

Authors' affiliations:

J.A. Bellanti, D.B. Wallerstedt, A.L. MacDowell-Carneiro, International Center for Interdisciplinary Studies of Immunology, Georgetown University School of Medicine, Washington, DC, USA

Correspondence to:

Joseph A. Bellanti, MD
Georgetown University Medical Center
3800 Reservoir Road NW
Washington, DC 20007
USA

The management of food allergy continues to be one of the most clinically perplexing challenges for those entrusted with the care of patients with allergic disease. The problem of therapy is compounded both by the complexity of the myriad of food substances and their allergenic components that give rise to food allergy and by the lack of understanding of the immunopathologic mechanisms which are involved in tissue injury. For ease of discussion, the management of food allergy includes the following three components:

- 1) the identification of the offending food
- 2) the elimination of the suspected food(s)
- 3) modification of the inflammatory mediator(s) responsible for the clinical expression of food allergy.

This presentation will include a description of both the classic approaches to each of these components and new therapeutic perspectives in food allergy.

Identification of offending food(s)

A carefully taken history is the first step in identifying the presence of food allergy (1). Although patients may present to the clinician with a history of food allergy, it is important to recognize that very often food allergy is unsuspected, and the manifestations of the patient's complaints may masquerade as those of another disorder. It is therefore imperative that the clinician maintain a high index of suspicion of food allergy particularly when any of the major shock organs are involved. Equally important to the therapeutic approach to food allergy is the need to elicit whether the reactions are "immediate" or "delayed", since this very often will elucidate possible immunopathologic mechanisms which ultimately determine therapeutic

To cite this article:

Bellanti J.A., Wallerstedt D.B. & MacDowell-Carneiro A.L. Therapeutic perspectives in food allergy. *Allergy* 1999, 54, Suppl 58, 46-49.

Copyright © Munksgaard 1999

ISSN 0105-4538

Table 1. Shock organs, pathogenetic mechanisms, and clinical expressions of food allergy

Major shock organs	Portal of entry of food allergens	Immunopathologic mechanism	Clinical expression
Generalized	Ingestion	IgE-mediated	Anaphylaxis
Skin	Ingestion	IgE-mediated	Urticaria
	Contact	IgE-mediated, ?CMI*	Urticaria
			Atopic dermatitis
Respiratory tract	Ingestion, inhalation	IgE-mediated	Asthma
	Ingestion	Non-IgE-mediated	Hemosiderosis
		(?IgG, IgA, C3)	(Heiner's syndrome)
Gastrointestinal tract	Ingestion	IgE- and non-IgE-mediated	Gastroenteritis
			Malabsorption
	Contact	CMI	Oral allergy syndrome ⁵
Central nervous system	Ingestion	Unknown	?Autism
			?ADHD

*CMI: cellular mediated immunity.

choices. Table 1 shows the major shock organs involved in food allergy together with portals of entry, suspected immunopathologic mechanisms, and therapeutic choices. Although most offending food antigens consist of macromolecular substances, particularly proteins, it is imperative to recognize the importance of low-molecular-weight chemicals present in food preparations which can give rise to allergic symptoms (2). Such additives as sorbic acid, food coloring agents, and monosodium glutamate (MSG) and sulfites have been known to give rise to allergic symptoms. Therefore, a careful search for these agents is mandatory in the management of patients who present with food allergy.

In recent years, it has become increasingly apparent that patients may be exposed to allergens through portals of entry distinct from the gastrointestinal tract (Table 1). An example of such an exposure is shown in Table 2, which describes a 25-year-old woman who presented to our clinic with a history of generalized urticaria. The patient was known to be allergic to peach, almond, and apricot and was advised by her allergist to avoid these in her diet. Unknown to her, the shampoo which she was using contained the apricot responsible for her food-related allergic reaction (3). Therefore, it is incumbent upon the physician to be aware of

these hidden food allergens which may be responsible for allergic disease, and which may masquerade as other clinical entities.

The generally accepted methods of diagnosis of food allergy include:

- 1) *in vivo* skin testing using commercial extracts
- 2) *in vitro* immunologic assays including RAST or ELISA (1, 4).

Ortolani and associates have extensively published results on the use of skin test antigens prepared from fresh fruits and vegetables (5-7). These investigators suggest that the putative food antigen(s) may be destroyed during the preparation of commercial extracts, leading to false negative skin test results. Therefore, the use of freshly prepared food extracts, which retain these critical labile antigens, is recommended by these investigators and appears to be more accurate for diagnosis.

Elimination of the suspected food

Once the offending food has been identified, the next step in the therapeutic regimen is to eliminate it (1). Not only should

Table 2. Clinical case of urticaria related to hidden food allergen (3)

White woman 25 years old with 5-year history of recurrent urticaria known to be allergic to peach, almond, peanut, walnut, and strawberry. Past history of allergic rhinitis due to inhalant aeroallergens.
Skin prick test was positive to trees, grasses, weeds, molds, cat, house dust, and mites; also skin test positive to peach (1+), strawberry (1+), almond (2+), and walnut (2+). Class 1 positive RAST to egg yolk, milk, peanut, wheat, soybean, and apricot.
Despite food-antigen elimination, symptoms of urticaria persisted. Patient's shampoo discovered to contain apricot (to which she was RAST positive and which is known to be cross-reactive with peach and almond). After discontinuation of shampoo, urticaria improved.

Table 3. Examples of cross-reacting foods

Food family	Members	Cross-reacting inhalants
Prunoideae	Peach, cherry, apricot, plum, almond (7)	–
Melon (gourd)	Watermelon, cantaloupe, honeydew melon	Ragweed (8)
–	Apple, carrot, potato	Birch (9)
Legumes	Peanut, peas, beans including soy (10, 11)	–
Cereals (grains)	Wheat, rye, oat, barley, rice, corn (12)	–
–	Celery, apple, peanut, kiwi fruit	Mugwort (13)
–	Banana, avocado, kiwi fruit, chestnut, papaya	Latex (14)
Citrus	Orange, lemon, grapefruit, lime, tangerine	–
Walnut	English walnut, black walnut, pecan, hickory nut	–
Mollusk	Oyster, clam, abalone, mussel	–
Crustacean	Crab, lobster, shrimp	–

the principal offending food be eliminated but also those closely related food substances containing cross-reacting antigens which can also give rise to the manifestations of food allergy (7–14). Table 3 shows some examples of selected food antigens together with closely related cross-reacting foods. These cross-reacting antigens, moreover, may not be solely restricted to food cross-reacting allergens, but may, on occasion, involve food-inhalant interactions (15), as in the ragweed-sensitive allergic rhinitis patient who developed urticaria after eating watermelon because of the known cross-reactivity between ragweed and watermelon (8).

Inherent in the identification and elimination of offending foods is the need for the clinician to instruct patients to read labels on food products carefully so as to identify hidden food antigens or additives, which may comprise only minor components of the food; e.g., cooking oil labeled as corn oil but containing small amounts of peanut oil (16).

Modification of the medications responsible for food allergy

Although the identification and elimination of food antigens represents the mainstay of clinical management of food

allergy, very often these procedures alone are insufficient, and the clinical manifestations persist and may require the use of pharmacologic agents to modify or block the inflammatory mediators responsible for the clinical reaction. Table 4 shows selected mediators or pathogenetic mechanisms responsible for “immediate” or “delayed” manifestations of food allergy, together with examples of pharmacologic agents which have been shown to be clinically effective. Thus, antihistamines, serotonin antagonists, and steroids are generally recognized as the mainstay of therapy. Recently, new families of pharmacologic agents, such as leukotriene-modifying agents (17–19), which block the expressions of or the synthesis of inflammatory mediators have become available and are being used clinically in the food-allergic patient. Although originally developed for the treatment of asthma (20), these agents are now finding wider clinical application to other allergic diseases.

Summary

The therapeutic perspectives in food allergy are thus based upon known principles and mechanisms of tissue injury

Table 4. Examples of pharmacologic agents based upon pathogenetic mechanism/mediators

Type of reaction	Pathogenetic mechanism/mediator		Pharmacologic agent
Immediate	IgE	Histamine	Antihistamines
		Serotonin	Cyproheptadine
		Leukotriene	Antagonist
		Inhibitor	Zafirlukast/montelukast Zileuton
Late	CMI and others		Steroids
			Systemic
			Topical
			Nasal
			Inhaler

mediated by immunologic reactions. A thorough knowledge of these, together with new approaches to the identification,

elimination, and modification of these reactions, is essential in the management of the patient with food allergy.

References

1. Bellanti JA. *Immunology*. Vol. III. Philadelphia: WB Saunders, 1985.
2. Kanwar AJ, Greaves MW. Approach to the patient with chronic urticaria. *Hosp Pract* 1996;31:175-179.
3. Abaci AS, MacDowell-Carneiro AL, Bellanti JA. Exacerbation of urticaria with natural cosmetics containing fruit. *Ann Allergy Asthma Immunol* 1998;80:133.
4. Sampson HA. Adverse reactions to foods. In: Middleton EJ, Reed CE, Ellis EF, et al, editors. *Allergy: principles and practice*. St Louis, MO: Mosby, 1998;1162-1182.
5. Ortolani C, Ispano M, Pastorello EA, et al. The oral allergy syndrome. *Ann Allergy* 1988;61:47-52.
6. Ortolani C, Ispano M, Pastorello EA, et al. Comparison of results of skin prick tests (with fresh foods and commercial food extracts) and RAST in 100 patients with oral allergy syndrome. *J Allergy Clin Immunol* 1989;83:683-690.
7. Pastorello EA, Ortolani C, Farioli L, et al. Allergenic cross-reactivity among peach, apricot, plum, and cherry in patients with oral allergy syndrome: an *in vivo* and *in vitro* study. *J Allergy Clin Immunol* 1994;94: 699-707.
8. Anderson L, Dreyfuss E, Logan J, et al. Melon and banana sensitivity coincident with ragweed pollinosis. *J Allergy Clin Immunol* 1970;45:310-319.
9. Dreborg S, Foucard T. Allergy to apple, carrot and potato in children with birch-pollen allergy. *Allergy* 1983;38:167-172.
10. Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. *J Allergy Clin Immunol* 1989;83:435-440.
11. Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. II. *J Allergy Clin Immunol* 1989;84:701-709.
12. Jones SM, Sampson HA. The role of allergens in atopic dermatitis. In: Leung DYM, editor. *Atopic dermatitis: from pathogenesis to treatment*. Georgetown, TX: RG Landes, 1996.
13. Valenta R, Kraft D. Type I allergic reactions to plant-derived food: a consequence of primary sensitization to pollen allergens. *J Allergy Clin Immunol* 1970;45:310-319.
14. Ahlroth M, Alenius H, Turjanmaa K, et al. Cross-reacting allergens in natural rubber latex and avocado. *J Allergy Clin Immunol* 1995;96:167-173.
15. Kalogeromitros D, Armenaka M, Galatas I, et al. Anaphylaxis induced by lentils. *Ann Allergy Asthma Immunol* 1996;77:480-482.
16. Munoz-Furlong A. Deciphering food ingredient statements. *Pediatr Allergy Immunol* 1998;12:217-218.
17. MacDowell-Carneiro AL, Hurtado RC, Bellanti JA. Improvement of atopic eczema with a leukotriene inhibitor: a new therapeutic use? *Ann Allergy Asthma Immunol* 1998;80:177.
18. Spector S, Tan RA. Antileukotrienes in chronic urticaria. *Ann Allergy Asthma Immunol* 1998;101:572.
19. MacDowell-Carneiro AL, Hassan MH, Cotronei-Cascardo C, et al. Use of a leukotriene inhibitor in the treatment of chronic urticaria. *Ann Allergy Asthma Immunol* 1999;82:113.
20. O'Byrne PM. Leukotrienes in the pathogenesis of asthma. *Chest* 1997;111: 27S-34S.