Introduction to Special Issue on Food Allergy

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Received: 3 August 2012 / Accepted: 17 August 2012 / Published online: 4 September 2012
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This special issue of *Seminars in Immunopathology* reviews recent progress in our understanding of food allergy. Food-sensitive enteropathies can be defined as reproducible clinical response(s) to a given food (or foods) that are governed by an aberrant (typically Th2-mediated) immune response. Pathological responses to innocuous food antigens can be both IgE- and non-IgE-mediated. This volume will focus primarily on the IgE-mediated anaphylactic reactions to food that are a growing public health concern in westernized countries [1]. Food allergies are increasingly common, especially in children. In the USA three million children (four out of every 100) were reported to have an allergic response to food in 2007, an increase of almost 20 % in just 10 years [2]. Similar trends have been reported in the UK [3] and in Australia [4]. Several reports indicate that, in the USA, allergic responses to food are the most frequent cause of anaphylactic reactions evaluated in the emergency room [5, 6].

For reasons that are not yet clear, 90 % of hypersensitivity reactions are attributable to only eight major types of food: milk, eggs, shellfish (particularly crustaceans), peanuts, soybeans, tree nuts, and wheat. Allergic responses to milk, soybeans, eggs, and wheat are typically transient and restricted to childhood; while peanuts, tree nuts, and shellfish are more likely to induce life-long anaphylactic hyperreactivity. In the first article in this issue, Ruiter and Shreffler discuss the molecular basis for allergenicity. Helminths and allergens uniquely induce Th2-biased immune responses. The authors review the literature on innate Th2 immune activation to glean novel insights into the immunogenic properties of food

allergens. The allergic effector response is mediated by IgE, most commonly considered in the context of the mast cell cross-linking and degranulation induced by binding to its high-affinity receptor FcεR1. However, as discussed by Berin, each of the three isotypes of immunoglobulin present at mucosal surfaces play a particular role in promoting tolerance or immunity to foods by facilitating antigen uptake. IgA, the dominant isotype, is secreted into the lumen and acts to prevent allergen from crossing the epithelial barrier. Antigen-specific IgA levels inversely correlate with clinical reactivity to food and aeroallergens. Conversely, IgG contributes to non-responsiveness to dietary antigen by facilitating antigen sampling. The neonatal Fc receptor transports antigen: IgG complexes from breast milk to induce tolerance to potential allergens early in life. By contrast, IgE-facilitated antigen delivery via CD23 contributes to clinical reactivity by delivering antigen:IgE complexes to allergic effector cells [7].

Food allergic patients do not present with a consistent set of complaints. Symptoms can range from transient urticaria or extend beyond the skin and gastrointestinal tract to the respiratory and cardiovascular collapse characteristic of a systemic anaphylactic response. Only some foods seem to trigger anaphylaxis; peanuts and tree nuts most commonly induce severe reactions, but there is currently no way to predict what kind of response will occur. A better understanding of allergic effector pathways may be helpful in predicting disease severity. Based on both murine model data and corroborative human studies, Hogan et al. suggest that intestinal mast cells play an important role in controlling the severity of food-induced anaphylaxis [8]. Two possible scenarios are presented: intestinal mast cells may lead to increased intestinal permeability and systemic antigen absorption, enabling systemic mast cell activation and potentiation of respiratory and cardiovascular collapse. Alternatively, in the presence of high intestinal mast cell numbers, mediators released in response to mast cell degranulation in the intestine may gain access to the systemic circulation and stimulate respiratory and cardiovascular collapse directly.

This article is published as part of the Special Issue on Food Allergy [34:5].

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Although genetic variants have been identified, allergic responses to food are governed by a poorly understood interplay between genetic, environmental, and epigenetic interactions [9]. Hong and Wang review current knowledge and examine whether epigenetic influences may provide a mechanistic link between the environmental exposures that have been associated with disease and susceptibility to food allergy. It has been more than 20 years since the “hygiene hypothesis” first suggested a relationship between the increasing prevalence of allergy and asthma and reduced exposure to infectious disease brought about by compulsory vaccination and improvements in sanitation [10]. Feehley et al. review the clinical and experimental evidence in support of a role for microbial stimulation in the regulation of allergic disease from its initial focus on pathogens to current insights into the role of the commensal microbiota. The authors propose that environmental stimuli that disturb naturally selected host–microbe interactions are altering the composition of the microbiota and driving the increasing prevalence of food allergy and other allergic diseases.

No treatment other than strict avoidance is currently available, making allergic responses to food particularly problematic in school and childcare settings. Hope may, however, be on the horizon. Rachid and Umetsu discuss the immunological mechanisms underlying the development of protocols to induce antigen-specific tolerance to dietary allergens to prevent or treat allergic responses to food. These include suppression of mast cell and basophil function, the generation of allergen-specific “blocking” IgG4 antibodies and the down-regulation of allergen-specific T and B cell effector responses. Henson and Burks review additional promising therapeutic strategies currently being explored for the treatment of food allergy. The addition of anti-IgE monoclonal antibodies to immunotherapy regimens, modified recombinant food protein vaccines, and the use of monoclonal antibodies to IL5 are among the approaches discussed.

During the last decade, a new group of food-related diseases, the eosinophilic gastrointestinal diseases (EGIDs) have emerged. The EGIDs are characterized by gastrointestinal symptoms that occur in the setting of dense eosinophilia in the gastrointestinal mucosa; eosinophilic esophagitis (EoE) is the most common of the EGIDs [11]. Although not a classical manifestation of food allergy, EoE has gained increasing attention as a food-related disease, particularly in children [12]. In the last article of this volume, Aceves et al. review the

EGIDs with a particular focus on EoE. The authors examine the clinical and histological features that define EoE and distinguish it from gastroesophageal reflux disease. Current insight into the pathogenesis of EoE, its management, and treatment are discussed.

Much remains to be discovered about the etiology, treatment, and prevention of food allergy. We hope the articles in this volume provide a comprehensive overview of our current understanding. I am grateful to have had the opportunity to serve as guest editor of this special issue and would like to conclude by thanking all of the authors for their outstanding contributions.

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