

## Original article

## Prevalence of food allergy and its relationship to asthma and allergic rhinitis in schoolchildren

**Background:** Food allergy (FA) is an important health problem. However, epidemiological studies at the population level are scarce. We assessed the prevalence of FA and its associations with respiratory manifestations among schoolchildren.

**Methods:** A total of 6672 schoolchildren aged 9–11 years recruited from 108 randomly chosen schools in six French cities underwent a clinical examination including skin prick test (SPT) to common food and aeroallergens and the standardized protocol of the run test to assess exercise-induced bronchial hyper-responsiveness (EIB). Asthma, allergic rhinitis (AR) and clinical symptoms of FA were determined using a standardized questionnaire completed by parents.

**Results:** About 2.1% of the children reported symptoms of FA, 1.9% were sensitized to food allergens, and 0.1% had SP-tested FA. The AR was more prevalent than asthma (20.0% lifetime, 11.9% past year vs 9.8%, 8.7% respectively). Reported FA, food sensitization and SP-tested FA were all positively associated with asthma and AR ( $P < 0.001$ ). These associations persisted also for FA not manifesting as respiratory symptoms ( $P < 0.001$ ). Asthma and AR remained significantly associated with reported symptoms of FA and allergic sensitization to food allergens after adjustment for confounders as well as for sensitization to aeroallergens. No relationship existed between EIB (9.0%) and FA.

**Conclusion:** The relationships between FA and asthma and AR could be totally explained neither by the existence of respiratory manifestations of FA nor by sensitization to aeroallergens. The FA might intervene differently in asthma and AR.

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Key words: allergic rhinitis; asthma; children; food allergy; sensitization to food allergens and to aeroallergens.

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Food allergy (FA) is an immunoglobulin E (IgE)-mediated disease (1), manifesting as cutaneous, gastrointestinal or respiratory symptoms (2), which in industrialized countries afflicts an increasing number of infants and children and is associated with both clinical and social burdens (3). Nevertheless, population-based data on FA are scarce because of the difficulty of confirming the reported diagnosis of FA (2, 4, 5) in population settings, where objective tests of allergic sensitization to food allergens [skin prick test (SPT), specific IgE] or of the implication of food (double-blind placebo-controlled food challenge) are not feasible. Therefore, also non-IgE-mediated reactions of food intolerance have been included in population studies having used a simple questionnaire (6, 7). According to such studies, the

prevalence of general adverse reactions to food varies between 3.3 and 34.9% (7–16). The few studies having included a subgroup of patients that had undergone an objective validation of the report of FA found a prevalence of FA between 1.4 and 4.4% (7, 11–13, 16, 17).

The interrelationships between FA and respiratory manifestations [asthma, allergic rhinitis (AR), exercise-induced bronchial hyper-responsiveness (EIB)] although investigated in patient-based studies have been scarcely examined at the population level. Three cross-sectional studies indicate that respiratory manifestations are more common in subjects with FA (10, 12, 15). Three cohort studies found that FA in early infancy is related to the development of asthma and AR in childhood (18–20). But, the mechanisms by which this is triggered are obscure.

The present study was intended to: (i) estimate the prevalence of FA (as assessed by reported symptoms of FA, allergic sensitization to food allergens according to SPT and SP-tested FA respectively) in a large French

**Abbreviations:** FA, food allergy; IgE, immunoglobulin E; SPT, skin prick test; EIB, exercise-induced bronchial hyper-responsiveness; AR, allergic rhinitis; PEF, peak expiratory flow; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval.

population-based sample of schoolchildren and (ii) evaluate the relationship of FA to respiratory manifestations of allergy and assess to what extent these could be explained by allergic sensitization to aeroallergens.

## Methods

### Study subjects

The initial population sample comprised 9615 children aged 9–11 years recruited to participate between March 1999 and October 2000 in a national survey on asthma and allergic diseases in childhood; namely all the children in the 401 relevant classes chosen from 108 schools randomly selected in six French cities (Bordeaux, Clermont-Ferrand, Créteil, Marseille, Strasbourg and Reims).

### Study design

The study protocol included a standardized questionnaire and a clinical examination. The parents completed an enriched version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (21, 22) containing questions concerning their child's allergic manifestations, how they were managed and their potential risk factors. To identify allergic symptoms (asthma, AR, atopic dermatitis, FA), 35 questions were used. The five questions on adverse reactions to food were partly based on a previous French standardized questionnaire on FA (15). Moreover, two specific modules consisting of complementary questions on asthma (21 questions) and on AR (seven questions) respectively were added. The clinical examination included objective evidence of allergic sensitization as assessed by SPT and a measure of EIB, which is not systematically assessed in school settings in France. Doctors especially trained for the survey performed the tests. Children were tested with the following common food and aeroallergens: egg, fish (cod), peanut, *Dermatophagoides pteronyssinus*, *D. farinae*, cat (Fel d 1), *Alternaria tenuis*, *Blatta germanica*, mixed grass and tree pollens (birch; Stallergènes Laboratories, Antony, France). Histamine (10 mg/ml) was used as a positive control and glycerine as a negative control. Reactions to each allergen were measured 15 min after the pricks. The size of each wheal was documented as the mean of the longest diameter and the diameter perpendicular to the middle of the longest diameter. The SPT positivity was defined as a wheal at least 3 mm and greater than the negative control. The EIB was assessed according to the standardized protocol of the run test (23). Peak expiratory flow (PEF) rate was measured three times immediately before and 5 min after, a 6-min period of running (1 min slow, 4 min fast, 1 min very fast) with a Mini-Wright Peak Flow Meter® (Harlow, UK). The maximum of each set of readings was used to calculate the percentage decrease in PEF after exercise. Pulse rate was measured for 15 s immediately after completion of the run, as an indicator of exercise intensity. Children receiving inhaler treatment for asthma were tested, when possible, at least 6 h after the last dose of medication.

All children and their parents gave informed consent. The study protocol obtained approval of the Ethics Board (Comité Consultatif de Protection des Personnes qui se prêtent à une Recherche Biomédicale).

### Health outcomes classification

We created three indicators of FA: (i) reported symptoms of FA if the child ever had an adverse reaction, including swelling of face,

swelling of lips, angio-oedema, urticaria, stomach pain or diarrhoea, shortness of breath or fainting, following the ingestion of a particular food (namely nuts, peanut, fruit or vegetables, milk, egg, fish, seafood). The adverse reaction should have happened after every ingestion of the suspected food (reproducibility of the symptoms); (ii) food sensitization as defined by at least one positive SPT to a food allergen (egg, fish or peanut); (iii) SP-tested FA if the child had reported symptoms of FA and if he was sensitized to at least one food allergen.

Using the replies to the questionnaire, the following respiratory manifestations were assessed: past year asthma ('Has your child had wheezing or whistling in the chest in the last 12 months?'); past year AR ('In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu? and 'In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?'); lifetime asthma ('Has your child ever had asthma?'); lifetime AR ('Has your child ever had hay fever? or 'Has your child ever had other types of AR?').

A child was considered to have EIB if the decrease in PEF after exercise exceeded 10%.

Sensitization to aeroallergens was defined as at least one positive SPT to one of the tested aeroallergens.

Potential confounders included age, sex, passive smoking, parental education, ethnic origins and family history of allergic diseases. A child had a family history of allergic diseases if his/her father or his/her mother had ever suffered from asthma, AR, eczema or FA.

### Statistical analyses

All the 6672 children who underwent clinical examination and whose parents completed the questionnaire were included in the analyses. In the case of prevalence, the confidence interval was estimated according to the normal distribution if number of diseased children exceeded 20 and according to the Poisson distribution elsewhere. To assess the associations between respiratory manifestations and FA, the chi-square test and the marginal odds ratio (OR) were used.

Logistic regression analysis was performed to estimate the adjusted odds ratio (aOR) after taking potential confounders and sensitization to aeroallergens into account. A marginal model (24) was applied in order to take into account the potential nonindependence of data between children living in a same city, because of the fact that they share the same environment, climate, pollens, social factors, and probably food products and diet. The parameters of the marginal model were estimated by the Generalized-Estimating Equation (GEE) approach using SAS GENMOD with independent working correlation structure using the city as stratum. Version 8.2 of SAS SYSTEM for Windows was used for statistical analysis. Statistical significance was provided by a *P*-value of <0.05 (two-tailed test).

## Results

### Participation rate

About 81% of the children (7781/9615) agreed to participate in the study. Completed valid data on both clinical examination and questionnaire were available for 6672 children (69%). Protocol completion rate among the children having accepted to participate ranged from 79 (Créteil) to 98% (Strasbourg). Characteristics of the 6672 children are given in Table 1.

Table 1. Characteristics of the children who underwent clinical examination and whose parents completed the questionnaire ( $N = 6672$ )

| Factors                                 | Child          | Mother         | Father         |
|-----------------------------------------|----------------|----------------|----------------|
| Age, years (mean $\pm$ SD)              | 10.4 $\pm$ 0.7 | 38.4 $\pm$ 5.2 | 41.5 $\pm$ 6.3 |
| Sex (male, %)                           | 49.2           |                |                |
| Passive smoking (%)                     | 43.9           |                |                |
| Family history of allergic diseases (%) | 43.2           |                |                |
| Ethnic origins (%)                      |                |                |                |
| Metropolitan France                     |                | 74.9           | 73.1           |
| French overseas departments             |                | 3.6            | 2.5            |
| South Europe                            |                | 3.8            | 4.3            |
| French-speaking Saharan Africa          |                | 8.5            | 10.1           |
| Sub-Saharan Africa                      |                | 3.3            | 3.5            |
| Asia                                    |                | 2.7            | 3.0            |
| Other                                   |                | 3.2            | 3.5            |
| Education (%)                           |                |                |                |
| Primary                                 |                | 11.7           | 12.5           |
| Secondary                               |                | 45.3           | 42.8           |
| High school and university              |                | 37.8           | 39.3           |
| Other                                   |                | 5.2            | 5.4            |

## Prevalence of allergic indicators

**Food allergy.** About 2.1% of the children had reported symptoms of FA (Table 2). Of the children with reported symptoms of FA, 39.4% related their symptoms to the ingestion of fruit or vegetables, 23.2% to seafood, 14.8%

Table 2. Prevalence of FA and respiratory manifestations of allergy ( $N = 6672$ )

|                            | $N^*$ | %†   | 95% CI‡   |
|----------------------------|-------|------|-----------|
| FA                         |       |      |           |
| Reported symptoms of FA    |       |      |           |
| At least one food          | 142   | 2.1  | 1.8–2.5   |
| Nuts                       | 10    | 0.2  | 0.1–0.3   |
| Fruit or vegetables        | 56    | 0.8  | 0.6–1.1   |
| Egg                        | 15    | 0.2  | 0.1–0.4   |
| Milk                       | 19    | 0.3  | 0.2–0.5   |
| Peanut                     | 21    | 0.3  | 0.2–0.4   |
| Fish                       | 10    | 0.2  | 0.1–0.3   |
| Seafood                    | 33    | 0.5  | 0.3–0.7   |
| Food sensitization         |       |      |           |
| At least one food allergen | 119   | 1.9  | 1.6–2.3   |
| Peanut                     | 70    | 1.1  | 0.9–1.4   |
| Fish                       | 46    | 0.7  | 0.5–1.0   |
| Egg                        | 23    | 0.4  | 0.2–0.5   |
| SP-tested FA               | 9     | 0.1  | 0.1–0.3   |
| Respiratory manifestations |       |      |           |
| Lifetime asthma            | 645   | 9.8  | 9.1–10.6  |
| Past year asthma           | 476   | 8.1  | 7.4–8.8   |
| Lifetime AR                | 1244  | 20.0 | 19.0–21.0 |
| Past year AR               | 688   | 11.9 | 11.0–12.7 |
| EIB                        | 543   | 8.7  | 8.0–9.4   |

AR, allergic rhinitis; EIB, exercise-induced bronchial hyper-responsiveness; FA, food allergy; SP, skin prick; CI, confidence interval.

\*Number of affected subjects.

†Proportion of affected subjects (%).

‡95% confidence interval of the proportion. It has been estimated according to the normal distribution if  $N > 20$  and according to the Poisson distribution elsewhere.

to peanut, 13.4% to milk, 10.6% to egg, 7.0% to nuts and 7.0% to fish. The most frequent symptoms were urticaria (38.7% of the children with reported symptoms of FA), stomach pain or diarrhoea (34.5%), swelling of lips (28.1%), swelling of face (18.3%), angio-oedema (9.1%), shortness of breath (7.7%) and fainting (1.4%). The prevalence of reported symptoms of FA was related neither to sex nor to city.

About 1.9% of the children were sensitized to at least one food allergen (Table 2). Of the children sensitized to food, 58.8% were sensitized to peanut, 38.7% to fish, 19.3% to egg and 20.2% to at least two food allergens. Food sensitization was significantly dependent on the city ( $P < 0.001$ ): 3.3% of the children from Bordeaux and 1.0% from Strasbourg were sensitized to food allergens. The prevalence of food sensitization was unrelated to sex.

Of the children with reported symptoms of FA, 6.3% were sensitized to at least one of the three tested food allergens. Thus, nine children had a SP-tested FA (Table 2).

**Respiratory manifestations.** About 9.8% of the children had lifetime asthma, 8.1% past year asthma, 20.0% lifetime AR and 11.9% past year AR. The prevalence of EIB was 8.7% (Table 2).

The prevalence of lifetime asthma, past year asthma, lifetime AR and past year AR was significantly higher in boys than in girls ( $P < 0.001$ ). But the prevalence of EIB was unrelated to sex. Except in the case of lifetime asthma, the prevalence of the indicators of respiratory manifestations significantly depended on the city ( $P < 0.05$  for past year asthma and past year AR;  $P < 0.001$  for lifetime AR and EIB). The highest prevalences of respiratory manifestations were observed in Bordeaux, Marseille and Créteil.

## Association between food allergy and respiratory manifestations

**Crude associations between FA and respiratory manifestations.** The prevalence of lifetime asthma, past year asthma, lifetime AR and past year AR was significantly higher in children with any of the three indicators of FA than in children without ( $P < 0.001$ ). The EIB was unrelated to FA (Table 3). After having excluded children with respiratory reported symptoms of FA (shortness of breath), the prevalence of lifetime asthma, past year asthma, lifetime AR and past year AR remained significantly higher in children with reported symptoms of FA than in those without ( $P < 0.001$ ). The AR was more related to sensitization to peanut and asthma to sensitization to egg.

Of the children with AR (lifetime and/or past year) and concomitant asthma (lifetime and/or past year), 6.4% reported symptoms of FA compared with 4.7% of those with only AR ( $P < 0.001$ ) and 4.5% were sensitized to food allergens compared with 3.4% ( $P < 0.05$ ). Of the children with only asthma, 2.9%

Table 3. Associations between FA and prevalence of respiratory manifestations of allergy

|                  | Reported symptoms of FA |               | Food sensitization |               | SP-tested FA  |             |
|------------------|-------------------------|---------------|--------------------|---------------|---------------|-------------|
|                  | No (N = 6480)           | Yes (N = 142) | No (N = 6056)      | Yes (N = 119) | No (N = 6121) | Yes (N = 9) |
| Lifetime asthma  | 608 (9.6)†              | 29 (20.7)*    | 543 (9.1)          | 27 (23.3)*    | 560 (9.3)     | 5 (55.6)*   |
| Past year asthma | 436 (7.6)               | 33 (27.5)*    | 401 (7.5)          | 20 (19.0)*    | 411 (7.6)     | 5 (62.5)*   |
| Lifetime AR      | 1161 (19.2)             | 65 (49.6)*    | 1072 (19.0)        | 48 (43.6)*    | 1097 (19.3)   | 7 (77.8)*   |
| Past year AR     | 634 (11.2)              | 41 (36.6)*    | 599 (11.4)         | 26 (24.1)*    | 609 (11.4)    | 6 (75.0)*   |
| EIB              | 527 (8.7)               | 12 (9.4)      | 499 (8.6)          | 13 (11.7)     | 506 (8.6)     | 2 (3.0)     |

AR, allergic rhinitis; EIB, exercise-induced bronchial hyper-responsiveness; SP, skin prick; FA, food allergy.

\* $P < 0.001$ .

†Number of subjects (%).

reported symptoms of FA and 3.2% were sensitized to food allergens.

**Influence of sensitization to aeroallergens.** About 1652 children (26.7%) were sensitized to at least one aeroallergen. Of the children with sensitization to aeroallergens, 51 (3.2%) had reported symptoms of FA vs 76 (1.7%) in those without ( $P < 0.001$ ), and 87 (5.3%) were sensitized to food allergens vs 32 (0.7%) in those without ( $P < 0.001$ ; Table 4). As expected, sensitization to birch pollen that affected 584 children (9.5%) was significantly associated with reported symptoms of FA [OR: 2.8 (CI: 1.5–5.1),  $P < 0.001$ ]. The strongest associations were found following the ingestion of nuts [7.4 (1.5–35.8),  $P < 0.01$ ] and fruit or vegetables [4.5 (2.0–10.1),  $P < 0.001$ ]. Among the 10 children (the 56 children respectively) who reported symptoms with nuts (fruit or vegetables respectively), 22.2% (14.6% respectively) were sensitized to birch pollen.

In children with sensitization to aeroallergens, those with reported symptoms of FA had significantly more

lifetime asthma, past year asthma, lifetime AR and past year AR than those without (Table 4); children with food sensitization had also more significantly lifetime asthma and lifetime AR than children without (Table 4). Reported symptoms of FA were significantly related to past year asthma, past year AR and lifetime AR also in children without sensitization to aeroallergens.

**Multivariate analysis.** After adjustment for confounders and sensitization to aeroallergens in a logistic regression model, lifetime asthma, past year asthma, lifetime AR and past year AR remained each significantly related to reported symptoms of FA (Table 5). Furthermore, they were related to food sensitization, although statistical significance was not attained in the case of past year asthma and past year AR.

The marginal models taking into account the nonindependence among children living in the same city confirmed the results obtained by the logistic regression models (Table 5). No significant association was found for EIB.

Table 4. Associations between FA and prevalence of respiratory manifestations of allergy after stratifying on sensitization to aeroallergens

|                                                            | Reported symptoms of FA |              | Food sensitization |              |
|------------------------------------------------------------|-------------------------|--------------|--------------------|--------------|
|                                                            | No (N = 4416)           | Yes (N = 76) | No (N = 4491)      | Yes (N = 32) |
| Subjects without sensitization to aeroallergens (N = 4523) |                         |              |                    |              |
| Lifetime asthma                                            | 258 (5.8)†              | 249 (5.7)    | 256 (5.8)          | 2 (6.2)      |
| Past year asthma                                           | 157 (3.9)               | 146 (3.7)    | 157 (3.9)          | 0 (0.0)      |
| Lifetime AR                                                | 522 (12.4)              | 491 (11.9)   | 519 (12.4)         | 3 (0.7)      |
| Past year AR                                               | 267 (6.7)               | 247 (6.3)    | 266 (6.7)          | 1 (0.5)      |
| EIB                                                        | 307 (7.1)               | 301 (7.1)    | 306 (7.1)          | 1 (0.4)      |
| Subjects with sensitization to aeroallergens (N = 1652)    |                         |              |                    |              |
| Lifetime asthma                                            | 312 (19.3)              | 291 (18.8)   | 287 (18.8)         | 25 (29.8)*** |
| Past year asthma                                           | 264 (18.9)              | 243 (18.0)   | 244 (18.5)         | 20 (25.6)    |
| Lifetime AR                                                | 598 (39.2)              | 557 (38.0)   | 553 (38.2)         | 45 (57.0)*   |
| Past year AR                                               | 358 (26.7)              | 330 (25.0)   | 333 (25.7)         | 25 (31.6)    |
| EIB                                                        | 205 (13.0)              | 195 (12.9)   | 193 (12.9)         | 12 (15.0)    |

AR, allergic rhinitis; EIB, exercise-induced bronchial hyper-responsiveness; FA, food allergy.

\* $P < 0.001$ , \*\* $P < 0.01$ , \*\*\* $P < 0.05$ .

†Number of subjects (%).

Table 5. Associations between FA and respiratory manifestations of allergy after adjustment for confounders and sensitization to aeroallergens in a logistic regression model and in a marginal model

|                  | Reported symptoms of FA [aOR (95% CI)] |                 | Food sensitization [aOR (95% CI)] |                  |
|------------------|----------------------------------------|-----------------|-----------------------------------|------------------|
|                  | Logistic regression model              | Marginal model  | Logistic regression model         | Marginal model   |
| Lifetime asthma  | 2.1 (1.3–3.6)**                        | 2.1 (1.3–3.5)** | 1.8 (1.1–3.0)***                  | 1.8 (1.2–2.5)**  |
| Past year asthma | 3.6 (2.0–6.2)*                         | 3.6 (2.0–6.4)*  | 1.5 (0.9–2.7)                     | 1.5 (1.0–2.2)*** |
| Lifetime AR      | 4.2 (2.6–6.6)*                         | 4.2 (2.9–6.0)*  | 1.8 (1.1–2.9)***                  | 1.8 (1.4–2.4)*   |
| Past year AR     | 4.0 (2.4–6.6)*                         | 3.9 (2.6–6.1)*  | 1.1 (0.6–1.9)                     | 1.1 (0.8–1.6)    |
| EIB              | 1.2 (0.6–2.3)                          | 1.2 (0.6–2.4)   | 1.3 (0.7–2.4)                     | 1.3 (0.9–2.0)    |

AR, allergic rhinitis; EIB, exercise-induced bronchial hyper-responsiveness; aOR, odds ratio adjusted for age, sex, passive smoking, parental education, ethnic origins, and family history of allergic diseases; CI, confidence intervals; FA, food allergy.

\* $P < 0.001$ , \*\* $P < 0.01$ , \*\*\* $P < 0.05$ .

## Discussion

We assessed for the first time in France the prevalence of allergic sensitization to major food allergens and reported symptoms of FA in a large population-based sample of schoolchildren and confirmed that asthma and AR were significantly more frequent in children with food sensitization, reported symptoms of FA and SP-tested FA respectively than in children without. However, our data show that the relationships of asthma and AR to food sensitization and reported symptoms of FA could not be totally explained by the existence of respiratory manifestations of FA or by the sensitization to aeroallergens. A better knowledge of FA, on which there has been so far little reliable information, may be important to limit its overall burden.

Although our study was based primarily on a questionnaire, the questions we used to identify reported symptoms of FA allowed limiting the overestimation of the prevalence of reported symptoms of FA because of the inclusion of food intolerance. Indeed, four elements were considered to assess FA: the questions concerning FA were deliberately placed after having focused on other allergic diseases; the reactions had to be associated with various specific food and not for the general diet as in other studies; the symptoms proposed were the classic symptoms of IgE-mediated FA and lastly the reproducibility of the reaction was taken into account (15, 25). However, among the children who reported symptoms of FA following the ingestion of fruit or vegetables, oral allergy syndrome may have been included. Concerning the food sensitization, the SPT to the three food allergens tested have an excellent negative predictive value (>80%) and a good positive predictive value (>60%) in assessing it (2). Thus, our estimation of the prevalence of sensitization to egg, fish and peanut was reliable. It can be criticized that the prevalence of food sensitization was probably underestimated in our study because only three food allergens were tested because of practical considerations. However, the three food allergens we chose are the most common at 10 years of age (26). Recently, clinical data showed that the most common food

allergens were: hen's egg (35%), peanut (24%), fish (4%) and cow's milk (8%) that considerably decreases after 7 years in toddlers (27). Testing fruit or vegetables was unfortunately not feasible because the antigens are labile without recombinant. Concerning respiratory manifestations, we use internationally validated indicators (21, 22, 28, 29).

The prevalence of reported symptoms of FA in our study is similar to those estimated in large population-based studies in France among children aged from 7 to 15 years (2.8%) (15) and teenagers (3.3%) (9). Similarly, the prevalence of food sensitization we observed is comparable with that of other studies. We found a prevalence of 0.4% for sensitization to egg compared with 0.1–0.8% in the literature (10, 12, 17), 0.7% to fish compared with 0.3–1.4% (10, 12) and 1.1% to peanut compared with 0.6–3% (10, 12, 17, 30). Only nine children of the 142 children with reported symptoms of FA had a FA-tested by SPT. Although the prevalence of SP-tested FA may be underestimated in our study because only three food allergens were tested, the rate of confirmed FA in a Swedish study based on 1812 subjects aged from 20 to 44 years was lower (12). Indeed, in this study, only 11 Swedish adults of the 521 with reported symptoms of FA had a FA validated by specific IgE. It has been observed that negative IgE and SPT to foods predicted well negative history of FA whereas the value of positive test results was limited (31).

The analyses of the association between FA and respiratory manifestations are scarce at the population level in the literature and do not take into account potential confounders, except in two studies (10, 12). In our analysis, an effort was made to correct for age, sex, passive smoking, parental education, ethnic origins and family history of allergic diseases, which are potential confounders (8, 10, 12, 15, 32–34). We found a significantly higher prevalence of asthma and AR in children with reported symptoms of FA than in children without. In the French study based on 33 100 subjects, the prevalence of asthma and AR was also significantly higher in subjects with reported symptoms of FA than in those without ( $P < 0.01$ ; 15). Moreover, in a

cross-sectional Canadian study, children with allergy to peanut had more asthma (56.3%) than children without (11.0%; 35). In our study, children sensitized to food allergens had also more asthma and AR than children without. This was in agreement with data from a case-control study in young Chinese children that found a significant association between asthma and the presence of food-specific IgE (36). Interestingly, asthma and AR remained significantly associated with FA not manifesting as respiratory symptoms in our study.

In order to better understand FA, we also stratified and adjusted respectively for allergic sensitization to aeroallergens. When the analysis was limited to children with sensitization to aeroallergens, asthma and AR were significantly more common in children with food sensitization than in children without. Moreover, the association between food sensitization and asthma and AR remained significant after adjustment for sensitization to aeroallergens. The Swedish study also revealed a significant association between food sensitization and asthma ( $P < 0.01$ ) and AR ( $P < 0.001$ ), after adjustment for sensitization to aeroallergens (12).

Thus, food sensitization may have a special relevance in the development of asthma and AR. In childhood, food sensitization may facilitate sensitization to aeroallergens, which is a major risk factor for the development

of asthma and AR. However, as shown by our findings, other mechanisms than sensitization to aeroallergens might be implicated in the relationships of FA to asthma and AR. Our results support the hypothesis of FA as a first step in the 'allergic march' leading to the development of allergic asthma or AR (18–20).

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