

Food Allergy: More Than Peanut



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The term “food allergy” covers a wide variety of clinical conditions that all involve a breakdown of clinical and immunologic tolerance against ingested foods. Food allergies can manifest as a wide variety of clinical conditions, including both IgE-mediated and non-IgE-mediated conditions.¹ Not all food allergies have received equal attention. Peanut allergy is perhaps the best studied. The large investment in research into peanut allergy over the past 10 years resulted in substantial progress in understanding its epidemiology and developing diagnostic, prevention, and treatment strategies, as reviewed in the theme issue of the *Journal of Allergy and Clinical Immunology: In Practice* in February 2019.

This theme issue of the *Journal of Allergy and Clinical Immunology: In Practice* moves beyond peanut allergy to highlight progress in understanding other food allergies, from food protein-induced enterocolitis syndrome (FPIES) in infancy to seafood allergy and alpha-gal syndrome, which have their greatest burden in adulthood. Clinical challenges in the diagnosis and management of these conditions are discussed in detail. This issue also highlights the importance of shared decision making in food allergy management as well as recent advances in food allergy prevention.

FPIES, a non-IgE-mediated food allergy estimated to affect 0.5% of infants in the United States, can be challenging to diagnose. There are currently no biomarkers of FPIES, with diagnosis relying on the recognition of symptoms after food ingestion, which can be complicated by delayed onset of symptoms (within 1-4 hours of ingestion) as well as the range of food triggers involved. Although often presenting in infancy with symptoms of repetitive, projectile emesis associated with lethargy, hypotonia, pallor, and/or hypothermia, the onset of FPIES in older age groups is increasingly being recognized, with fish and

shellfish being common triggers in adults. The first international consensus guidelines for FPIES published in 2017 helped to standardize the diagnosis of acute FPIES using a system of major and minor criteria for research and clinical practice; however, no such guidelines exist for chronic FPIES. Nowak-Węgrzyn et al² discuss current concepts in the epidemiology, pathophysiology, diagnosis, and management of FPIES. The authors also identify key unmet needs that must be addressed to improve patient care, including better understanding of the pathophysiology, development of diagnostic biomarkers, improved understanding of the natural history and long-term consequences of FPIES in children and adults, and development of therapeutic strategies to accelerate resolution.

Managing fish and shellfish allergy also presents clinical challenges. Davis et al³ review recent progress in improving the diagnosis and management of seafood allergy. Research into clinical cross-reactivity between fish, crustaceans, and mollusks has highlighted the importance of identifying the specific allergies involved. Some patients are allergic only to fish, and others to crustaceans but not mollusks, and even patients with fish allergy may tolerate certain fish types on food challenge despite sensitization to multiple fish extracts. Oral food challenges remain a mainstay for diagnosis and for avoiding unnecessary dietary restrictions due to the limitations of currently available tests. For example, several commercial skin prick test preparations for fish lack some of the critical fish allergens, resulting in false-negative results for some patients. Component-resolved diagnostics shows promise for improving diagnosis of seafood allergy, with IgE measurements to the major shrimp allergen tropomyosin producing superior positive predictive values for shrimp allergy compared with testing to whole shrimp protein. However, these tests are not yet commercially available. Other clinical challenges include distinguishing allergy from adverse reactions generated by contamination with toxins or parasites. Avoidance of seafood can be difficult due to cross-contamination, and there is a risk of reaction, including anaphylaxis to small doses of aerosolized allergens created during cooking.

Alpha-gal syndrome is an unusual food allergy first described around 10 years ago and now well recognized on many continents. Cases have been reported in the United States, Australia, Europe (including Sweden, France, Italy, Spain, and Germany), Asia (Japan and South Korea), South Africa, and Central and South America. Onset typically occurs in adulthood, and patients develop reactions generally 2 to 6 hours after consumption of meat of mammalian origin, ranging from localized hives or angioedema to severe anaphylaxis requiring hospital admission. More rarely, cases have also been reported in children, and reactions have been reported within 2 hours of consumption. Diagnosis of alpha-gal syndrome requires a blood test for IgE to alpha-gal because skin prick testing is unreliable. Important

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sources of sensitization leading to alpha-gal syndrome are tick bites, because the saliva of several tick species contains the alpha-gal oligosaccharide. Platts-Mills et al⁴ review current knowledge relating to the nature of the syndrome as well as strategies for diagnosis and management. The review also highlights challenges in management, including the presence of alpha-gal in a range of mammalian-derived foods and medical products. There are early reports of a potential association between IgE to alpha-gal and coronary artery disease, which requires further research. It is currently unclear whether consumption of alpha-gal-containing products can contribute to inflammation in sensitized individuals who may not develop allergic symptoms on the consumption of these products.

It is now widely accepted that prompt peanut introduction into the diet of high-risk infants can reduce the risk of peanut allergy. However, this prevention is allergen-specific, with no evidence of an associated reduction in any other food allergies. Because most food allergies are caused by triggers other than peanut, recent research has focused on developing and evaluating additional prevention strategies. Perkin et al⁵ review recent progress in food allergy prevention, including early introduction of foods other than peanut and studies aiming to improve the skin barrier to prevent early food sensitization and subsequent allergy through the intensive treatment of eczema. Strategies to address the role of the microbiome, dietary components, and other modifiable risk factors are also discussed. This review highlights the evidence relating to maternal consumption of allergenic foods, microbial exposure, pet exposure, and vitamin D supplementation. Implementation of the early food introduction to foods other than peanut with dosing similar to the Learning Early About Peanut allergy study can be challenging. Controversial issues are reviewed concerning the timing of introduction, and the amount, type, and preparation of allergenic foods optimal for induction of tolerance. Because the studies are heterogeneous and the acceptance of strategies to prevent food allergy has had varied uptake, clinicians will be on the front line of the impact of the new introduction guidelines on infant feeding behavior and food allergy outcomes.

Several treatment options for food allergy are currently in the late stages of development, providing for the first time the prospect of real choice for patients in how they manage their food allergy. Each treatment has specific risks and benefits, and patients and

clinicians will need to balance the importance of efficacy versus safety as well as a range of other attributes, including the convenience of the dosing regimen and associated activity restrictions, duration of the therapy, costs, and other factors. The decision on which is the “best” treatment will depend on the values and personal preferences of the patient. Anagnostou et al⁶ highlight the importance of a shared decision-making approach in food allergy and provide a practical approach for clinicians to apply this approach across different areas of food allergy management. Shared decision making in food allergy will often involve both parents and their children. Involving children in decisions where possible should be encouraged to prepare them for the transition to adulthood. This is likely to be critical for compliance with treatment as patients move into the teenage years.

With the burden of disease and public interest in food allergies, patients will continue to ask clinicians about the methods to diagnose, prevent, and treat this disease. This is an unprecedented time in the field of food allergy, and future food consumption will be shaped by new insights obtained during the next decade. Although tremendous advances have been achieved in our knowledge of food allergy and treatment of peanut allergy specifically, many questions remain. More research is needed. This themed issue on food allergies other than peanut is a helpful review for the most up-to-date information. FPIES, alpha-gal, seafood allergy, food allergy prevention, and shared decision-making tools are all comprehensively examined for the practitioner. These reviews are a great resource to help navigate the ever-changing landscape of food allergies beyond peanut.

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