

Symposium: Pediatric Food Allergy

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ABSTRACT. Food allergy seems to be increasing in prevalence,¹ significantly decreases the quality of life for patients and their families,² and has become a common diagnostic and management issue for the pediatrician.³ Studies now a decade old showed that 6% to 8% of children younger than 3 years experience documented adverse reactions to foods. Several studies have defined the prevalence of allergy to specific foods in childhood. Population-based studies document a prevalence of cow milk allergy in 1.9% to 3.2% of infants and young children,⁴ egg allergy⁵⁻⁷ in 2.6% of children by age 2.5 years,⁸ and peanut allergy in 0.4% to 0.6% of those younger than 18 years.^{9,10} Overall, the typical allergens of infancy and early childhood are egg, milk, peanut, wheat, and soy, whereas allergens that are responsible for severe reactions in older children and adults are primarily caused by peanut, tree nuts, and seafood. Allergy to fruits and vegetables are prominent but usually not severe.¹¹⁻¹³ For diagnostic purposes, it is instructive to consider the prevalence of food allergy as a cause of specific disorders. For example, food allergy accounts for 20% of acute urticaria,^{14,15} is present in 37% of children with moderate to severe atopic dermatitis^{16,17} and approximately 5% with atopic asthma,¹⁸ and is the most frequent cause of anaphylaxis outside the hospital setting.¹⁹⁻²² *Pediatrics* 2003; 111:1591-1594; food allergy, food hypersensitivity, allergic gastroenteropathy, anaphylaxis.

ABBREVIATIONS. IgE, immunoglobulin E; RAST, radioallergen sorbent test.

On April 20th, 2002, a symposium was held among food allergy specialists and a group of pediatricians, a pediatric gastroenterologist, and an allergist (Appendix 1) for the purpose of identifying specific issues of concern to pediatricians regarding food allergy. Lectures and question-and-answer sessions were held to formulate responses to particular concerns so as to generate a set of manuscripts that were clinically relevant for the pediatrician who is faced with the front-line recognition of

food-allergic disorders. A selection of specific questions that were posed by pediatricians and addressed by the group are shown in Table 1.

TOPICS ADDRESSED IN THE SYMPOSIUM

During the past decade, there has been an increased understanding of the immunopathogenesis of food-allergic disorders that carries crucial lessons for an improved diagnostic approach to these disorders. Food allergy is defined as an adverse immunologic response to food protein.²³ This is in contrast to toxic reactions exemplified by food poisoning or to a number of disorders that are considered food intolerance. Food intolerance is host specific but does not involve immune mechanisms and is exemplified by lactose intolerance. Food allergy (hypersensitivity) therefore represents an aberration of the normal immune responses to food proteins (oral tolerance). In immunoglobulin E (IgE) antibody-mediated allergy, T cells direct B cells to produce food-specific IgE antibodies that arm tissue mast cells (sensitization). Reexposure to the food is detected by these IgE antibodies on the surface of mast cells and results in the immediate release of mediators such as histamine that cause the observed reaction (clinical allergy). This mechanism underlies most of the acute reactions to food proteins resulting in symptoms such as hives, wheezing, and hypotension. The second mechanism, non-IgE-mediated, or cell-mediated, food allergy, results from the generation of T cells that respond directly to the protein with the elaboration of mediators that direct allergic inflammation (eosinophilic inflammation, increased vascular permeability), leading to a variety of subacute and chronic responses primarily affecting the gastrointestinal tract. In some cases, patients with phenotypically identical disorders may have a mixed pathology with both IgE antibody and cellular causes. Table 2 lists specific named disorders according to the recognized immunopathological basis.

A series of 4 reviews in this supplement address specific food-allergic disorders. The first article addresses food-induced anaphylaxis, an acute IgE antibody-mediated disorder that accounts for >30 000 episodes of anaphylaxis in the United States each year.²⁰ Although anaphylaxis is usually easy to identify, numerous issues regarding the identification of a specific cause, treatment, preparation for, and prevention of accidental exposures can be challenging and are discussed in detail. The variety of clinical manifestations of food allergy that affect the skin, gastrointestinal tract, and respiratory tree are dis-

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TABLE 1. Selected Questions Posed by Pediatricians

How often and to what extent might food allergy play a role in common disorders such as atopic dermatitis, asthma, colic, gastroesophageal reflux, constipation, failure to thrive, otitis media, behavioral problems, and others?
What types of complaints regarding foods would warrant an allergy evaluation?
Under what circumstances should self-injectable epinephrine be prescribed and administered?
At what point should the pediatrician consult an allergist, dermatologist, and/or gastroenterologist?
How should schools and camps be approached regarding food allergy and anaphylaxis?
Can allergy be prevented, and how should food be introduced to atopy-prone children?
Who is at risk for severe or fatal food anaphylaxis?
What tests should a pediatrician perform to diagnose food allergy?

cussed in articles divided by organ system. These disorders include acute, subacute, and chronic disease with significant morbidity and symptoms that often overlap nonallergic disorders or allergic disorders caused by nonfood allergens (eg, respiratory allergy induced by dust mite).

The pediatrician is usually the first to consider food allergy as a cause of specific complaints, symptoms, and physical signs. The diagnostic evaluation is reviewed in an article that highlights the concept that information obtained from a careful history in the context of a good understanding of the features of specific disorders is the most important step toward diagnosis. The laboratory tests currently available to assist in the diagnosis of food allergy are ones that detect food-specific IgE antibody. The test modalities include allergy prick skin tests, usually performed by allergists, and serum tests, radioallergen sorbent tests (RASTs), that are more widely available. Tests for IgE antibody can be informative but also carry limitations that must be fully appreciated. The tests detect only sensitization (IgE) and do not necessarily indicate clinical reactivity. Depending on the clinical history, a positive test correlates with reactions less than half of the time.¹ Positive test results are therefore “false positives” in many circumstances. Conversely, they may be negative tests despite a clinical food-allergic reaction because: 1) the pathophysiological cause of the reaction was cell mediated, not antibody mediated; 2) the wrong food was tested; or 3) the test was not sensitive enough. The group was tentative in recommending the use of such tests for screening or diagnostic purposes by pediatricians because of these limitations and the potential for errors in over-, under-, and misdiagnosis. In many cases, the diagnosis of food allergy

additionally requires the use of diagnostic elimination diets and physician-supervised oral food challenges, modalities that carry a risk of reactions and nutritional consequences and are generally beyond the scope of routine pediatric practice. Given the test limitations, the articles reflect caution in the use of RASTs for the purpose of making a definitive diagnosis of food allergy by pediatricians, although they may be useful as screening tests in an effort to identify children who may have underlying food allergy.

Once a diagnosis is secured, management involves elimination of causal foods. The requirement seems straightforward but is difficult to carry out successfully. Management issues include education about reading labels from commercial products, problems with cross-contact and contamination with allergens in restaurants and other settings, and numerous issues that arise in schools and camps. For children who are at risk for anaphylaxis, emergency plans must be in place for treatment with medications, particularly epinephrine, in the event of an accidental ingestion. Such plans carry numerous practical concerns that often require involvement by the pediatrician. In addition, elimination of >1 or 2 foods can result in nutritional consequences. These important issues are discussed in 2 of the reviews.

Parents often direct 3 important queries to pediatricians: 1) Will my child outgrow his or her food allergy? 2) Is there any way to prevent food allergy in another child? 3) Is there hope for better diagnosis and treatment in the near future? Recent advances in research have improved our ability to answer these questions. For example, the dogma that peanut allergy is permanent²⁴ has been revised on the basis of several studies showing that it is outgrown in ~20% of very young children.^{25,26} Conversely, it seems that the number of children who do not outgrow milk and egg allergy may have been generally underestimated. Attention has also turned to prevention of food allergy, and several recommendations were recently espoused by the American Academy of Pediatrics regarding infant feeding practices and concerns about maternal diet during breastfeeding in children at risk for atopic diseases.²⁷ Last, numerous avenues of research show promise for improved diagnostic and therapeutic strategies. These topics are considered in detail in 3 articles.

Two additional specific concerns were not addressed in detail in the articles but are often initially considered by pediatricians. One concern is the presence of food proteins in vaccines and medications. For vaccines, the *Red Book* contains the most up-to-date information on components that may trigger

TABLE 2. Named Food-Allergic Disorders According to Pathophysiology

IgE Antibody-Mediated	IgE Antibody-Mediated and/or Cell-Mediated	Cell-Mediated (Non-IgE)
Urticaria/angioedema	Atopic dermatitis	Dietary protein, enterocolitis
Immediate gastrointestinal reactions	Eosinophilic gastroenteropathies	Dietary protein proctitis
Oral allergy syndrome (pollen-related)		Dietary protein enteropathy
Rhinitis	Asthma	Celiac disease
Anaphylaxis		Dermatitis herpetiformis
Food-associated, exercise-induced anaphylaxis		Pulmonary hemosiderosis

TABLE 3. Role of the Pediatrician and Specialists in the Management of Pediatric Food Allergy: A Partnership

	Pediatrician	Specialist
Initial diagnosis	XX	X
Definitive diagnosis		XX
Few food restrictions	X	X
Many food restrictions	X	XX
Provision of measles-mumps-rubella vaccine	XX	
Management of anaphylaxis education	X	X
Instruction of school and camp	X	X
Reevaluation for tolerance		XX
Allergy prevention	X	X

X, indicates important role; XX, primary role.

allergic reactions. For example, the measles-mumps-rubella vaccine is generally safe for egg-allergic patients, but the influenza and yellow fever vaccines may contain relevant amounts of egg protein that could elicit reactions. Gelatin is another food-derived protein found in vaccines that is sometimes problematic. A variety of medications contain food proteins, and so this concern must be considered on an individual basis. The other issue often faced by pediatricians that was not otherwise discussed in detail was the role of food or additive allergy and other adverse reactions on behavior and development. This topic remains controversial, but there is little evidence for a significant impact of food allergy on behavior and no evidence of "sugar allergy."²⁸

Several themes that emerged from the conference were that pediatricians are recognizing an increasing number of patients with food allergy, need to address parental concerns about the relationship of various disorders to foods, and are being called on increasingly for diagnosis and management of a variety of food-allergic disorders. The "division of labor" among pediatricians, allergists, and other subspecialists (gastroenterologist, dietitian, dermatologist, etc) for the care of food-allergic patients was discussed with a variety of opinions given. Although specific roles may vary by disease, severity, availability of specialists, and other factors, a general scheme for the roles of specialists and generalists in the care of food-allergic patients and their families is best viewed as a partnership as shown in Table 3. Educational materials that are helpful for the management of families with food allergy are available from resources listed in Appendix 2. In closing, the organizers, editors, and participants in this symposium hope that these articles serve as a valuable resource for the improved diagnosis and management of food-allergic disorders in infants and children.

APPENDIX 1: PARTICIPANT LIST

Speakers: S. Allan Bock, MD, National Jewish Medical and Research Center, Boulder, CO; A. Wesley Burks, MD, Arkansas Children's Hospital, Little Rock, AR; John James, MD, Colorado Allergy and Asthma Center, Fort Collins, CO; Lloyd Mayer, MD, Mount Sinai School of Medicine, New York, NY; Shideh Mofidi, MS, RD, CSP, Mount Sinai School of Medicine, New York, NY; Anne Muñoz-Furlong, BA,

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Invited Guests: Joel Forman, MD; Reza Keshavarz, MD; John Larsen, MD; Chris Liacouras, MD; Rosanna Mirante, MD; Laura Popper, MD; Harold Raucher, MD; Kenneth Schuberth, MD; Barry Stein, MD.

APPENDIX 2: RESOURCES FOR PATIENT EDUCATION

Allergy and Asthma Network/Mothers of Asthmatics, 2751 Prosperity Ave, Ste 150, Fairfax, VA 22031, (800) 878-4403, www.aanma.org

American Academy of Allergy, Asthma & Immunology, 611 E. Wells St, Milwaukee, WI 53202, (800) 822-ASMA, www.aaaai.org

American Academy of Pediatrics, 141 Northwest Point Blvd, Elk Grove Village, IL 60007-1098, (800) 433-9016, www.aap.org

American College of Allergy Asthma & Immunology, 85 W. Algonquin Rd, Ste 550, Arlington Heights, IL 60005, (800) 842-7777, www.allergy.mcg.edu

American Dietetic Association, 216 W. Jackson Blvd, Chicago, IL 60606-6994, (800) 877-1600, www.eatright.org

Asthma & Allergy Foundation of America, 1233 20th St NW, Ste 402, Washington, DC 20036, (800) 7ASTHMA, www.aafa.org

The Eczema Association for Science and Education, 1220 SW Morrison, Ste 433, Portland, OR 97205, (800) 818-7546, www.eczema-assn.org

Food Allergy & Anaphylaxis Network, 10400 Eaton Place, Ste 107, Fairfax, VA 22030, 800-929-4040, www.foodallergy.org

Inflammatory Skin Disease Institute, PO Box 1074, Newport News, VA 23601, (757) 223-0795, www.isdionline.org

Medic Alert Foundation, PO Box 1009, Turlock, CA 95381, (800) 344-3226

For information about supporting food allergy research to find a cure, contact the Food Allergy Initiative, 625 Madison Avenue, 4th Floor, New York, NY 10022, (212) 527-5835, www.FoodAllergyInitiative.org

REFERENCES

1. Sampson HA. Food allergy. Part 1: immunopathogenesis and clinical disorders. *J Allergy Clin Immunol.* 1999;103:717-728
2. Sicherer SH, Noone SA, Munoz-Furlong A. The impact of childhood food allergy on quality of life. *Ann Allergy Asthma Immunol.* 2001;87:461-464
3. Sampson HA, Anderson JA. Summary and recommendations: classification of gastrointestinal manifestations due to immunologic reactions to foods in infants and young children. *J Pediatr Gastroenterol Nutr.* 2000;30:S87-S94
4. Jakobsson I, Lindberg T. A prospective study of cow's milk protein intolerance in Swedish infants. *Acta Paediatr Scand.* 1979;68:853-859
5. Host A, Halken S. A prospective study of cow milk allergy in Danish infants during the first 3 years of life. *Allergy.* 1990;45:587-596

6. Schrandt JJP, van den Bogart JPH, Forget PP, Schrandt-Stumpel CTRM, Kuijten RH, Kester ADM. Cow's milk protein intolerance in infants under 1 year of age: a prospective epidemiological study. *Eur J Pediatr*. 1993;152:640–644
7. Eggesbo M, Botten G, Halvorsen R, Magnus P. The prevalence of CMA/CMPI in young children: the validity of parentally perceived reactions in a population-based study. *Allergy*. 2001;56:393–402
8. Eggesbo M, Botten G, Halvorsen R, Magnus P. The prevalence of allergy to egg: a population-based study in young children. *Allergy*. 2001;56:403–411
9. Sicherer SH, Muñoz-Furlong A, Burks AW, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol*. 1999;103:559–562
10. Emmett SE, Angus FJ, Fry JS, Lee PN. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members. *Allergy*. 1999;54:380–385
11. Ortolani C, Spano M, Pastorello E, Bigi A, Ansaloni R. The oral allergy syndrome. *Ann Allergy*. 1988;61:47–52
12. Asero R. Detection and clinical characterization of patients with oral allergy syndrome caused by stable allergens in Rosaceae and nuts. *Ann Allergy Asthma Immunol*. 1999;83:377–383
13. Ortolani C, Spano M, Pastorello EA, Ansaloni R, Magri GC. 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
14. Sehgal VN, Rege VL. An interrogative study of 158 urticaria patients. *Ann Allergy*. 1973;31:279–283
15. Champion R, Roberts S, Carpenter R, Roger J. Urticaria and angioedema: a review of 554 patients. *Br J Dermatol*. 1969;81:588–597
16. Eigenmann PA, Sicherer SH, Borkowski TA, Cohen BA, Sampson HA. Prevalence of IgE-mediated food allergy among children with atopic dermatitis. *Pediatrics*. 1998;101(3). Available at: www.pediatrics.org/cgi/content/full/101/3/e8
17. Lever R, MacDonald C, Waugh P, Aitchison T. Randomised controlled trial of advice on an egg exclusion diet in young children with atopic eczema and sensitivity to eggs. *Pediatr Allergy Immunol*. 1998;9:13–19
18. James JM, Bernhisel-Broadbent J, Sampson HA. Respiratory reactions provoked by double-blind food challenges in children. *Am J Respir Crit Care Med*. 1994;149:59–64
19. Novembre E, de Martino M, Vierucci A. Foods and respiratory allergy. *J Allergy Clin Immunol*. 1988;81:1059–1065
20. Yocum MW, Butterfield JH, Klein JS, Volcheck GW, Schroeder DR, Silverstein MD. Epidemiology of anaphylaxis in Olmsted County: a population-based study. *J Allergy Clin Immunol*. 1999;104:452–456
21. Pumphrey RSH, Stanworth SJ. The clinical spectrum of anaphylaxis in north-west England. *Clin Exp Allergy*. 1996;26:1364–1370
22. Kemp SF, Lockey RF, Wolf BL, Lieberman P. Anaphylaxis: a review of 266 cases. *Arch Intern Med*. 1995;155:1749–1754
23. Bruijnzeel-Koomen C, Ortolani C, Aas K, et al. Adverse reactions to food. Position paper. *Allergy* 1995;50:623–635
24. Bock SA, Atkins FM. The natural history of peanut allergy. *J Allergy Clin Immunol*. 1989;83:900–904
25. Skolnick HS, Conover-Walker MK, Koerner CB, Sampson HA, Burks W, Wood RA. The natural history of peanut allergy. *J Allergy Clin Immunol*. 2001;107:367–374
26. Hourihane JO, Roberts SA, Warner JO. Resolution of peanut allergy: case-control study. *Br Med J*. 1998;316:1271–1275
27. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106:346–349
28. Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritsy MC. Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. *N Engl J Med*. 1994;330:301–307