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The figures for food allergy present two contrasting clinical perspectives in children and in adults. In children, the prevalence of food allergy is approximately 8%, the clinical presentation is atopic dermatitis, and the most commonly involved foods are milk, eggs, fish, and nuts (1). In contrast, stringent investigation of adults suspected of having food allergy revealed that less than 1% had clinically significant manifestations (2). In part, these differences may be related to the observation that most infants spontaneously "out grow" sensitization to most foods by the age of 2 years, with the notable exceptions of certain foods such as peanut (3). On the other hand, the occurrence of sensitization of adults to vegetable foods is relatively common, with the highest frequency seen in pollen-sensitive subjects, who may manifest their food allergy as a consequence of the known antigenic cross-reactivity between pollen and foods (4). In southern Europe, fruits and vegetables known not to be cross-reactive with pollens are also very important, as shown by recent studies. In challenge tests of 112 food-allergic patients, in whom the most involved food was peach (5), the major peach allergen was cross-reactive with the other Prunoideae fruits, but not with pollens (6).

The typical clinical picture of IgE-mediated food allergy shows a high rate of anaphylactic reactions and oral allergy syndrome (OAS).

Anaphylaxis is characterized by the classic symptoms of immediate hypersensitivity, involving the cutaneous, respiratory, gastrointestinal, and cardiovascular systems, and this hypersensitivity results from the generation and release of a number of potent, pharmacologically active mediators such as histamine and leukotrienes. Recent reports indicate that foods are the most common cause of anaphylaxis (7, 8), and peanut is the most common causative agent in fatal reactions (9). However, in Italy, because of its

To cite this article:

Pastorello E.A., Pravettoni V., Incorvaia C. & Bellanti J.A.
Food allergy: an update.
Allergy 1999, 54, Suppl 58, 43-45.

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ISSN 0105-4538

scant consumption, peanut has not played a major role, as evidenced by the results of an epidemiologic study we recently conducted to evaluate the incidence of anaphylaxis in 1997 in a general hospital in Milan. The incidence of anaphylaxis in approximately 20 000 patients referred to the hospital was found to be 0.4%, and analysis of the different causes showed not only that foods were the most common cause of anaphylaxis but also that fresh fruits and vegetables were the most frequently involved foods (paper in preparation).

The OAS is defined by symptoms caused by an IgE-mediated reaction occurring at the mucosal surface when the causative food, mainly fresh fruits and vegetables but also eggs, milk, meats, and seafood, comes into contact with sensitized cells (10). This definition focuses on the requirement of direct contact between the oral mucosa and the causative food; afterward, the rapidly released water-soluble allergens at the mucosal surface react with mucosal mast cells. The OAS is often the initial manifestation of the IgE-mediated reaction, and systemic symptoms of varying severity may follow, including laryngeal edema and anaphylactic shock.

When fresh fruits and vegetables are involved, most patients are sensitized to pollens, with well-defined clinical associations such as allergy to birch pollen, apple, and hazelnut; allergy to ragweed, melon, and other members of the gourd family; and allergy to grass and tomatoes (11). This is due to cross-sensitization to certain proteins which naturally occur with similar structures in different sources, giving rise to clusters of hypersensitivity; this is true, for example, for Bet v 1 and Bet v 2, the major birch allergens, which are present with a high degree of homology in all the foods cross-reacting with birch (12).

Since 1995, with the aim of improving our knowledge in this field, we have studied patients with pollinosis in order to evaluate the prevalence and clinical features of OAS resulting from fresh fruits and vegetables. Of patients with pollinosis thus far evaluated, about 25% reported OAS, with or without systemic symptoms, after eating fresh vegetable foods. Prospective analysis of the results has shown that sensitization to these foods seems to be increasing, since the incidence rose by approximately 2% per year. We have confirmed well-known clusters of association between birch pollinosis and apple, pear, and hazelnut allergy, and between grass hay fever and tomato and melon allergy. In frequency of sensitization to the different foods, peach was first, followed by apple, hazelnut, tomato, and kiwi. The extent of the consumption, as well as the characteristics of the foods, may account for

such frequency. In Italy, the most important food allergen source seems to be peach and the other Prunoideae fruits. In 1994, we demonstrated that a major allergen of peach was a low-molecular-weight protein that was the only allergen recognized by sera from patients allergic to peach but not to birch, and the same pattern of reactivity was demonstrated for other Prunoideae fruits such as apricot, plum, and cherry (6). More recently, using cationic exchange and gel filtration, we have purified this allergen and established its molecular mass at 9 kDa, demonstrating that it belongs to a family of recently described proteins referred to as lipid transfer proteins (13). This protein has not been detected previously in peach or other Prunoideae fruits and has been designated Pru p 3 by the WHO/IUIS subcommittee on allergen nomenclature.

Having found a relationship between clinical allergy to peach and allergy to apple and pear, we reasoned that the association could be the result of the presence of homologous Bet v 1 proteins in all these fruits; however, this association can be found also in patients without birch allergy, in whom other allergens are likely to be involved. By immunoblotting of an apple extract with sera from patients allergic to apple and birch pollen, we detected a reactivity to allergens of 19 (Bet v 1), 14 (Bet v 2), and 9 kDa, but if sera from patients allergic to apple with no birch pollinosis were used, IgE binding only to the 9-kDa protein was found. We purified this allergen by cationic exchange and gel filtration, obtaining a well-purified protein, and amino-acid sequencing demonstrated it to be a lipid transfer protein, thus far not described in apple, which demonstrates a high percentage of homology with that from peach (paper submitted).

In the diagnosis of allergic reactions to foods of plant origin, the main problem is the lack of knowledge of the allergenic proteins of these foods and of their relationship with clinical symptoms or simply with sensitization. A clear example is the introduction of transgenic soybean enriched with a 2S albumin from Brazil nut, disregarding the allergenic activity of this protein (14), which demonstrated a strict correlation with occurrence of anaphylaxis in subjects sensitized to Brazil nut (15). This makes the current diagnosis by SPT and RAST unreliable; therefore, the clinical demonstration of reactivity to the food item by the double-blind, placebo-controlled food challenge (DBPCFC) is needed (3). Especially with hidden foods such as peanut, sesame seed, and mustard seed, which subjects consume unawares with potentially fatal reactions, the diagnosis must be absolutely verified by DBPCFC.

However, the DBPCFC also needs a standardized procedure. This is available for peanut, and is generally performed

with lyophilized preparations in capsules (16), but not for other vegetable foods. The type of procedure must depend on the different food items as well as on the different clinical syndromes. In a European Union contract (FAIR-CT 97-3224), we recently set up an original and reliable test meal designed for the DBPCFC with vegetable foods that can be powdered, but this method is not suitable for fresh vegetable foods.

Future advances in identification and purification of food allergens should help greatly in improving diagnosis, and the availability of sensitive tests should aid in recognizing the

presence of hidden foods in commercial preparations. Such tests are expected to reduce the incidence of reactions resulting from unaware consumption, a factor which hampers the optimal treatment of food allergy – allergen avoidance.

As to specific immunotherapy, the first attempts in peanut allergy were discouraging because of severe adverse reactions (17). New approaches are being developed which consist of modifying the IgE-binding epitopes so as to achieve recombinant vaccines that do not cause anaphylaxis (18), and using peanut proteins encoded within plasmid-DNA vectors (19).

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