Symposium: Pediatric Food Allergy

Scott H. Sicherer, MD§; Anne Muñoz-Furlong, BA*; Ramon Murphy, MD‡; Robert A. Wood, MD||; and Hugh A. Sampson, MD§

ABSTRACT. Food allergy seems to be increasing in prevalence, significantly decreases the quality of life for patients and their families, and has become a common diagnostic and management issue for the pediatrician. 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, egg allergy in 2.6% of children by age 2.5 years, and peanut allergy in 0.4% to 0.6% of those younger than 18 years. 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. 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 and is present in 37% of children with moderate to severe atopic dermatitis and approximately 5% with atopic asthma, and is the most frequent cause of anaphylaxis outside the hospital setting. Pediatrics 2003; 111:1591–1594; food allergy, food hypersensitivity, allergic gastroenteropathy, anaphylaxis.

ABBREVIATIONS. IgE, immunoglobulin E; RAST, radioallergosorbent 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. 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. 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-

From the Department of Pediatrics, Mount Sinai School of Medicine, New York, New York; §Elliott and Roslyn Jaffe Food Allergy Institute, Division of Allergy and Immunology, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland; and ‡Division of Allergy and Immunology, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Received for publication Sep 11, 2002; accepted Oct 30, 2002.
Reprint requests to (H.A.S.) Division of Allergy/Immunology, Mount Sinai School of Medicine, Box 1198, One Gustave L. Levy Pl, New York, NY 10029-6574. E-mail: hugh.sampson@msm.edu
PEDIATRICS (ISSN 0031-4005). Copyright © 2003 by the American Academy of Pediatrics.
TABLE 2. Named Food-Allergic Disorders According to Pathophysiology

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

Discussing articles divided by organ system. These disorders include acute, subacute, and chronic disease with significant morbidity and chronic disorders caused by nonfood allergens (e.g., 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, radioallergosorbent 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
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.

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, Food Allergy & Anaphylaxis Network, Fairfax, VA; Ramon J.C. Murphy, MD, Uptown Pediatrics, PC, New York, NY; Anna Nowak-Wegrzyn, MD, Mount Sinai School of Medicine, New York, NY; Hugh A. Sampson, MD, Mount Sinai School of Medicine, New York, NY; Scott Sicherer, MD, Mount Sinai School of Medicine, New York, NY; Robert A. Wood, MD, Johns Hopkins Hospital Lutherville, MD; and Robert Zeiger, MD, Kaiser Permanente, San Diego, CA.

**Invited Guests:**

- Joel Forman, MD; Reza Kesha-varz, MD; John Larsen, MD; Chris Liacouras, MD; Rosanna Mirante, MD; Laura Popper, MD; Harold Raucher, MD; Kenneth Schubert, 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 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
- 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**


Symposium: Pediatric Food Allergy
Scott H. Sicherer, Anne Muñoz-Furlong, Ramon Murphy, Robert A. Wood and Hugh A. Sampson

*Pediatrics* 2003;111;1591

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/111/Supplement_3/1591.full.html