

Review

Criteria to Determine Food Allergen Priority

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ABSTRACT

The emergent health issue of food allergens presents an important challenge to the food industry. More than 170 foods have been reported in the scientific literature as causing allergic reactions. Clearly, it would be impossible to deal with the presence of trace amounts of all these in the context of food labeling. If the decision to classify major allergens is based solely on the knowledge and experience of allergists and food scientists in the field, without scientifically defined criteria, it is likely to lead to a proliferation of lists. Such practices may lead to an unnecessary elimination of foods containing important nutrients. This paper defines food allergy, food intolerance, and food anaphylaxis and identifies criteria for classifying food allergens associated with frequent allergic reactions. A practical list of food allergens that may result in potentially life-threatening allergic reactions is provided. A mechanism-based (i.e., immunoglobulin E mediated), acute life-threatening anaphylaxis that is standardized and measurable and reflects the severity of health risk is proposed as the principal inclusion criterion for food allergen labeling. Where available, prevalence in the population and threshold levels of allergens should be used as an additional guide to identify possible future labeling needs.

A variety of adverse reactions can occur following exposure to foods, and these can be confused with a true food allergy, since both may exhibit similar signs and symptoms. The general public perceives adverse reactions to food and food additives as a major health problem. Approximately 30% of American households were found to alter their eating habits because one of the family members was believed to have food allergies (59), and about 20% of households surveyed in the United Kingdom reported a food intolerance (68). In fact, less than 2% of the adult population has a true food allergy, which can be confirmed by the “gold standard” double-blind, placebo-controlled food challenge (4, 8, 48, 51). About 5% of infants and young children are diagnosed as having food allergies, most of which are evident in the first 3 years of life (7, 10, 20, 36, 72). Some allergies to foods such as milk and egg are often outgrown, whereas allergies to peanuts and tree nuts are thought to be lifelong (6, 11, 31, 49). Recently, an exciting finding of apparent resolution of clinical peanut allergy in preschool children was reported (29); it is important that such a finding can be confirmed by others.

The term *allergy* has been overused and abused (2, 4, 19, 53). Food allergy denotes an abnormal immunologic reaction that results from exposure to a food or food additive. For most, the term *food allergy* is synonymous with reactions that involve an immunoglobulin E (IgE) mechanism (15, 21, 37, 41, 42, 52), although other immunologic mechanisms can be involved, such as complex formation (14, 45, 55) and cell-mediated immune reactions (60, 65).

This is in contrast to other adverse reactions that are non-immunologic (13, 16, 18, 22, 35, 58, 62, 63). These may include the following: (i) food intolerance, which is an abnormal physiological response to an ingestion of food or a food additive (e.g., sulfite in fruits); (ii) food poisoning, basically a toxic reaction (e.g., histamine in scombroid fish poisoning); (iii) pharmacological reactions due to chemicals that produce a druglike effect (e.g., tyramine in aged cheese); or (iv) metabolic disorders such as an enzyme deficiency (e.g., lactase deficiency).

Although the pathogenesis of food allergy is multifactorial, IgE-mediated anaphylactic reactions will be the focus of this paper. In the scope of food allergy, only IgE-mediated reactions and cell-mediated celiac disease are understood well enough to allow accurate documentation with respect to prevalence, severity, and threshold levels, and only food-dependent, IgE-mediated anaphylaxis poses a serious health risk to sensitive consumers. Food anaphylaxis is a severe and potentially life-threatening form of systemic allergic reaction. It is characterized by rapidly developing postprandial, IgE-mediated allergen-specific generalized reactions, including itching, hives, sweating, swelling of the throat, breathing difficulty, lowered blood pressure, unconsciousness, and, in rare occasions, death (3, 12, 24, 47, 50, 51, 54, 57, 66, 67, 69, 70).

Although any food protein can be potentially allergenic, relatively few are known to cause most allergic reactions as defined above. It is also essential to realize that the effect of “food allergens” only exists in those people who react to them. A food allergen is a protein found in food that is capable of stimulating the immune system to produce IgE antibodies, and on subsequent contact, it is capable of in-

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ducing mast cell degranulation to produce clinical signs and symptoms (1, 34, 41, 61). Foods frequently recognized to trigger severe systemic allergic reactions in sensitive consumers include the following: (i) peanut and peanut products; (ii) soy and soy products; (iii) egg and egg products; (iv) milk and milk products; (v) tree nuts (brazil nut, cashew, walnut, almond, pecan, hazelnut) and nut products; (vi) fish and fish products; (vii) crustacea (shrimp, crab, crayfish, and lobster) and products of these; (viii) cereals containing gluten (wheat) and products of these; and (ix) sesame seed and sesame seed products.

Gluten is not to be confused with celiac disease (gluten-sensitive enteropathy or celiac sprue), which is believed to be a cell-mediated gluten intolerance. Cereal gluten in a meal impairs the absorption of starch and fat, depending on the dose, to sensitive individuals. Clinical manifestations predominately reflect the consequences of malabsorption (18).

The first eight items in the list are often listed as the top eight foods associated with allergic reactions (9, 17, 71). Gluten is included in this allergen list, because it appears in allergen lists worldwide. (Sulfite is included in the Codex list but not included in the International Life Sciences Institute (ILSI) list and the present allergen lists, since it does not meet our inclusion criteria as an allergen.) However, an IgE-mediated allergic reaction to ingested gluten is generally mild and cutaneous. Sesame has been included in the list, since there has been an increasing frequency of reports of allergic reactions to sesame seeds noted in recent literature. With the emerging popularity of vegetarian food and exotic sesame preparations, an escalating prevalence of sesame-induced reactions is expected (5, 25, 30, 32, 39, 40, 46, 64).

In the future, the statement "and products of," which is included in the allergen list, should be clarified or defined. For example, peanut oil and soy oil are products of peanuts and soy, yet it is unlikely that the hot-pressed, highly refined oils contain any allergenic proteins. Clinical studies of people with peanut allergy found that most did not react to crude peanut oil and none reacted to refined peanut oil (26). Similarly, lactose is a milk product not known to be allergenic. As stated above, lactose intolerance is a non-immunologic metabolic disorder due to lactase deficiency. Because these oils and lactose may be used as carriers or diluents for food additives, required labeling for these ingredients may be misleading and may cause sensitive people to avoid the food unnecessarily.

This paper is an attempt to define scientifically, on the basis of current knowledge, a list of food allergen priorities for labeling based on the criteria proposed below. The list of foods and food ingredients in the 1995 Food and Agricultural Organization Technical Consultation on Food Allergies (17) provided a starting point for this discussion. Their list includes those foods known to cause food hypersensitivity and, therefore, includes sulfite. Our criteria proposal for food allergen is a variation from the one recommended by Bousquet et al. (9). They used positive double-blind, placebo-controlled food challenge and anaphylactic reaction as the main criteria for inclusion, whereas we pro-

pose to use severity of health risk based on IgE-mediated anaphylaxis as our principal criterion for allergen labeling. It is hoped that this proposal will stimulate debates and identify areas for further research, which will lead to an improved criteria for redefining the allergen list to better protect food allergic consumers. Without defined criteria, it is possible that certain important candidate foods, for example, sesame seeds, may not be included in the list.

CRITERIA FOR IDENTIFYING FOOD ALLERGENS ASSOCIATED WITH FREQUENT ALLERGIC REACTIONS

One of the major difficulties in interpreting the medical literature has been the lack of uniform definition of terms to define the clinical problems that are observable. These terms have now been standardized (3, 4, 24, 54, 67, 69, 70) and form the basis for the following criteria. The principal criteria to be used for identifying food allergens that are associated with frequent allergic reactions are severity of the reaction, prevalence in the population, and threshold levels of the allergen. These three criteria are further defined below.

SEVERITY OF REACTION

The severity of adverse reactions was considered by Codex Alimentarius of the Food and Agricultural Organization (17) as the principal criterion for identifying allergenic foods. Unfortunately, the term *severity* is not defined. The Australia New Zealand Food Authority defined severe reactions as being those that lead to a significant morbidity or mortality outcome; however, neither the term *significant* nor *morbidity* was defined. We propose to use an acute life-threatening anaphylaxis as a guideline to meter the severity of reactions that lead to "significant morbidity." Life-threatening food anaphylaxis is mechanism based, that is, an IgE-mediated, allergic reaction that is standardized (i.e., a systemic allergic reaction with manifestations of a cutaneous symptom and an additional symptom from the respiratory, cardiovascular, or gastrointestinal system) and measurable and reflects the severity of health risk (3, 12, 24, 47, 50, 54, 66–69).

PREVALENCE IN THE POPULATION

The prevalence of allergic conditions and the threshold levels at which allergens trigger allergic reactions are important criteria to be considered. Unfortunately, it is generally agreed that prevalence data are limited (27, 38, 39, 43, 48, 51, 57), perhaps except for milk allergy in infants (43, 51, 57), and problematic because the inclusion criteria used in the studies are often undefined. Regardless, prevalence data, if available, should be used as an additional guide to identify labeling needs, e.g., when incidences of sesame seed-induced anaphylactic reactions are documented and appear to be on the rise, its inclusion into the food allergen list is warranted.

THRESHOLD LEVELS OF ALLERGENS

Threshold levels are problematic as well, since the amount of an allergen in foods that is required to cause an

allergic reaction varies from individual to individual (i.e., individual variation to threshold levels). Further, the levels of an allergen that may sensitize atopic individuals are unknown. However, it is likely that threshold levels for food allergens capable of inducing allergic reactions do exist. In fact, some information regarding threshold levels is available for a limited number of foods but is still lacking for many others. For example, in an open oral challenge, 10 mg of lyophilized ovalbumin was required to elicit symptoms in children (33). As little as 6 mg of fish induced a positive double-blind, placebo-controlled food challenge (23). In another double-blind, placebo-controlled food challenge study, the amount of peanut allergen required to induce allergic symptoms was found to be as low as 0.1 to 1 mg (28). In an oral provocation study, 25% of the peanut allergic cases reacted to a total reactive dose of less than 100 mg of peanut seeds, and the threshold of peanut reactivity was lower than the threshold of egg reactivity (44). It is recognized that data are scarce and seldom reported; such data are also accumulating from samples obtained from allergy-related complaints. It is anticipated that when analytical tools become available, more data can be collected. Despite these problems, the prevalence and threshold criteria are important, since they will allow food allergens to be included as new problems are identified.

CONCLUSION

More than 170 foods have been reported in the scientific literature as causing "allergic" reactions. Clearly, it would be impossible to deal with the presence of trace amounts of all these in the context of food labeling. Therefore, the food industry should focus its attention on those food allergens that produce true allergic reactions (IgE mediated) that manifest a significant degree of severity in symptoms, i.e., at least involving a cutaneous symptom and an additional symptom from the respiratory, cardiovascular, or gastrointestinal system. The criteria for identifying these allergens should include the severity of the reaction, prevalence in the population, and threshold levels of the allergen if known.

The issue of labeling deficiencies in the case of allergens continues to be debated. Recently, Codex Alimentarius has adopted an amendment to the General Standard for Labeling of Pre-Packaged Food to require ingredient declaration of all compound ingredients present in the food at 5% or more. (These ingredients are defined as those with a common name but composed of multiple ingredients, e.g., fat replacer blend such as whey and soy lecithin.) This amendment, when proposed, initiated the discussion of the allergen labeling subject in Codex Alimentarius, although it was generally recognized by delegations to Codex that the percentage of compound ingredients is irrelevant to the issue of allergen declaration, since thresholds of food allergens that trigger an allergic reaction are mostly not identified. Codex Alimentarius also has decided to require the ingredient declaration of specific known allergens and their products, irrespective of the quantity present in the food. Current U.S. Food and Drug Administration policy recommends that allergenic ingredients be declared, since they

would not be considered "incidental additives" even at trivial levels (56).

To the extent possible, the food industry strives to ensure that individuals with severe food allergies are not exposed to hidden allergens. The industry is taking a leadership role in finding solutions to this problem. However, it would be beneficial to establish a permanent International Expert Panel on Food Allergens to deliberate issues associated with food allergens, including but not limited to the following: (i) establishing specific criteria for identifying and defining allergens in the food supply; (ii) developing mechanisms and materials for educating the public and the international food industry on food allergen issues; and (iii) providing recommendations on labeling the presence of inadvertent allergens in the event of cross contact. The expert panel would be expected to provide a sound scientific basis for harmonizing an international allergen definition, criteria, and labeling—a definite benefit to food safety programs throughout the international community. The panel should consist of established allergy experts from the food industry, medical profession, government, academia, and allergy associations.

REFERENCES

1. Aalberse, R. C. 1997. Food allergens. *Environ. Toxicol. Pharmacol.* 4:55–60.
2. Aas, K. 1994. Expert views as expressed in a lay consensus statement: Nordic consensus statement on investigation of allergy and other disorders of hypersensitivity. *Allergy* 49:573–575.
3. Allergy Section, Canadian Paediatric Society. 1994. Position statement: fatal anaphylactic reactions to food in children. *Can. Med. Assoc. J.* 150:337–344.
4. Anderson, J. A. 1994. Milestones making the knowledge of adverse reactions to food in the decade of the 1980s. *Ann. Allergy* 72:143–154.
5. Asero, R., G. Mistrello, D. Roncarolo, P. L. Antonioti, and P. Falagiani. 1999. A case of sesame seed-induced anaphylaxis. *Allergy* 54:526–527.
6. Bock, S. A. 1987. Prospective appraisal of complaints of adverse reactions in children during the first three years of life. *Pediatrics* 79:683–688.
7. Bock, S. A., and H. A. Sampson. 1994. Food allergy in infancy. *Pediatr. Clin. North Am.* 41:1047–1067.
8. Bock, S. A., H. A. Sampson, F. M. Atkins, R. S. Zeiger, S. Lehrer, M. Sachs, R. K. Bush, and D. D. Metcalf. 1988. Double-blind, placebo-controlled food challenge (DBPCFC) as an official procedure: a manual. *J. Allergy Clin. Immunol.* 82:986–997.
9. Bousquet, J., B. Bjorkstein, C. A. F. M. Bruijnzeel-Koomen, A. Huggett, C. Ortolani, J. O. Warner, and M. Smith. 1998. Scientific criteria and selection of allergenic foods for labelling. *Allergy* 53:3–21.
10. Brigino, E., and S. L. Bahna. 1995. Clinical features of food allergy in infants. *Clin. Rev. Allergy Immunol.* 13:329–345.
11. Brostoff, J., and L. J. Hawk. 1991. Food allergy in children. *Eur. J. Clin. Nutr.* 45(Suppl. 1):11–15.
12. Burks, A. W., and H. A. Sampson. 1993. Food allergies in children. *Curr. Probl. Pediatr.* 23:230–252.
13. Burks, W., G. A. Bannon, S. Sicherer, and H. A. Sampson. 1999. Peanut-induced anaphylactic reactions. *Int. Arch. Allergy Immunol.* 119:165–172.
14. Carini, C., J. Brostoff, and D. G. Wraith. 1987. IgE complexes in food allergy. *Ann. Allergy* 59:110–116.
15. Crowe, S. E., and M. H. Perdue. 1992. Gastrointestinal food hypersensitivity: basic mechanisms of pathophysiology. *Gastroenterology* 103:1075–1095.
16. Eigenmann, P. A., and H. A. Sampson. 1994. An update on food hypersensitivity. *Fund. Clin. Immunol.* 23:121–133.

17. FAO Technical Consultation on Food Allergies, Rome, Italy, 13–14 Nov 1995. 1995. Food and Agriculture Organization of the United Nations, Rome, Italy.
18. Ferguson, A. 1997. Gluten-sensitive enteropathy (celiac disease), p. 287–301. *In* D. D. Metcalfe, H. A. Sampson, and R. A. Simon (ed.), Food allergy: adverse reactions to foods and food additives, 2nd ed. Blackwell Science, Oxford.
19. Finn, R. 1992. Food allergy—fact or fiction: a review. *J. Royal Soc. Med.* 85:560–564.
20. Foucard, T. 1984. Developmental aspects of food sensitivity in childhood. *Nutr. Rev.* 42:98–104.
21. Gaye, A. M., and A. Gungor. 1997. IgE-mediated food allergy, p. 23–35. *In* R. J. Trevino and H. S. Dixon (ed.), Food allergy. Thieme, New York.
22. Grammer, L. C. 1994. Hypersensitivity. *Nephrol. Dial. Transplant.* 9(Suppl. 2):29–35.
23. Hansen, T. K., and C. Bindslev-Jensen. 1992. Codfish allergy in adults: identification and diagnosis. *Allergy* 47:610–617.
24. Hide, D. W. 1993. Food induced anaphylaxis—death can be and must be avoided. *Br. J. Clin. Practice* 47:6–7.
25. Hill, D. J., H. S. Hosking, C. Y. Zhie, R. Leung, K. Baratwidjaja, Y. Iikura, N. Iyngkaran, A. Gonzalez-Andaya, L. B. Wah, and K. H. Hsieh. 1997. The frequency of food allergy in Australia and Asia. *Environ. Toxicol. Pharmacol.* 4:101–110.
26. Hourihane, J. O., S. J. Bedwani, T. P. Dean, and J. O. Warner. 1997. Randomized, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts. *Br. Med. J.* 314:1084–1088.
27. Hourihane, J. O. 1998. Prevalence and severity of food allergy—need for control. *Allergy* 53:84–88.
28. Hourihane, J. O., S. A. Kilburn, J. A. Nordlee, S. L. Hafle, and S. L. Taylor. 1997. An evaluation of the sensitivity of peanut allergic subjects to very low doses of peanut proteins: a randomized, double-blind, placebo-controlled food challenge study. *J. Allergy Clin. Immunol.* 100:596–600.
29. Hourihane, J. O., S. A. Roberts, and J. O. Warner. 1998. Resolution of peanut allergy: case control study. *Br. Med. J.* 316:1271–1275.
30. Kanny, G., C. Hauteclouque, and D. A. Moneret-Vautrin. 1996. Sesame seed and sesame seed oil contain masked allergens of growing importance. *Allergy* 51:952–957.
31. Kivity, S., K. Dunner, and Y. Marian. 1993. The pattern of food hypersensitivity in patients with onset after 10 years of age. *Clin. Exp. Allergy* 24:19–22.
32. Kolopp, M. N., D. A. Moneret-Vautrin, B. Gobert, G. Kanny, M. Brodschii, M. C. Bene, and G. C. Faure. 1997. Specific humoral immune responses in 12 cases of food sensitization to sesame seed. *Clin. Exp. Allergy* 27:1285–1297.
33. Lau, S., M. Thiemeier, R. Urbanek, M. Kemeny, and U. Wahn. 1988. Immediate hypersensitivity to ovalbumin in children with hen's egg white allergy. *Eur. J. Pediatr.* 147:606–608.
34. Lehrer, S. B., W. E. Horner, and G. Reese. 1996. Why are some proteins allergenic? Implications for biotechnology. *Crit. Rev. Food. Sci. Nutr.* 36(Suppl.):S553–S564.
35. Lesof, M. H., and D. M. Kemeny. 1987. Non-IgE-mediated reactions to food: how much is allergic? *Ann. Allergy* 59:90–92.
36. Levy, Y., B. Kornboth, I. Ofer, G. B. Zarty, and Y. Danon. 1994. Food allergy in infants and children: clinical evaluation and management. *Isr. J. Med. Sci.* 30:873–879.
37. Loza, C., and J. Brostoff. 1995. Peanut allergy. *Clin. Exp. Allergy* 25:493–502.
38. Madsen, C. 1997. Prevalence of food allergy/intolerance in Europe. *Environ. Toxicol. Pharmacol.* 4:163–167.
39. Malish, D., M. M. Glovsky, D. R. Hoffman, L. Ghekiere, and J. M. Hawkins. 1981. Anaphylaxis after sesame seed ingestion. *J. Allergy Clin. Immunol.* 67:35–38.
40. Martin, K., M. A. Kagi, and B. Wuthrich. 1993. Falafel-burger anaphylaxis due to sesame seed allergy. *Lancet* 338:582.
41. Metcalfe, D. D. 1985. Food allergens. *Clin. Rev. Allergy* 3:331–349.
42. Metcalfe, D. D. 1997. Food allergy in adults, p. 183–191. *In* D. D. Metcalfe, H. A. Sampson, and R. A. Simon (ed.), Food allergy: adverse reactions to foods and food additives, 2nd ed. Blackwell Science, Oxford.
43. Moneret-Vautrin, D. A. 1999. Cow's milk allergy. *Allerg. Immunol.* 31:201–210.
44. Moneret-Vautrin, D. A., F. Range, G. Kanny, A. Olsewski, J. L. Gueant, G. Dutau, and L. Guerin. 1998. Food allergy to peanuts in France—evaluation of 142 observations. *Clin. Exp. Allergy* 28: 1113–1119.
45. Panganelli, R., G. Cavagni, and F. Pallone. 1986. The role of antigenic absorption and circulating immune complexes in food allergy. *Ann. Allergy* 57:330–336.
46. Pecquet, C., F. Leynadier, and P. Saiag. 1998. Immediate hypersensitivity to sesame in foods and cosmetics. *Contact Dermatitis* 39: 313.
47. Rumsaeng, V., and D. D. Metcalfe. 1998. Asthma and food allergy. *Nutr. Rev.* 56:S153–S160.
48. Sampson, H. A. 1996. Epidemiology of food allergy. *Pediatr. Allergy Immunol.* 7(Suppl. 9):42–50.
49. Sampson, H. A. 1996. Managing peanut allergy. *Br. Med. J.* 312: 1050–1051.
50. Sampson, H. A. 1998. Fatal food-induced anaphylaxis. *Allergy* 53: 125–130.
51. Sampson, H. A. 1999. Food allergy, part 1: immunopathogenesis and clinical disorders. *J. Allergy Clin. Immunol.* 103:717–728.
52. Sampson, H. A., and A. W. Burks. 1996. Mechanism of food allergy. *Ann. Rev. Nutr.* 16:161–177.
53. Schreiber, R. A., and W. A. Walker. 1989. Food allergy: facts and fiction. *Mayo Clin. Proc.* 64:1381–1391.
54. Schwartz, H. J. 1994. Anaphylaxis: a potentially fatal, avoidable, and often ignored clinical problem. *Mayo Clin. Proc.* 69:93.
55. Shakib, F. 1990. IgE-mediated hypersensitivity an autoimmune disease? *Allergy* 45:1–9.
56. Shank, F. R. 1996. Label declaration of allergenic substances in foods. U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition. Available at: <http://vm.cfsan.fda.gov/~1rd/allerg7.html>.
57. Sicherer, S. H., and H. A. Sampson. 1999. Food hypersensitivity and atopic dermatitis: pathophysiology, epidemiology, diagnosis, and management. *J. Allergy Clin. Immunol.* 104:S114–S122.
58. Simon, R. A. 1986. Sulfite sensitivity. *Ann. Allergy* 56:281–288.
59. Sloan, A. E., and M. E. Powers. 1986. A perspective on popular perceptions of adverse reactions to foods. *J. Allergy Clin. Immunol.* 78:127–133.
60. Targan, S. R., M. F. Kagnoff, M. D. Brogan, and F. Shanahan. 1987. Immunological mechanisms in intestinal diseases. *Ann. Intern. Med.* 106:853–870.
61. Taylor, S. L., and S. B. Lehrer. 1996. Principles and characteristics of food allergens. *Cri. Rev. Food Sci. Nutr.* 36(Suppl.):S91–S118.
62. Taylor, S. L., J. A. Nordlee, and J. H. Rupnow. 1989. Food allergy and sensitivities, p. 255–295. *In* S. L. Taylor and A. Scanlan (ed.), Food toxicology: perspective on the relative risks. Marcel Dekker, New York.
63. Taylor, S. L., J. E. Stratton, and J. A. Nordlee. 1989. Histamine poisoning (scombroid fish poisoning): an allergy-like intoxication. *Clin. Toxicol.* 27:225–240.
64. Vadas, P., and M. Gold. 1998. Criteria for development of a priority allergen list: application to sesame seed. *Allergy* 3:174–176.
65. Walker-Smith, J. A. 1986. Food sensitivity enteropathies. *Clin. Gastroenterol.* 15:55–69.
66. Weiler, J. M. 1999. Anaphylaxis in the general population: a frequent and occasionally fatal disorder that is underrecognized. *J. Allergy Clin. Immunol.* 104:271–273.
67. Yocum, M. W., and D. A. Khan. 1994. Assessment of patients who have experienced anaphylaxis: a 3-year survey. *Mayo Clin. Proc.* 69:16–23.
68. Young, E., M. D. Stoneham, A. Petrukevitch, J. Barton, and R. Rona. 1994. A population study of food intolerance. *Lancet* 343: 1127–1130.
69. Yunginger, J. W. 1992. Anaphylaxis to foods, p. 543–557. *In* R. E. Reisman and P. Lieberman (ed.), Immunology and allergy clinics of

- North America: anaphylaxis and anaphylactoid reactions, vol. 12, no. 3. W. B. Saunders Co., Philadelphia.
70. Yunginger, J. W. 1992. Anaphylaxis. *Ann. Allergy* 69:87–96.
71. Zarkadas, M., W. S. Scott, and A. Ham Pong. 1999 Common allergenic foods and their labeling in Canada—a review. *Can J. Allergy Clin. Immunol.* 4:118–141.
72. Zeiger, R. S. 1990. Prevention of food allergy in infancy. *Ann. Allergy* 65:430–441.