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Preface: Food Allergy in Children **xv**

Hemant P. Sharma, Robert A. Wood, and Max J. Coppes

Clinical Presentations of Food Allergy **315**

Darlene K. Mansoor and Hemant P. Sharma

Food allergies are immune-mediated responses to food proteins. Because of differences in the underlying immunologic mechanisms, there are varying clinical presentations of food allergy. This article discusses the manifestations of IgE-mediated disorders, including urticaria and angioedema, rhinoconjunctivitis, asthma, gastrointestinal anaphylaxis, generalized anaphylaxis, food-dependent exercise-induced anaphylaxis, and oral allergy syndrome. It also reviews the presentations of mixed IgE- and cell-mediated disorders, including atopic dermatitis and eosinophilic gastrointestinal disorders. Finally, the manifestations of cell-mediated food allergies are discussed, including dietary protein-induced proctitis and proctocolitis, food protein-induced enterocolitis syndrome, celiac disease, and food-induced pulmonary hemosiderosis.

Epidemiology of Food Allergy **327**

Carina Venter and S. Hasan Arshad

Food allergy (FA) is perceived as a common problem, especially during childhood. Accurate assessment of incidence and prevalence of FA has been difficult to establish, however, due to lack of universally accepted diagnostic criteria. Although many foods are reported to cause IgE-mediated FA, most studies focus on 4 common food groups: cow's milk, hen's egg, peanut/tree nuts, and fish/shellfish. There may be variation in the prevalence of FA in regions of the world and a likely increase in prevalence has been observed in recent decades. This cannot be stated with confidence, however, without the use of consistent methodology and diagnostic criteria.

Diagnostic Testing in the Evaluation of Food Allergy **351**

Philippe A. Eigenmann, Jae-Won Oh, and Kirsten Beyer

Food-related symptoms are frequent in childhood, and pediatricians are often requested to initiate a food allergy diagnostic workup. A careful history is the cornerstone for assessing whether tests are needed and which diagnostic procedures are most appropriate. Skin prick tests should be performed only according to standard procedures by a skilled health professional. Determining serum IgE levels (in vitro tests) are available for a wide range of foods. Of utmost importance is the need to correlate test results to the clinical picture. When a conclusion cannot be reached, oral food challenges should be performed for a definite diagnosis.

Pathophysiology of Food Allergy **363**

Brian P. Vickery, Stacy Chin, and A. Wesley Burks

In this article we review the pathophysiology of food allergy, which affects 4% of US children and 2% of adults, and is increasing in prevalence. Most

food allergens share certain specific physicochemical characteristics that allow them to resist digestion, thus enhancing allergenicity. During allergic sensitization, these allergens are encountered by specialized dendritic cell populations in the gut, which leads to T-cell priming and the production of allergen-specific IgE production by B cells. Tissue-resident mast cells then bind IgE, and allergic reactions are elicited when mast cells are reexposed to allergen. Adjacent IgE molecules bound to the surface of the mast cell become cross-linked, causing mast cell degranulation and release of powerful vasoactive compounds that cause allergic symptoms.

Recognition and Management of Food-Induced Anaphylaxis

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Corinne Keet

Food-induced anaphylactic reactions are common and increasing in frequency. Despite the existence of a consensus definition of anaphylaxis, many cases are missed, recommended treatments are not given, and follow-up is inadequate. New aspects of its pathophysiology and causes, including atypical food-induced causes, are still being uncovered. Epinephrine remains the cornerstone for successfully treating anaphylaxis; H1 and H2 antihistamines, glucocorticoids, and β -agonists are ancillary medications that may be used in addition to epinephrine. Early recognition of anaphylaxis, appropriate emergency treatment, and follow up, including prescription of self-injectable epinephrine, are essential to prevent death and significant morbidity from anaphylaxis.

Gastrointestinal Manifestations of Food Allergies

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Jaime Liou Wolfe and Seema S. Aceves

The rates of eosinophilic gastrointestinal disorders appear to be increasing. The most common of these is eosinophilic esophagitis (EoE) which is a clinicopathologic condition consisting of characteristic symptoms and endoscopic features accompanied by a pan-esophageal, acid resistant epithelial eosinophilia of greater than equal to 15 per high power field. Typical symptoms include dysphagia and abdominal pain. Typical endoscopic features include pallor, plaques, furrows, concentric rings. Complications include food impactions and strictures. EoE resolution with food elimination diets provides evidence that EoE is a food-antigen driven process. In vitro and microarray studies have identified specific immunologic factors underlying EoE pathogenesis. Other gastrointestinal manifestations of food intolerances/allergy include food protein induced enterocolitis syndrome.

Milk and Soy Allergy

407

Jacob D. Kattan, Renata R. Cocco, and Kirsi M. Järvinen

Cow's milk allergy (CMA) affects 2% to 3% of young children and presents with a wide range of IgE and non-IgE-mediated clinical syndromes, which have a significant economic and lifestyle effect. It is logical that a review of CMA would be linked to a review of soy allergy because soy formula is often an alternative source of nutrition for infants who do not tolerate cow's milk. This review examines the epidemiology, pathogenesis, clinical features, natural history, and diagnosis of cow's milk and soy allergy. Cross-reactivity and management of milk allergy are also discussed.

Jean-Christoph Caubet and Julie Wang

Egg is one of the most important allergens in childhood feeding, and egg allergy can pose quality-of-life concerns. A clear clinical history and the detection of egg white-specific immunoglobulin E (IgE) will confirm the diagnosis of IgE-mediated reactions. Non-IgE-mediated symptoms, such as those of eosinophilic diseases of the gut, might also be observed. Egg avoidance and education regarding the treatment of allergic reactions are the cornerstones of management of egg allergy. This article discusses epidemiology, risk factors, diagnosis, treatment, and natural history of egg allergy.

Peanut Allergy**445**

Jonathan O'B Hourihane

Peanut allergy may affect up to 2% of children in some countries, making it one of the most common conditions of childhood. Peanut allergy is a marker of a broad and possibly severe atopic phenotype. Nearly all children with peanut allergy have other allergic conditions. Peanut accounts for a disproportionate number of fatal and near fatal food-related allergies. Families with a child or children with peanut allergy can struggle to adapt to the stringent avoidance measures required. Although oral induction of tolerance represents the cutting edge of peanut allergy management, it is not yet ready for routine practice.

Living with Food Allergy: Allergen Avoidance**459**

Jennifer S. Kim and Scott H. Sicherer

The primary treatment of food allergy is to avoid the culprit foods. This is a complex undertaking that requires education about reading the labels of manufactured products, understanding how to avoid cross-contact with allergens during food preparation, and communicating effectively with persons who are providing allergen-safe meals including relatives and restaurant personnel. Successful avoidance also requires a knowledge of nuances such as appropriate cleaning practices, an understanding of the risks of ingestion compared to skin contact or inhalation, that exposure could occur through unanticipated means such as through sharing utensils or passionate kissing, and that food may be a component of substances that are not ingested such as cosmetics, bath products, vaccines and medications. The authors review the necessary tools of avoidance that physicians and medical practitioners can use to guide their patients through the complexities of food avoidance.

Managing Food Allergies in Schools and Camps**471**

Kim Mudd and Robert A. Wood

Managing food allergy in school and camp environments involves creating an individualized plan that addresses safety, and supports growth and development of the food-allergic child. The result is a dynamic strategy that meets the needs of a food-allergic child and promotes the development of a food-allergic adolescent.

Can Food Allergy Be Prevented? The Current Evidence

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George Du Toit and Gideon Lack

Food allergy is a recognized public health concern, for which preventative strategies are required. Although an intervention that adequately protects against the development of food allergy has still to be identified, limited benefits have been shown for the prevention of related allergic conditions such as eczema, and to a lesser extent asthma and rhinitis; these benefits are usually limited to at-risk populations. Prevention strategies need to be tested using randomized controlled study designs that account for the numerous methodological challenges, safety concerns, and necessary ethical limitations.

Food Allergy Therapy: Is a Cure Within Reach?

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Anna Nowak-Wegrzyn and Antonella Muraro

There is an unmet medical need for an effective food allergy therapy; thus, development of therapeutic interventions for food allergy is a top research priority. The food allergen-nonspecific therapies for food-induced anaphylaxis include monoclonal anti-IgE antibodies and Chinese herbs. The food allergen-specific therapies include oral, sublingual, and epicutaneous immunotherapy with native food allergens and mutated recombinant proteins. Diet containing heated milk and egg may represent an alternative approach to oral immunomodulation. Oral food immunotherapy remains an investigational treatment to be further studied before advancing into clinical practice.