

The Mouth and Pharynx

Elide A. Pastorello, Cristoforo Incorvaia, Claudio Ortolani

- Symptoms appear immediately at the site of contact with the food when a susceptible allergic patients eats the offending food.
- Allergy to fresh fruits and vegetables, associated with all kinds of pollinosis, is the more frequent cause of Oral Allergy Syndrome.

Key words: Food allergy, Oral Allergy Syndrome, food intolerance

IgE-mediated food allergy

Definition and epidemiology

One of the most common forms of IgE-mediated food allergy in adults is the Oral Allergy Syndrome (OAS). This term is currently used to describe the complex of clinical symptoms localized to the oral mucosa and pharynx that arise on direct oral contact with a provocative food (1). Though foods such as seafood (2), milk and egg (3) may give rise to oropharyngeal symptoms besides systemic ones, fresh fruits and vegetables are the foods most frequently involved in OAS. This chapter will focus on these.

OAS from fruits and vegetables occurs mainly in patients allergic to pollens. A recent study found that about 40% of patients suffering from hay

fever from various pollens had symptoms upon eating fresh fruits and vegetables (4). Considering that in civilized areas about 7-8% of people suffer from pollinosis, it is therefore reasonable to assume that about 3% will present this kind of food allergy. Birch pollen allergy seems particularly to favor sensitization to fresh fruits and vegetables, as it has been reported that 75% of birch pollen allergic patients complained of allergic symptoms after eating apples (5). However all sorts of pollinosis facilitate the appearance of food sensitization and the topographic prevalence of the local flora is often the most influential environmental factor in inducing the common

Author	(Ref)	Year	Pollen	Fruit/vegetable
Anderson	(6)	1970	Ragweed	Melon/banana
Eriksson	(7)	1978	Birch	Apple hazelnut, carrot, potato
Pauli	(8)	1985	Birch, mugwort	Celery
Enberg	(9)	1987	Ragweed	Watermelon, gourd family
Ortolani	(1)	1988	Grass	Tomato, melon, watermelon
Ebne	(5)	1991	Birch	Apple
Hirschwehr	(14)	1992	Hazel	Hazelnut
Ortolani	(10)	1993	Birch	Fennel, celery
			Grass	Kiwi
Gall	(10)	1994	Birch	Kiwi

Table 1. Associations between pollinosis an allergy to fresh fruits and vegetables

sensitizations to vegetable foods in a given area. Table 1 reports the most frequent associations between pollinosis and allergy to fruits/vegetables.

Sensitization to a certain fruit or vegetable is usually associated with sensitization to other foods belonging to the same botanical family, in well-defined "clusters" of hypersensitivity. The most frequent clusters are various nuts, apple and pear, potato and carrot (12), melon, watermelon and tomato (1), peach, apricot, plum and cherry (13).

Etiopathogenesis

The pathogenesis is truly IgE-mediated. The IgE response is directed toward a series of allergens, most as yet unidentified. One of the pivotal factors in inducing hypersensitivity to fruits and vegetables seems to be cross-sensitization with pollens because of cross-reacting allergens in these two sources. The first studies used RAST inhibition experiments to demonstrate high cross-reactivity between some pollens and vegetable foods. However only recent studies using SDS-PAGE and immunoblotting techniques have shown that this is due to allergens with similar immunochemical characteristics. In particular it has been demonstrated that birch pollen and apple have a common allergen with molecular weight of 17 Kd (which is the major allergen of birch, named Bet v 1) showing very high cross-reactivity and significant nucleic acid homology (5). Similarly hazel and hazelnut share the same major allergens, which are 17 and 14 Kd proteins respectively representing the major allergen of hazel Cor a 1 and hazel profilin, homologous to birch allergens (14).

The nature of these cross-reacting allergens is still being investigated and recent findings indicate that profilin, the 14 Kd protein, is present in almost all eukaryotic organisms, where it serves to regulate actin polymerization (15).

This allergen seems to be the major allergen of celery, cross-reacting with profilin of birch and artemisia. Thus, cross-reacting allergens could be ubiquitous structures with the same biological functions in the different plant and animal sources. It has been recently suggested that even carbohydrate structures or glycoproteins of vegetable could play a role in cross-reactivity between vegetable foods and pollens (16), but the clinical impact of this observation is still under discussion.

In other cases the major allergens of fruits and vegetables are exquisitely specific. For example SDS-PAGE followed by immunoblotting and

blotting inhibition using sera of patients with OAS from peach and other Prunoideae detected a major allergen of 13 Kd shared by all the fruits of this botanical subfamily but not by pollens (13).

Clinical symptoms

The symptoms elicited in allergic subjects by eating the culprit fruit or vegetable characteristically immediately involve the anatomical areas coming into contact with the food. They seem related to the very high concentration of mast cells in the oropharyngeal mucosa leading to a wide interaction between the allergen rapidly released from the vegetable foods and the specific IgE bound on the mast cell surface.

Symptoms are oropharyngeal itching and tingling, papulae/blisters on the mucosa and swelling of the lips. They occur within a few minutes of contact and most patients in our population complained of local symptoms within five minutes from eating; almost all symptoms occurred within 30 minutes(1). If the patient ingests the food despite the local disturbances, symptoms arise related to contact with the gastrointestinal mucosa, such as vomiting and diarrhea, and even systemic reactions, ranging in severity from urticaria to glottis edema and anaphylactic shock may occur. Glottis edema is particularly frequent, and in a first study we observed 62 cases with this reaction out of 262 patients (26%) with OAS from fresh fruits and vegetables(1). Four of the 262 patients (1.5%) presented anaphylactic shock and the foods involved were apricot, peach, lentil and tomato, while celery was the vegetable most frequently causing glottis edema.

We recently confirmed the high prevalence of severe reactions, as 92 out of 706 patients (13%) had at least one documented episode of glottis edema and 15 (2.1%) had anaphylactic shock (10).

The foods mainly involved in causing OAS are reported in Table 2. It is important to underline that these foods elicit symptoms only when eaten raw; once they are cooked they are absolutely safe for the patient.

Diagnosis

The diagnosis of allergy to fresh fruits and vegetables is based on the demonstration of clinical intolerance to the suspected food and of the IgE-mediated mechanism by skin tests and *in vitro*

Food	No of pts	(%)	Food	No of pts	(%)
Apple	139	(53)	Fennel	46	(17)
Peach	104	(40)	Melon	42	(16)
Hazelnut	98	(37)	Orange	42	(16)
Peanut	93	(35)	Banana	39	(15)
Apricot	60	(23)	Carrot	39	(15)
Almond	57	(22)	Potato	39	(15)
Pear	57	(22)	Watermelon	26	(10)
Tomato	54	(21)	Pea	26	(10)
Cherry	53	(20)	Celery	26	(10)

Less than 10 %: Lettuce, lentil, kiwi, cabbage, garlic, lemon, tangerine, parsley, strawberry, blackberry.

Table 2. Frequency of allergy to individual food items in 262 patients suffering from OAS

tests such as RAST. However, the marked lability of the allergens in these foods, which cannot resist the usual procedures for preparation of allergenic extracts, makes the reliability of the IgE tests questionable. Skin prick tests with commercial extracts of fruits are often reliable and the currently recommended technique is the prick+prick, which involves pricking the fruit first and then the patient's skin with the same lancet (17). *In vitro* IgE tests are also affected by loss of allergenicity during preparation of commercial material. For instance RAST showed unsatisfactory sensitivity for most commercial extracts of fruits and vegetables (18), whereas using fresh fruits as coating material for RAST discs gave good results (19).

In food allergy in general the diagnostic value of the IgE tests is held up against a "gold standard", which is the double-blind placebo-controlled food challenge (DBPCFC), as this assesses the appearance of symptoms in response to a given food in strictly controlled conditions.

This principle of how to obtain a diagnosis with certainty is also valid for OAS. However the lability of the allergens of fruits and vegetables affects not only the results of skin tests and RAST but also DBPCFC, since both lyophilization (necessary to give the foods in capsules) and gastric acidity once the food comes into contact with gastric mucosa can inactivate the allergens, making the results unreliable. Moreover, administration of foods in capsules prevents the contact with the oral mucosa and consequently the occur-

rence of local symptoms, thus exposing the patient to the risk of systemic reactions once the capsule dissolves. Therefore fruits and vegetables should be administered by alternative methods, for example using masking solutions, but so far no technique is free of criticism. However in OAS, unlike other kinds of food allergy, the relationship between contact with food and appearance of symptoms (often severe) is unequivocal, so DBPCFC is rarely indispensable.

Food intolerance

Angioedema of lips, tongue, cheeks, palate and, more rarely, of the pharynx (associated in this case with choking) can present as a syndrome in subjects intolerant to non-steroidal anti-inflammatory drugs (NSAID). These substances are rarely used as additives in foods, so intolerance to NSAID can be considered a problem of drug more than food intolerance. However, in subjects intolerant to NSAID certain food additives can elicit symptoms, especially in the oropharynx. The list includes benzoic acid derivatives, which have structural similarities with ASA, azo and non-azo dyes and sulfites (20). The main problem in diagnosing intolerance to a food additive in subjects suffering from chronic urticaria/angioedema relies on applying the correct diagnostic procedure which, considering the variability of symptoms in these patients, must be based on double-blind placebo-controlled challenges, which have to be repeated at least three times.

Elide A. Pastorello, M.D.
Cristoforo Incorvaia, M.D.
Istituto di Medicina Interna
Malattie Infettive e Immunopatologia
Universita degli Studi di Milano

Claudio Ortolani, M.D.
Head, Dept Allergy and Clinical
Immunology
Divisione Bizzozzero
Ospedale Niguarda Ca' Granda
Piazza Ospedale Maggiore 3
20100 Milan, Italy

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