Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2010

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This review highlights some of the research advances in anaphylaxis; hypersensitivity reactions to foods, drugs, and insects; and allergic skin disease that were reported in the *Journal* in 2010. Key epidemiologic observations include an apparent increase in peanut allergy, with more than 1% of children affected, and increasing evidence that early food allergen exposure, rather than avoidance, might improve allergy outcomes. Advances in food allergy diagnosis include improved insights into prognosis and estimation of severity through component-resolved diagnostics and characterization of IgE binding to specific epitopes. Regarding treatment, oral and epicutaneous immunotherapy show promise. Studies of drug allergies show insights into pathophysiology, and studies on insect hypersensitivity reveal improved diagnostic methods. Genetic and functional studies have revealed the important role of epidermal differentiation products in the pathogenesis of atopic dermatitis. Cross-talk between the atopic immune response with the innate immune response have also been found to predispose to infection in patients with atopic dermatitis. New therapeutic approaches to control chronic urticaria have also been identified during the past year. (J Allergy Clin Immunol 2011;127:326-35.)

Key words: *Dermatology, skin disease, urticaria, atopic dermatitis, anaphylaxis, allergy, hypersensitivity disorders, food, drug, insect venom*

This review highlights key advances in allergic skin disease, anaphylaxis, and hypersensitivity to foods, drugs, and insect venom selected primarily from more than 100 articles on these topics published in the *Journal of Allergy and Clinical Immunology* in 2010. Some of the key advances are summarized in Table I.

Abbreviations used

AD:	Atopic dermatitis
ADEH−:	Atopic dermatitis without a history of eczema herpeticum
ADEH+:	Atopic dermatitis with a history of eczema herpeticum
EH:	Eczema herpeticum
EoE:	Eosinophilic esophagitis
FACU:	Familial atypical cold urticaria
FLG:	Filaggrin
NIAID:	National Institute of Allergy and Infectious Diseases
NMF:	Natural moisturizing factor
OR:	Odds ratio
PPAR:	Peroxisome proliferator-activated receptor
TCI:	Topical calcineurin inhibitor
TCS:	Topical corticosteroid
TSLP:	Thymic stromal lymphopoietin
WTVZV:	Wild-type varicella zoster virus

FOOD ALLERGY

A milestone publication toward improving care of patients with food allergies is the National Institute of Allergy and Infectious Diseases (NIAID)–sponsored "Guidelines for the diagnosis and management of food allergy in the United States."[1,2] The guidelines were based on a comprehensive independent literature review with evidence grading, which was used by an expert panel. The expert panel received guidance from a coordinating committee of diverse stakeholders and from public comment to provide evidence-based advice and summaries of findings in the areas of epidemiology, natural course, diagnosis, prevention, and treatment. The guidelines are designed not only for allergists/immunologists but also for researchers and practitioners in the areas of pediatrics, family medicine, internal medicine, dermatology, gastroenterology, emergency medicine, pulmonary and critical care medicine, and others. The NIAID is also maintaining a Web site with supporting information (http://www.niaid.nih.gov/topics/foodallergy/clinical/Pages/default.aspx). Also of note is a similarly comprehensive guideline focusing on milk allergy developed in a similar fashion through the World Allergy Organization[3] and a comprehensive general review of food allergy.[4] Collectively, these should provide tremendous guidance for improved diagnosis and management.

Epidemiology and risk factors

Three studies used population-based surveys to estimate the prevalence of common food allergies.[5-7] In separate studies in the United States[5] and Canada,[6] random calling methodologies showed overall rates of self-reported allergies as follows: peanut,

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TABLE I. Summary of selected key advances reported in the *Journal* in 2010

Topic	Clinical or basic research concerns	Advances and observations
Food allergy	Epidemiology	• Childhood peanut allergy appears to have increased and exceeds a prevalence of 1%. • Delayed introductions of milk and egg are associated with increased risk of atopic outcomes. • Maternal ingestion of peanut during pregnancy was associated with increased risk of infant peanut sensitization among a cohort of atopic infants.
	Pathophysiology	• Allergen-induced *IL4* expression was related to milk allergy in the absence of *GATA3* expression.
	Diagnostic testing	• Binding to Ara h 2 provided the best peanut allergy diagnostic discrimination in a population-based cohort. • Studies of epitope binding provide insights on the prognosis, severity, and phenotypic expression of milk allergy.
	Treatment/management	• Oral immunotherapy shows promise for the treatment of peanut allergy. • A preliminary study of epicutaneous immunotherapy with milk protein shows a trend toward efficacy.
Anaphylaxis	Epidemiology	• A database of >1 million person-years shows increased risk for anaphylaxis among persons with asthma, particularly severe asthma.
Insect venom hypersensitivity	Diagnosis/treatment	• Use of nonglycosylated recombinant allergens for testing improves diagnostic accuracy. • Risks of side effects during vespid venom immunotherapy are related to baseline tryptase levels. • Gene expression profiling differentiated those having effective from ineffective immunotherapy.
Drug allergy	Pathophysiology and treatment	• Identification of plasmacytoid dendritic cells plays a role in drug reactions with eosinophilia and systemic symptoms. • Among those with serious reactions to cephalosporins, 25% had positive results to penicillin.
AD	Mechanisms and treatment	• *FLG* breakdown products are antimicrobial. • Aside from defects in *FLG* expression, broad defects of epidermal cornification exist. • Reduced IL-17 production distinguishes hyper-IgE syndrome from AD. • Patients prone to eczema herpeticum are highly atopic and have *FLG* mutations and *TSLP* polymorphisms. • Barrier proteins can be increased with topical anti-inflammatory therapy.
Urticaria and angioedema	Diagnosis and treatment	• Identification of FACU as a new form of cold urticaria • Use of high-dose antihistamine and anti-IgE for treatment-refractory cases

0.8% in the United States and 1.0% in Canada; tree nut, 0.6% in the United States and 1.2% in Canada; and sesame, 0.1% for both. The Canadian study[6] applied various algorithms to determine "probable" allergy, and Slightly lower rates were calculated. They also considered a category of "confirmed" allergies, rates of which were much lower, but were also difficult to determine accurately because of unavailable data that were required for this category. The US study[5] presented the opportunity to compare survey results over time because the study had been administered in a similar fashion in 1997, 2002, and 2008. The rates of surrogate-reported allergy in children increased significantly for tree nuts (0.6% to 1.2% and finally 2.1%) and peanut (0.4%, 0.8%, and finally 1.4%). Limitations of the studies included decreasing participation rates and self-assessment of allergy.

A study in Singapore and the Philippines[7] used a similar questionnaire and focused on 4- to 6- and 14- to 16-year-old children. Interestingly, the rates of peanut and tree nut allergy among local inhabitants were on the order of 0.5% and 0.3%, respectively (eg, lower than the US and Canadian estimates). However, the rates among expatriates in Singapore were on the order of 1.2% for each food, which was similar to what was seen in the US and Canadian studies. The Canadian and Asian studies evaluated additional foods. Interestingly, shellfish allergy in children was reported on the order of 0.5% in Canadians, 0.7% in expatriates, and 4% in the children native to Singapore and the Philippines.

In another epidemiologic study, Liu et al[8] took advantage of the serologic testing performed during the National Health and Nutrition Examination Survey in the United States in 2005-2006. Estimations of clinical food allergy risk were based on prior studies correlating clinical outcomes to food-specific IgE concentrations. The rates of clinical food allergy varied by food type and age group and overall showed the following: milk, 0.4%; egg, 0.2%; peanut, 1.3%; and shrimp, 1%. In the children aged 1 to 5 years, clinical allergy to milk, egg, and peanut was estimated at 1.8% each. Although the rates of estimated peanut allergy in these various studies appear spectacularly high, a United Kingdom birth cohort study that included testing and oral food challenges also arrived at a rate nearing 2%.[9] Evidence for increases in food allergy rates are also possibly reflected in greater numbers of emergency department visits for food-induced anaphylaxis.[10]

Adding to the concern of increasing prevalence, there continues to be evidence that food allergies are more persistent than previously appreciated. Savage et al[11] reported in a referral practice that soy allergy resolved in 25% by age 4 years, 45% by age 6 years, and only 69% by age 10 years.