (33.2%)
Maternal history of FHS	189 (19.5%)
Sibling with FHS	122 (21.5%)
Method of feeding at 3 months of age	
Exclusively breast-fed	198 (20.4%)
Breast-fed and formula-fed	128 (13.2%)
Exposure to pets (cat/dog) during the first year of life	534 (55.1%)
Medium/high socioeconomic status (based on maternal level of education)	589 (60.8%)
Mean cord IgE (SD), n = 859	0.52 kU/L (1.95)

hospital to undergo the challenge procedure. Challenges were performed at home when the history indicated delayed development of symptoms and negative skin prick test (SPT). Some of these home challenges started at hospital and were continued at home. Reactions during a home challenge were reported by parents on a food and symptom diary. We ensured that after a negative challenge, all children consumed a normal portion of the suspected food. Children with 1-day challenges consumed a normal portion on the day of challenges. Children with 1-week challenges consumed normal portions for 1 week. In addition all children were contacted 4 to 6 weeks after the negative challenges to find out whether they were eating the food regularly without any reaction.

Analysis of data

All data were double-entered by different operators on SPSS versions 10 and 11 (SPSS Inc, Chicago, Ill) and were compared and verified. Frequency tables were constructed to obtain estimates of food sensitization rates, and 95% CIs were computed. Contingency table analyses were performed to investigate associations between sensitivity to allergens and gender, sibship, maternal, and family history of atopy. The effects of exposure to individual predictors are presented in the form of relative risks together with 95% CIs.

RESULTS

Characteristics of participants

A total of 969 pregnant women were recruited for the study (91% of the target population, which was 1063). Reasons for nonconsent/recruitment included lack of interest (56), moving from the island (12), stillbirths (6), missed opportunities to recruit (11), language issues (4), and antenatal complications (5). Characteristics of the recruited babies are shown in Table I.

Parental reported food hypersensitivity

At 3, 6, 9, and 12 months, 927 (95.6%), 912 (94.1%), 900 (92.9%), and 900 (92.9%) follow-up questionnaires were completed, respectively. Symptoms of FHS were reported by 132 (14.2%) parents at 3 months, 83 (9.1%) at 6 months, 49 (5.5%) at 9 months, and 65 (7.2%) at 12 months of age. Some parents reported symptoms on more than 1 occasion, and some reported a problem at 1 point

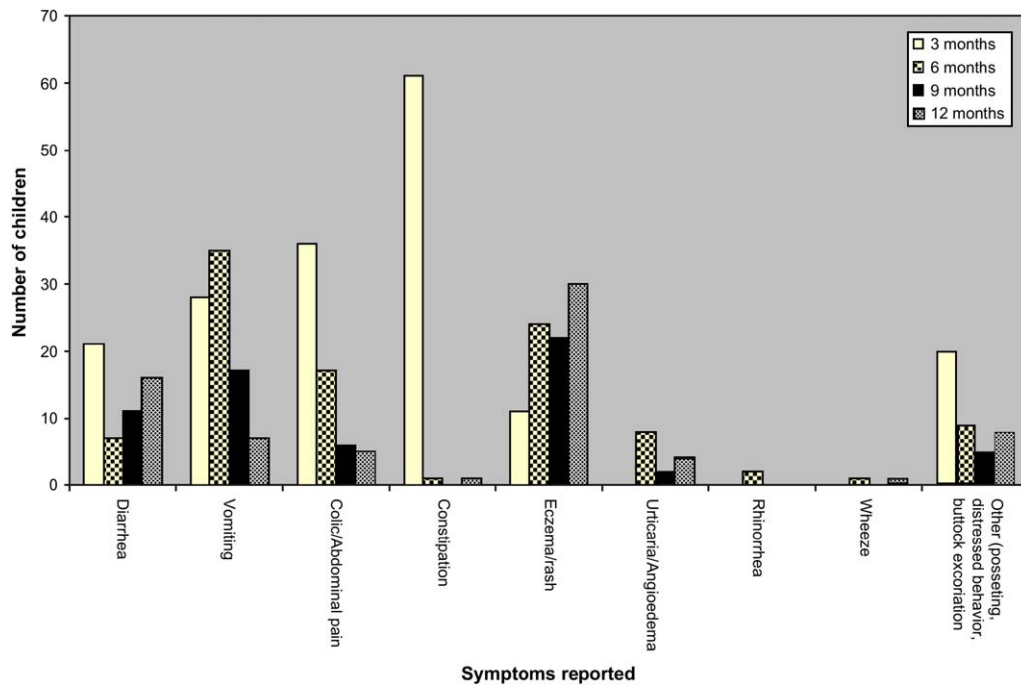


FIG 1. Reported problems to food at 3, 6, 9, and 12 months.

only. Fig 1 demonstrates the frequency of different symptoms reported in the infant's first year of life. The foods most commonly implicated in these reported symptoms were cow's milk formulas at 3 months; cow's milk formulas, noncitrus fruits, baby rice, and oats at 6 months; cow's milk or cow's milk formulas, egg, and tomato at 9 months; and cow's milk or cow's milk formulas, egg, tomato, and fish at 12 months. In total, 487 of 900 (54%) infants were avoiding some foods at 1 year of age. Food additives and nuts (including peanuts) were the most common foods/ingredients avoided.

Sensitization rates at 12 months

A total of 763 infants were skin prick tested at 1 year of age. Lack of parental consent was the main reason that other infants were not tested. The rate of sensitization to any of the predefined allergens tested was 2.6% (20/763; 95% CI, 1.6% to 4%). Children born to atopic mothers were significantly more likely to be sensitized to any allergen (3.2% vs 1.1%; $P = .04$). The rate of sensitization to the predefined aeroallergens (house dust mite, cat, and grass) was 1.0% (8/763; 95% CI, 0.4% to 2%): 3 infants to house dust mite, 4 to grass, and 1 to cat. SPTs to other aeroallergens were performed in 4 infants on the basis of indicated history (3 dog and 1 *Alternaria*). One infant had a positive SPT to dog. The rate of sensitization to any of the predefined food allergens (milk, egg, fish, peanut, sesame, and wheat) was 2.2% (17/763; 95% CI, 1.3% to 3.5%). Fourteen infants were sensitized to egg, 3 to peanut, 2 to milk, 2 to fish, and 2 to sesame. Three infants were sensitized to more than 1 food. Where history indicated, the infants were skin prick tested to other foods. Sixteen

infants were skin prick tested to other foods. Only 1 had a positive SPT to corn, potato, and rice in addition to egg.

We further investigated the predictors of sensitization. Within this relatively small cohort, sex, position in sibship, and family history of atopy were not significantly associated with sensitization to either food allergens or aeroallergen.

Prevalence of food hypersensitivity assessed by food challenges between 6 and 9 months of age

Parents who reported adverse reactions to food at 3 and 6 months of follow-up were contacted by the research dietitian and invited for a medical examination and food challenges. Two hundred two mothers reported a problem with food at either 3 or 6 months, with 13 reporting a problem at both 3 and 6 months. A total of 177 infants were excluded from undergoing challenges because they had subsequently tolerated the food or were eating other foods from the same food group. Twenty-five infants were invited for OFCs. Two mothers declined the food challenge because of lack of interest ($n = 1$) and social issues ($n = 1$). The first infant had a positive SPT to milk at 6 months, and the infant's eczema improved with milk avoidance. The other infant had a negative SPT to milk, but eczema improved on milk avoidance. This infant subsequently became sensitized to milk, egg, and peanut.

In total, 28 OFCs to milk, egg, wheat, and citrus fruit were performed on 23 infants between the ages of 6 and 9 months. Twelve OFCs were positive among 12 infants (11 milk and 1 wheat). Sixteen OFCs were negative; these included 12 challenges to milk, 3 egg challenges, and

1 OFC to citrus fruit. The 12 infants with a positive OFC were invited to undergo DBPCFC, and 9 challenges were performed in 9 infants. One mother declined because she did not want her infant to undergo another challenge (6-mm SPT to egg). One infant only reacted on skin contact with milk (confirmed in OFC) and consumed milk without any reaction. The other infant had multiple food allergies and other allergic symptoms, and the consultant allergist requested no further interventions (SPT: potato = 7 mm; egg = 8 mm; fish = 4 mm; peanut = 3 mm). Hence, a total of 9 DBPCFCs were performed in 9 infants, and 4 challenges (in 4 infants) were positive to milk.

The incidence of FHS at 9 months was 1.2% (12/969; 95% CI, 0.6% to 2.2%) on the basis of OFC and 0.4% (4/969; 95% CI, 0.1% to 1.1%) on the basis of DBPCFC. If infants with a clear history ($n = 2$) who declined challenges are included with infants who were positive on OFC, then the incidence of FHS is 1.4% (14/969; 95% CI, 0.8% to 2.4%). If infants with a positive OFC who declined further challenges ($n = 3$) and infants with a clear history who declined all challenges ($n = 2$) are included with infants who were positive on DBPCFC, then the incidence of FHS is 0.9% (9/969; 95% CI, 0.4% to 1.8%).

Prevalence of food hypersensitivity assessed by food challenges between 9 and 12 months of age

Between 9 and 12 months, a similar approach for food challenges was followed. Ninety-seven mothers reported a problem to foods at either 9 or 12 months, with 17 mothers reporting problems at both times. Fifty-four infants were excluded from challenges for similar reasons outlined under the section discussing children at 6 to 9 months. A total of 43 infants were invited for an OFC. An additional 8 infants, identified by means of a positive SPT without previous consumption of the food, were also invited for food challenges. Four mothers declined. One infant had a negative SPT to egg, but the eczema improved on egg avoidance. Another developed a rash with egg, but was SPT negative. Two infants had positive SPT (4 mm) but no history of exposure to egg.

Forty-seven infants underwent a total of 57 food challenges to a variety of foods (milk, egg, wheat, citrus, strawberry, tomato, fish, corn, salicylates, and soya). Twenty-five of these infants had 30 positive OFC to milk ($n = 12$), egg (13), wheat (2), tomato (1), corn (1), and salicylates (1), with 5 infants having a positive challenge to more than 1 food. Between them, these 25 infants underwent 17 one-day OFCs and 13 one-week OFCs, with some having both 1-day and 1-week challenges. These 25 infants were invited to undergo DBPCFC, and 18 challenges were performed in 15 infants. The reasons for not performing DBPCFC were as follows: moved to the mainland (egg SPT = 5 mm); lack of interest (milk SPT = 1 mm; egg SPT = 3 mm); parents agreed only to a repeat OFC (1 infant with 2 positive milk OFCs and another with 2 positive wheat OFCs; 2 other infants had a second OFC that was negative to either milk or tomato); medical reasons (2 infants with

severe reactions, 1 with celiac disease); and lack of time (egg SPT negative). Of these 15 infants, 13 infants had 15 positive DBPCFCs. Six DBPCFCs were to milk (1 one-day and 5 one-week), 8 challenges were to egg (all 1 day), and 1 infant had a positive 1-week wheat challenge. Two infants had positive DBPCFC to milk and egg.

By the age of 12 months, the incidence of FHS was 2.6% (25/969; 95% CI, 1.7% to 3.8%) on the basis of OFC and 1.2% (12/969; 95% CI, 0.6% to 2.2%) on the basis of DBPCFC. If infants with a clear history who did not undergo challenges ($n = 3$) are included with those with a positive OFC, then the incidence of FHS is 2.8% (27/969; 95% CI, 1.8% to 4.3%). If infants with a positive OFC who declined further challenges ($n = 9$) and infants with a clear history who did not take part in the challenges ($n = 3$) are included with those with a positive DBPCFC, then the incidence of FHS is 2.5% (24/969; 95% CI, 1.6% to 3.7%).

Cumulative incidence of FHS at 1 year of age

Food hypersensitivity was confirmed in 3.6% (35/969; 95% CI, 2.5% to 5%) infants using 85 OFCs and 1.5% (15/969; 95% CI, 0.9% to 2.5%) using 27 DBPCFCs (Tables II and III) during the first year of life. If infants with a clear history who did not undergo challenges ($n = 4$) are included, then the cumulative incidence of FHS is 4.0% (39/969; 95% CI, 2.9% to 5.5%). The prevalence was lower because 2 infants had outgrown their FHS on repeat challenge. If infants with a positive OFC who declined further challenges ($n = 12$) and infants with clear history who did not take part in the challenges ($n = 4$) are included with those with a positive DBPCFC, then the cumulative incidence of FHS is 3.2% (31/969; 95% CI, 2.2% to 4.5%), but the prevalence at 1 year of age is 3% (29/969; 95% CI, 2.0% to 4.3%) because 2 infants outgrew their FHS.

The cumulative incidence of reported parental perceived food hypersensitivity was 25.8% (250/969; 95% CI, 23.1% to 28.7%) by 12 months of age. Of these, only 14% (35/250) and 6% (15/250) were diagnosed with FHS by means of OFC and DBPCFC, respectively.

DISCUSSION

This is the first study conducted in the United Kingdom that investigates the rates of parentally reported FHS and clinically diagnosed FHS during the first year of life. The rate of sensitization to any food allergen was 2.2%. We have established that adverse reactions to food were reported by 14.2% parents at 3 months, and this declined to 7.2% at 12 months of age.

Bock⁶ diagnosed 7.7% (37/480; 95% CI, 5.5% to 10.5%) of infants with FHS by 3 years of age. This was achieved by using either OFC or DBPCFC. Unfortunately, no data regarding FHS at 1 year are available, and therefore, we cannot compare these data with our study. Also, Bock et al⁶ used only food challenges aimed at

TABLE II. Summary of positive OFC between 6 and 12 months**A. Challenges with immediate reactions (within 1 h)**

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (min)	Symptom
1	M	Milk	0	1 drop	5	Urticaria
2	F	Egg	5	Labial rub	7	Urticaria
3	M	Egg	7.5	1 g	15	Angioedema
4	M	Egg	5	0.5 g	6	Urticaria
5	F	Milk	1	3.5 mL	45	Urticaria
6	M	Egg	2	Labial rub	5	Urticaria
7	M	Tomatoes	0	Labial rub	10	Rash/eczema flared
8	F	Egg	7	1 g	5	Urticaria
9	F	Egg	3.5	3 g	30	Urticaria/vomiting
10	F	Corn	5	1 g	20	Vomiting

B. Challenges developing over hours (1-5 h)

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (min)	Symptom
11	M	Egg	4.5	7g	120	Rash Eczema flared
12	F	Egg	0	18 g	100	Urticaria
13	M	Egg	0	18 g	210	Rash
14	F	Salicylates	NA	250 mL Black currant juice	120	Angioedema Swollen/stiff joints
15	F	Egg	3	18 g	210	Erythema
16	F	Wheat	0	5 g	80	Vomiting/urticaria
10*	M	Milk	0	200 mL	12 h	Wheeze (2 challenges performed)

C. Challenges with reactions over days (1-7 d)

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (d)	Symptom
11	M	Milk	0	170 mL	1	Eczema flared
4	M	Milk	6.5	15 mL	1	Rash/excessive crying
17	M	Milk	0	230 mL	1	Vomiting
17	M	Egg	0	2.5 g	2	Red facial flush
12	M	Milk	0	580 mL	6	Vomiting
18	M	Milk	0	230 mL	6	Diarrhea
19	M	Milk	0	500 mL	2	Diarrhea
20	M	Milk	0	300 mL	2	Distressed behavior/abdominal pain
					4	Rash
21	M	Milk	0	230 mL	4	Rash
21	M	Wheat	0	3-4 portions	2	Vomiting
					3	Excessive crying
					4	Rash
22	M	Milk	1	230 mL	1	Diarrhea/angioedema
23	M	Milk	0	230 mL	3	Vomiting
24	F	Wheat	0	1 Weetabix†	2	Rash
25	M	Wheat	0	1 portion	2	Diarrhea
26	M	Milk	0	30 g margarine	1	Diarrhea/buttock excoriation
8	F	Milk	0	120 mL	2	Eczema flared
27	M	Milk	0	30 mL	1	Vomiting
28	M	Milk	0	300 mL	1	Buttock excoriation
29	F	Milk	0	420 mL	1	Urticaria
30	F	Milk	0	300 mL	2	Diarrhea/vomiting
31	M	Milk	6	180 mL	1	Rash
32	M	Milk	0	580 mL	4	Eczema flared
33	F	Milk	0	5 g margarine	2	Diarrhea
34	M	Egg	0	32 g	6	Rash

*This child had received Nutramigen (Mead Johnson Nutritionals, Evansville, Ill) from birth because of a strong family history of allergy. He reacted to milk when introduced at home on his doctor's advice. The same reaction reoccurred during the challenge, which was approximately 6 weeks after the first episode.

†Weetabix Ltd, Northamptonshire, United Kingdom.

TABLE III. Summary of positive DBPCFCs**A. Challenges with immediate reactions (within 1 h)**

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (min)	Symptom
3	F	Egg	7.5	250 mg	15	Urticaria
4	M	Milk	6.5	12 mL	30	Urticaria
4	M	Egg	5	250 mg	5	Rash
17	M	Egg	0	1 g	7	Itch/urticaria
6	M	Egg	0	<1 g	25	Urticaria
8	F	Egg	6.8	1.5 g	25	Urticaria

B. Challenges developing over hours (1-5 h)

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (min)	Symptom
16	F	Egg	3	8 g	90	Rash
25	F	Egg	3.5	25 g	90	Erythema/urticaria
34	M	Egg	2	60 g	55	Urticaria/facial flush

C. Challenges with reactions over days (1-7 d)

Unique case identification number	Sex	Food	SPT (mm)	Reactive dose	Total time to reaction (d)	Symptom
11	M	Milk	0	400 mL	1	Itch/rash
17	M	Milk	0	230 mL	2	Eczema flared
21	M	Milk	0	200 mL	4	Rash/vomiting
21	M	Wheat	0	5 portions	3	Rash/vomiting
22	M	Milk	1.3	480 mL	2	Diarrhea
26	F	Milk	0	500 mL	1	Eczema flared/diarrhea
8	F	Milk	0	500 mL	2	Eczema flared
29	F	Milk	0	400 mL	3	Urticaria
30	F	Milk	0	250 mL	2	Diarrhea/vomiting
33	F	Milk	0	250 mL	4	Diarrhea/vomiting

identifying immediate-type symptoms. Foods implicated in this study⁶ were milk, egg, soy, peanut, chocolate, corn, rice, and wheat, which were foods very similar to those identified in our study.

Four studies have examined the incidence of cow's milk FHS during the first year of life.⁶⁻⁹ One further study looked at egg and milk hypersensitivity at 2.5 years of age.³ Our findings on the prevalence of cow's milk hypersensitivity (2.3% on the basis of OFC and 1.0% on the basis of DBPCFC) are similar to those reported by these 4 studies.^{3,6-8} One Canadian study⁹ suggested that 7.5% Canadian infants had milk FSH in the first year of life. This study used only OFC, perhaps explaining these higher rates. Food hypersensitivity to egg has been reported to be 1.6% at 2.5 years of age.⁴ The point prevalence of egg hypersensitivity in our study was 1.3% (13/969) by means of OFC and 0.8% (8/969) by means of DBPCFC. Food hypersensitivity to egg does not usually emerge until the second year of life, and this could potentially explain the difference between our study and the published study that looked at egg hypersensitivity at 2.5 years of age.⁴

Two previous studies have looked at parentally reported adverse reactions to food. One reported the rate of parentally perceived adverse reactions to foods was 35%

by 2 years of age,¹⁰ whereas the study by Bock⁶ suggested it was 28% by 3 years of age. In our population, the reported rate of perceived adverse reactions to food is 25.8% by 1 year of age. In the study by Bock,⁶ only a quarter of infants with apparent adverse reactions had evidence of FHS. In our population, an eighth of infants with symptoms had evidence of FHS.

One possible limitation of the study is the low uptake of the DBPCFC. Although more than 90% of mothers consented to OFC at both 6 to 9 and 9 to 12 months, only 75% and 60% consented to DBPCFC between 6 and 9 and 9 and 12 months, respectively. However, this compares well with the most cited previous study, in which only 44% (16/37) of the infants with positive food challenges underwent DBPCFC.⁶ In addition, 6 of the 14 infants not undergoing a DBPCFC in our study were excluded because of severity of reaction on open challenge or a SPT diameter above the 95% positive predictive levels.¹² In addition, 2 other infants outgrew their FHS before undergoing DBPCFC. Therefore, only 6 infants did not undergo a DBPCFC when this was indicated. A second limitation was the lack of challenges in the 5 infants sensitized to peanut or sesame. It was decided that infants should not be exposed to these allergens before 1 year of age.¹³ This may have resulted in us underestimating the

rate of food hypersensitivity in infancy. Also, it is possible that some infants were sensitized to foods that were not in our allergen panel, although this is unlikely to have significantly affected the rate of clinical allergy because infants were also tested to other foods to which they had had an adverse reaction.

In conclusion, we have established that a quarter of parents report adverse reactions to foods in their infants during the first year of life. Of these, only an eighth were confirmed as FHS by OFC.

Our data describes the magnitude of the problem of FHS in the first year of life and highlights the most frequent foods associated with FHS. They also emphasize the need for accurate diagnosis to prevent infants being on unnecessarily restricted diets, which may be associated with inadequate nutrition in this important period of growth and development.

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REFERENCES

1. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol* 2004;113:832-6.
2. Sicherer SH, Leung DYM. Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insect stings. *J Allergy Clin Immunol* 2004;114:118-24.
3. Eggesbo M, Botten G, Halvorsen R, Magnus P. The prevalence of CMA/CMPI in young children: the validity of parentally perceived reactions in a population-based study. *Allergy* 2001;56:393-402.
4. Eggesbo M, Botten G, Halvorsen R, Magnus P. The prevalence of allergy to egg: a population-based study in young children. *Allergy* 2001;56:403-11.
5. Bock SA, Sampson HA, Atkins FM, Zeiger RS, Lehrer S, Sachs M, et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. *J Allergy Clin Immunol* 1988;82:986-97.
6. Bock SA. Prospective appraisal of complaints of adverse reactions to foods in children during the first 3 years of life. *Pediatrics* 1987;79:683-8.
7. Schrandt JJ, van den Bogart JP, Forget PP, Schrandt-Stumpel CT, Kuijten RH, Kester AD. Cow's milk protein intolerance in infants under 1 year of age: a prospective epidemiological study. *Eur J Pediatr* 1993;152:640-4.
8. Host A, Halken S. A prospective study of cow milk allergy in Danish infants during the first 3 years of life: clinical course in relation to clinical and immunological type of hypersensitivity reaction. *Allergy* 1990;45:587-96.
9. Gerrard JW, MacKenzie JW, Goluboff N, Garson JZ, Maningas CS. Cow's milk allergy: prevalence and manifestations in an unselected series of newborns. *Acta Paediatr Scand Suppl* 1973;234:1-21.
10. Eggesbo M, Halvorsen R, Tambs K, Botten G. Prevalence of parentally perceived adverse reactions to food in young children. *Pediatr Allergy Immunol* 1999;10:122-32.
11. Pereira B, Venter C, Grundy J, Clayton B, Arshad SH, Dean T. Prevalence of sensitisation to food allergens, reported adverse reaction to foods, food avoidance and food hypersensitivity amongst teenagers. *J Allergy Clin Immunol* 2005;116:884-92.
12. Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin Exp Allergy* 2000;30:1540-6.
13. Committee on toxicity of chemicals in food, consumer products and the environment. Peanut allergy. London: Department of Health; 1998.