

Short communication

Bronchial challenges with aerosolized food in asthmatic, food-allergic children

Background: Allergic asthma is usually considered to be provoked by aeroallergens. However, we have recently recognized a group of children with food allergies who also develop asthma when exposed to the aerosolized form of the food.

Methods: Between 1997 and 1999 we prospectively identified children with an immunoglobulin (Ig)E-mediated food allergy who develop asthma on inhalational exposure to the relevant food allergen while it is being cooked. Subjects were exposed for 20 min to the aerosolized form of the allergen and the symptoms and the lung function were monitored. Aerosolization was achieved by cooking the food in a small room. Where possible challenges were double-blinded.

Results: We identified 12 children with an IgE-mediated food allergy who developed asthma on inhalational exposure to food. The implicated foods were fish, chickpea, milk, egg or buckwheat. Nine out of the 12 children consented to undergo a bronchial food challenge. Five challenges were positive with objective clinical features of asthma. Additionally, two children developed late-phase symptoms with a decrease in lung function. Positive reactions were seen with fish, chickpea and buckwheat. There were no reactions to the seven placebo challenges.

Conclusions: We have presented a prospective series of children with food allergy who developed symptoms of asthma with exposure to aerosolized food allergens. Our data demonstrates that, as in the case of other aeroallergens, inhaled food allergens can produce both early- and late-phase asthmatic responses. This highlights the importance of considering foods as aeroallergens in children with coexistent food allergy and allergic asthma. For these children, dietary avoidance alone may not be sufficient and further environmental measures may be required to limit exposure to aerosolized food.

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Airborne allergens are known to play a key role in the etiology of allergic asthma (1) as well as being important triggers of exacerbations (2). Allergic asthma is usually considered to be provoked by allergens such as house dust mite, cat dander or grass pollen (2). Identification of a significant aeroallergen and avoidance measures can result in a considerable improvement in allergic asthma (4, 5). Foods, meanwhile, are generally considered to induce allergic reactions by direct physical contact via the skin or mouth; they are usually more readily avoidable than aeroallergens (5). Within the paediatric chest and allergy clinic at St Mary's we have recognized children with food allergies who seem to develop symptoms when they are present in a room where the food is being cooked. This suggests that food may act as an aeroallergen as well as a contact or oral allergen. In order to

evaluate this further, we prospectively documented all such cases seen in the clinic between 1997 and 1999. The preliminary results of this study have been published in abstract form (7).

Methods

Subjects

Between 1997 and 1999 we prospectively identified children and teenagers with well defined IgE-mediated food allergy who, in addition, suffered from asthmatic symptoms on inhalational exposure to the relevant food allergen while it was cooking. These exacerbations occurred at home while the food was being cooked (boiled, fried or steamed). Food allergy was diagnosed if the subjects had convincing histories of immediate reactions on at least two occasions within an hour of oral exposure to the food. These histories were confirmed by either a positive skin prick test (SPT) (ALK, Horsholm, Denmark;

positive defined as wheal ≥ 3 mm) (8) or detectable IgE antibodies in serum [Pharmacia CAP (Pharmacia Diagnostics, Uppsala, Sweden), positively defined as class ≥ 2]. Subjects were diagnosed as having allergic asthma by one of the clinic paediatricians according to the American Thoracic Society definition (8). All the subjects had a positive SPT or IgE antibodies. All the subjects were seen in the tertiary paediatric chest and allergy clinic at St Mary's Hospital. A total of 750 new patients with food allergy were seen in the study period, 30% had coexistent asthma.

Design

Bronchial food challenges were performed in this group of children with food allergy, for clinical reasons, to determine whether subjects needed to completely eliminate the food from the home environment. In order to differentiate between a nonspecific bronchial response and an allergic bronchial reaction, subjects were, where possible, also exposed to a nonallergenic placebo food. Prior to challenge, short-acting bronchodilators were stopped for 12 h and long-acting bronchodilators, inhaled steroids, antihistamines or leukotriene antagonists for 72 h. We attempted to mimic the circumstances provoking symptoms in each subject (Table 1). The food was kept out of sight during the challenge and nose clips were used to prevent subjects and evaluators recognizing the food. Subjects were challenged separately within a small cubicle (2×4 m) on the paediatric wards with full resuscitation equipment available. The subjects were exposed to the food for 20 min within this cubicle as it was cooking. Symptoms and, where possible, peak expiratory flow measurements (Mini Wright), were followed at 20-min intervals initially, then hourly, for the subsequent 12 h. A positive challenge was defined as one where symptoms (wheeze, chest tightness, shortness of breath or prolonged coughing) and, for older children, a drop in lung function of at least 15%, occurred within an hour of the exposure. A positive late phase reaction was defined as symptoms and a drop in lung function of at least 15% occurring after complete resolution of the early phase reaction. Fully informed parental consent was obtained for all challenges.

Results

Between 1997 and 1999 we prospectively identified 12 children with IgE-mediated food allergy who, in addition, suffered from asthmatic symptoms (wheeze, chest tightness or cough within minutes) on inhalational exposure to the particular food allergen on more than

one occasion (Fig. 1). All children were successfully practising dietary avoidance of the food. Their average age was 7 years (range 4–13). Six subjects were boys. The subjects had asthma and food allergy for an average duration (range) of 5 (1–9) and 5 (2–8) years, respectively. The implicated foods were fish (6 subjects), milk (2), chickpea (2), buckwheat (1) and egg (1). All subjects had convincing histories of immediate hypersensitivity reactions (urticaria, angioedema, wheeze, or stridor within an hour) on at least two occasions following oral exposure to the food (Table 1). These histories were confirmed by either a positive SPT or IgE antibody results in all subjects (Table 1). The majority of subjects had results above those shown to be associated with 95% chance of clinical allergy on food challenge (10,11).

Nine out of the 12 children consented to undergo a bronchial food challenge (Fig. 1). Six challenges were double-blind, placebo-controlled (DBPCBFC); one was single-blind, placebo-controlled (SBPCBFC); and two were open challenges (Table 2). Five challenges were positive and four negative. Positive challenges were seen with fish ($n=3$), chickpea ($n=1$) and buckwheat ($n=1$). In each of the five positive challenges, children developed objective respiratory symptoms and signs with a decrease in lung function of at least 15% within an hour of challenge. Two children developed late phase symptoms and lung function changes after they had recovered from the early phase symptoms. Additionally, three subjects also developed nonbronchial symptoms (Table 2). No symptoms, signs or changes in lung function were seen following any of the placebo challenges. Five families completely removed the food allergen from the home and all these children showed improvement in asthma control accompanied by a reduction in inhaled steroid medication in two children. The other seven children, who were either noncompliant or had negative challenges, continued to have significant symptoms and five had an ongoing requirement for inhaled steroids.

Table 1. Summary of presenting details of the cases. All had convincing histories of immediate hypersensitivity to ingested food with positive specific IgE (RAST or skin prick testing)

Case	Age (years)	Food (method of cooking)	Presenting food allergy history		Immunological test to food		Aeroallergen sensitisation
			Oral exposure	Air exposure	Skin prick test wheal diameter results (mm)	Specific IgE results IU/ml (class)	
1	5	Fish (frying)	U	C, W	ND	8.29 (3)	Cat and dog
2	7	Fish (steaming)	W	U, A, W	ND	5.90 (3)	House dust mite
3	8	Fish (baking or steaming)	U, W	U, W	10	ND	None
4	11	Fish (steaming or frying)	U, W	C	ND	7.29 (3)	Aspergillus
5	13	Fish (steaming or frying)	U, A	C, W	ND	> 100 (6)	Grass pollen, house dust mite
6	13	Fish (steaming or frying)	U, S	W, T	20	> 100 (6)	Grass pollen, cat, dog, house dust mite
7	2	Chickpea (baking)	U, W	R, C	ND	6.07 (3)	Grass or tree pollen
8	6	Chickpea (baking)	U, R	U, W	4	0.00 (0)	Grass pollen or house dust mite
9	4	Milk (boiling)	V, L	C, W	10	18.10 (4)	None
10	5	Milk (boiling)	A, U	C	ND	85.70 (5)	Dog and cat
11	4	Egg (boiling)	V, W	W	6	53.40 (5)	None
12	7	Buckwheat (baking)	U, W	W	16	ND	Grass pollen

U, urticaria; W, wheeze; V, vomiting; A, angioedema; S, stridor; R, rhinoconjunctivitis; L, lethargy; C, cough; T, chest tightness; ND: not done.

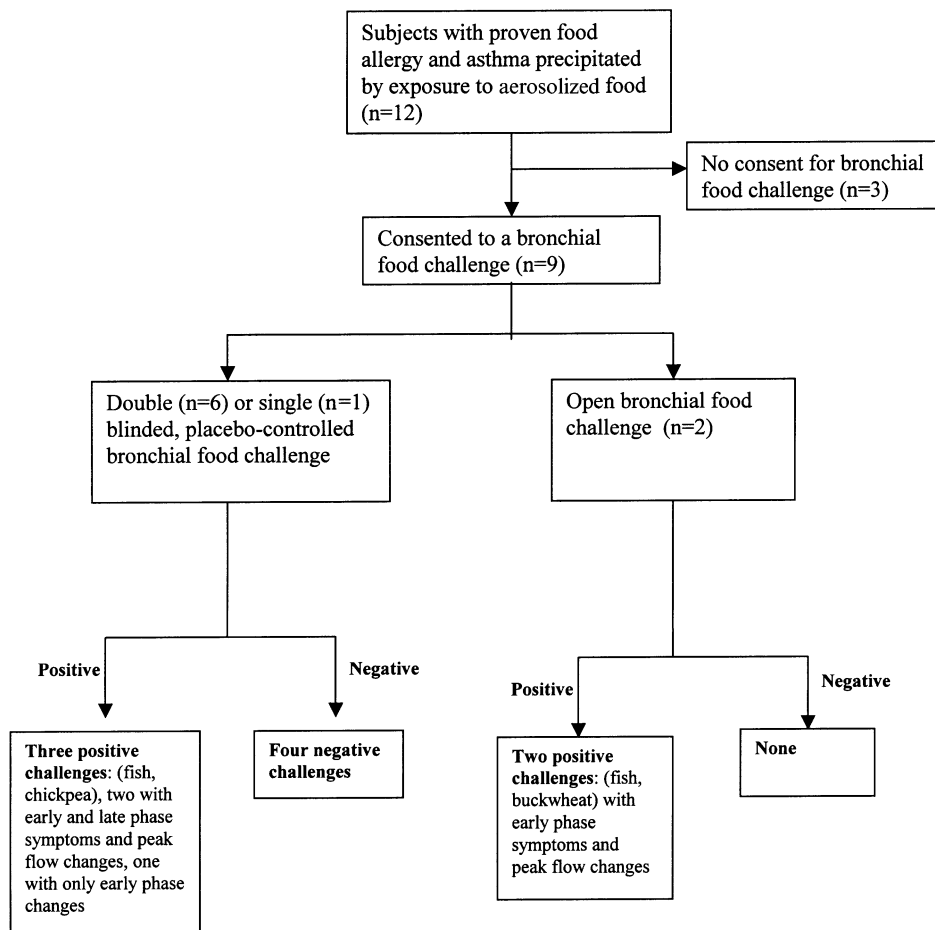


Figure 1. Flow diagram presenting the investigations undertaken in these subjects.

Discussion

We have presented a prospective series of 12 children with proven IgE-mediated food allergy whose asthma seemed to worsen on inhalational exposure to the food to which they react. The foods implicated as the cause of these reactions were fish, milk, chickpeas, buckwheat or eggs (Table 1). All the children were able to successfully avoid allergic symptoms by dietary avoidance. However, the families continued to cook with the foods and the children continued to have symptoms of chronic asthma. Uniquely, these subjects have been systematically investigated with bronchial food challenges. Of the nine subjects who consented to challenge, five developed objective asthmatic signs and lung function changes when exposed to the food while it was being cooked. Two of these children also had late phase responses, suggesting that aerosolized food allergens can induce bronchial inflammation (12). When the families stopped cooking the food in the house, there was a considerable reduction in both symptoms and inhaled steroid requirements. These results demonstrate that foods can behave as aeroallergens, causing both early and late phase bronchospasm.

There has been a long-standing debate as to whether foods and diet play a role in allergic asthma (13). Up to

8% of asthmatic subjects have a coexistent food allergy (14, 15). Co-existent food allergy has also been implicated as a risk factor for severe asthma (16). The ingestion of an allergenic food is a recognized cause of bronchospasm and this is an important pathophysiological mechanism in anaphylactic reactions to foods (17). In a series of 320 children and young adults undergoing double-blind, placebo-controlled oral food challenges, 15% developed lower respiratory tract symptoms and 7% dropped their FEV₁ by more than 20% (18). Airway hyper-responsiveness (AHR), as measured by methacholine challenge, has also been evaluated by the same group in children and teenagers with food allergy and asthma (19). Significant increases in AHR were seen in subjects after a food challenge, whether or not they experienced chest symptoms. It is therefore apparent that ingestion of food can increase airway hyper-reactivity without necessarily inducing symptoms of asthma.

Foods are also known to cause bronchospasm in the context of occupational exposure. Examples include baker's asthma (20), buckwheat (21), cow's milk (22) or egg in the food industry (23). In the latter, egg is sprayed onto food with a spray gun prior to baking. This inevitably results in aerosolization of potentially aller-

Table 2. Summary of results of bronchial challenges

Case	Age (years)	Food	Challenge type	Challenge result		Outcome after complete avoidance
				Early phase	Late phase	
1	5	Fish	Moved away	ND	ND	Improved symptom control
2	7	Fish	DBPCBFC (boiling fish or chicken)	Wheeze and cough with 15% peak flow drop	Cough with a peak flow drop of 20%	Improved symptom control
3	8	Fish	Refused challenge	ND	ND	Non-compliant, symptoms when the family cooks with fish
4	11	Fish	DBPCBFC (boiling fish or chicken)	No symptoms, signs or peak flow change	No symptoms, signs or peak flow change	Still symptomatic despite 400 µg inhaled fluticasone per day
5	13	Fish	DBPCBFC (steamed fish or chicken)	Rhinitis and tight chest with 30% peak flow drop	No symptoms, signs or peak flow change	Improved symptom control
6	13	Fish	Open (steamed fish)	Wheeze, cough and 20% peak flow drop	No symptoms, signs or peak flow change	Non-compliant, symptoms when the family cooks with fish
7	2	Chickpea	Refused challenge	ND	ND	Non-compliant, still requires 400 µg budesonide daily
8	6	Chickpea	SBPCBFC (milled chickpea or wheat flour)	Rhinitis, urticaria, wheeze and 60% drop in peak flow	Wheeze and 50% drop in peak flow	Successfully stopped 400 µg daily budesonide dose
9	4	Milk	DBPCBFC (boiling cow's milk or soy)	No symptoms or signs	No symptoms or signs	Continues to require oral montelukast and inhaled budesonide 200 µg a day
10	5	Milk	DBPCBFC (boiling cow's milk or soy)	No symptoms or signs	No symptoms or signs	Successfully stopped 200 µg daily beclomethasone dose
11	4	Egg	DBPCBFC (boiled egg and chicken)	No symptoms or signs	No symptoms or signs	Still requires inhaled fluticasone 100 µg a day
12	7	Buckwheat	Open (milled buckwheat)	Urticaria, angioedema and wheeze	No symptoms or signs	Only symptomatic when family cooks with buckwheat

DBPCBFC: double-blind, placebo-controlled, bronchial food challenge; SBPCBFC single-blind, placebo-controlled, bronchial food challenge; ND: not done.

genic egg proteins within the work place. Foods have also been found to act as more general environmental aeroallergens. The asthma epidemics of Cartagena and Barcelona in Spain were connected with the unloading of soya beans at the port (24). It is therefore clear that inhalation of food allergens can cause occupational and epidemic asthma.

The ability of common food allergens to behave as aeroallergens has been previously recognized (25–31) and aerosolized food allergens have been detected in environmental sample (32). This is not widely appreciated by physicians although approximately 5% of children presenting to our clinic with food allergy and asthma have bronchial symptoms with only inhalational exposure to the food. In this paper, we have, for the first time, systematically investigated a group of subjects with food allergy and asthma using objective double-blind, placebo-controlled bronchial food challenges (DBPCBFC). We have demonstrated that food allergens may have a significant role as aeroallergens in the etiology of asthmatic symptoms in children with food allergies. Fish seems to be especially able to cause symptoms via the inhaled route; 3 out of 4 children in this series reacted on challenge to aerosolized fish. It seems that fish allergen is able to become aerosolized in sufficient quantities without the need for cooking (32). Many other food allergens also have the potential to become aerosolized without cooking (24, 32). In

particular, there is now considerable concern that peanut allergens may be able to behave in a similar way, particularly within the confined cabin of commercial airliners (26). It is intriguing that none of the milk or egg-allergic children reacted on aerosolized challenge, despite apparently convincing histories. For these foods, we may have failed to deliver sufficient quantities of allergenic particles in the respirable range; this might have been overcome by nebulizing a solution containing the allergen but we wished to replicate the actual domestic circumstances. It is possible that peak expiratory flow measurements may have been too insensitive to detect changes in lung function. Other measures such as spirometry or inflammatory markers may have proved to be more sensitive. Alternatively, the children may have outgrown their bronchial reactivity prior to outgrowing their gastrointestinal and cutaneous reactivity.

We have presented a prospective series of children with food allergy who develop symptoms of asthma as a result of exposure to aerosolized food allergens. This highlights the importance of considering foods as aeroallergens in children with coexistent food allergy and asthma. Even with rigorous dietary avoidance, continued environmental exposure may contribute to a child's persistent asthma symptoms. In such a situation, dietary elimination of the food may not suffice and complete environmental elimination may be required.

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