Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2012

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This review highlights some of the research advances in anaphylaxis; hypersensitivity reactions to foods, drugs, and insects; and allergic skin diseases that were reported in the *Journal* in 2012. Studies support an increase in peanut allergy prevalence in children and exposure to the antibacterial agent triclosan and having filaggrin *(FLG)* loss-of-function mutations as risk factors for food sensitization. The role of specific foods in causing eosinophilic esophagitis is elucidated by several studies, and microRNA analysis is identified as a possible noninvasive disease biomarker. Studies on food allergy diagnosis emphasize the utility of component testing and the possibility of improved diagnosis through stepped approaches, epitope-binding analysis, and bioinformatics. Treatment studies of food allergy show promise for oral immunotherapy, but tolerance induction remains elusive, and additional therapies are under study. Studies on anaphylaxis suggest an important role for platelet-activating factor and its relationship to the need for prompt treatment with epinephrine. Insights on the pathophysiology and diagnosis of non–IgE-mediated drug allergy are offered, with novel data regarding the interaction of drugs with HLA molecules. Numerous studies support influenza vaccination of persons with egg allergy using modest precautions. Evidence continues to mount that there is cross-talk between skin barrier defects and immune responses in patients with atopic dermatitis. Augmentation of the skin barrier with reduction in skin inflammatory responses will likely lead to the most effective intervention in patients with this common skin disease. (J Allergy Clin Immunol 2013;131:55-66.)

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

Abbreviations used

AD:	Atopic dermatitis
α-Gal:	Galactose-α-1,3-galactose
APT:	Atopy patch test
EoE:	Eosinophilic esophagitis
FAAN:	Food Allergy & Anaphylaxis Network
FLG:	Filaggrin gene
miRNA:	MicroRNA
NIAID:	National Institute of Allergy and Infectious Diseases
OFC:	Oral food challenge
OIT:	Oral immunotherapy
OR:	Odds ratio
PAF:	Platelet-activating factor
SLIT:	Sublingual immunotherapy
SPT:	Skin prick test
TNP:	Trinitrophenyl

This review highlights key advances in allergic skin disease, anaphylaxis, and hypersensitivity to foods, drugs, and insect venom selected primarily from articles published in the *Journal of Allergy and Clinical Immunology* in 2012. Some of the key advances are summarized in Tables I to III, providing additional insights on these topics since our last review.[1]

FOOD ALLERGY

Epidemiology, risk factors, and prevention

Food allergy is a worldwide problem, with evidence of increasing prevalence in many countries,[2] but there are few population-based studies that have estimated allergy to any food rather than to specific ones. Soller et al[3] examined the results of a random telephone survey that included data for 9667 subjects from 10 Canadian provinces to estimate the prevalence of food allergy to any food. There are many caveats for studies providing prevalence estimates of food allergy,[4] including the possibility that a high number of self-reports of food allergy are not physician diagnosed,[5] and the main limitation in the study by Soller et al[3] was a reliance on self-reporting. Overall, they found that 8.07% (95% CI, 7.47% to 8.67%) of subjects reported at least 1 food allergy. When they excluded adults reporting unlikely allergies (eg, isolated reactions to milk, wheat, soy, or egg) and adjusted for nonresponders using imputation, the final estimate was 6.69% (95% CI, 6.15% to 7.24%) in the overall population, with 7.14% of children and 6.56% of adults reporting allergy. Milk (2.23%), peanut (1.77%), and tree nuts (1.73%) were the most common allergens in children, and shellfish (1.91%), fruits (1.61%), and vegetables (1.29%) were the most common allergens in adults. The authors point out that these high rates are similar to estimates from other sources.

Whether there has been an increase in food allergy prevalence remains uncertain,[6] but studies using consistent methods over

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TABLE I. Key advances in food allergy in 2012

Clinical or basic research concerns	Advances and observations
Epidemiology/risk factors/prevention	• A Canadian study reported that 8% of the population reports at last 1 food allergy. • A population-based medical records review in Minnesota showed a 3-fold increase in childhood peanut allergy from 1999-2007. • Data from the National Health and Nutrition Examination Survey support exposure to the antibacterial agent triclosan as a risk factor for food sensitization in male subjects. • *FLG* gene loss-of-function mutations were associated with food sensitization but not clinical allergy. • A maternal pregnancy diets including peanut was protective for asthma outcomes.
Gastrointestinal allergy	• miRNA analysis of EoE suggests a means to diagnose and monitor disease activity, including a noninvasive biomarker. • Several studies characterize the role of diet in management of EoE, including the utility of allergy testing. • Food protein–induced enterocolitis syndrome is described outside the pediatric age group.
Molecular aspects/ pathophysiology	• Murine models suggest that mast cells do not impair tolerance induction and that immunotherapies inducing IgG responses might protect against systemic and localized reactions, and identified Pim1 kinase as a potential target for therapy. • Gelatin allergy might be related to delayed-onset mammalian meat allergy by reactivity to α-Gal.
Diagnostic testing	• Multiple studies provide diagnostic insights on predicting reactivity to products containing baked egg or milk. • Evaluation of SPT, peanut IgE, and Ara h 2 results for peanut allergy diagnosis in young children suggested a 2-step approach with SPTs followed by Ara h 2 testing would be most likely to reduce the number of diagnostic OFCs needed. • Patients with isolated reactivity to Ara h 8 are unlikely to react to roasted peanut. • Epitope analysis with peanut using a bioinformatics approach shows high diagnostic accuracy.
Treatment/management	• A study of milk SLIT and OIT shows a more robust response to OIT but with comparatively more side effects; loss of protection was common after cessation of daily dosing. • Salivary peanut-specific IgA levels might be a biomarker for response to peanut SLIT. • Children able to tolerate egg in baked foods and ingesting such products regularly were almost 15 times more likely to have tolerance to whole egg products compared with control subjects. • Pepsin-digested cashew proteins showed promise as an immunotherapeutic approach based on a murine model. • A randomized trial of Lactobacillus GG for children with milk allergy suggested efficacy for enhancing resolution of the allergy.

TABLE II. Key advances in anaphylaxis, insect venom, and drug allergy in 2012

Topic	Clinical or basic research concerns	Advances and observations
Anaphylaxis	Epidemiology, risk, pathophysiology and management	• The NIAID/FAAN anaphylaxis criteria performed well in a validation study. • Data from an inner-city pediatric emergency department suggests inadequate use of epinephrine with patients on Medicaid and an increased risk of not having prehospital treatment. • Having increased PAF levels correlated with severity of anaphylaxis, but this was not the case for histamine or tryptase. • An *in vitro* system suggested earlier treatment with epinephrine was more likely to disrupt the PAF pathway.
Insect venom hypersensitivity	Risk, diagnosis, and treatment	• Risk factors for severe reactions included increased baseline tryptase levels, prompt symptoms after a sting, absence of urticaria/angioedema, and senior age. • A basophil activation test and component-resolved diagnostics might elucidate the clinical ramifications of double positivity to bee and wasp venom caused by cross-reactive carbohydrate determinants. • A study compared ultrarush and semirush initiation of jack jumper ant immunotherapy, revealing more reactions and more severe reactions with the faster approach.
Drug allergy	Pathophysiology, diagnosis, and management	• An extensive study of nonimmediate cephalosporin allergy suggests intradermal testing with the culprit agent might be effective. • The HLA risk factor for Stevens-Johnson syndrome was elucidated, finding direct interaction of drug with HLA to activate T cells. • Numerous studies and practice parameters support influenza vaccination of persons with egg allergy using modest precautions.

time are most informative. Rinaldi et al[7] took advantage of the data available in the Rochester Epidemiology Project, a population-based medical records linkage system in Olmsted County, Minnesota, and sought records coded for diagnoses possibly related to peanut allergy among children. They applied clinical and laboratory criteria to determine cases of peanut allergy over a period from 1999 to 2007 and noted a statistically significant 3-fold increase in diagnoses of peanut allergy in children over that time period, with a final prevalence rate of 0.65% in 2007.

TABLE III. Key advances in allergic skin diseases in 2012

Topic	Clinical or basic research concerns	Advances and observations
AD	Mechanisms	• Filaggrin deficiency enhances percutaneous allergen penetration and IL-1 responses. • Polarized T_H2 and T_H22 immune responses play a critical role in driving AD skin inflammation.
	Treatment	• Early-life exposure, including probiotics, might play a key role in prevention of AD. • Phototherapy reduces systemic immune activation and increases serum vitamin D levels.
Chronic urticaria	Pathophysiology and treatment	• Early diagnosis of hereditary angioedema might reduce fatal laryngeal attacks. • Complement activation by the complement controller domain of thyroperoxidase might contribute to chronic urticaria in patients with thyroid autoimmunity.

The risk factors for food allergy can include heredity, route and timing of exposure to food allergens, skin barrier defects, vitamin D sufficiency, dietary fat, antioxidants, obesity, exposure to infection, and other factors.[6] Keet et al[8] used data from the National Health and Nutrition Examination Survey 2005-2006 to investigate how sensitization to foods in those younger than 21 years related to being born in or outside of the United States and the age of immigration. They found that US-born children were at greater risk (odds ratio [OR] 2.05; 95% CI, 1.5-2.8; $P <$ .001), and among those born outside the United States, arriving before age 2 years was a risk factor (OR, 2.68; 95% CI, 1.2-6.1; $P <$ .02); however, among children born in the United States, children of immigrants were at higher risk. These findings suggest a relative environmental risk factor for US residents but also suggest that there might be complex interactions of genetics and environment putting immigrant children at greater risk. The hygiene hypothesis is a proposed explanation for increasing allergy prevalence. The same researchers[9] used the National Health and Nutrition Examination Survey database to evaluate rates of food sensitization against urinary levels of endocrine-disrupting compounds, considering those with and without antimicrobial properties. Only the compound triclosan, which has an antimicrobial effect, was associated with an increased risk of food sensitization (among male subjects), perhaps reflecting an additional risk factor within an already higher-risk group. An Australian study[10] generated additional support for the vitamin D hypothesis by showing a latitude gradient for IgE-mediated egg and peanut allergy, with higher rates in regions farther from the equator with less ambient UV radiation. Another Australian study[11] sought to address the hypothesis that skin barrier defects associated with eczema might also be a risk for food allergy because of an increased chance of sensitization by allergens permeating the skin, bypassing oral tolerance. Filaggrin gene (*FLG*) loss-of-function mutations were determined in a subset (n = 700) from a large cohort extensively tested for sensitization and for clinical food allergy. After adjusting for eczema, *FLG* mutations were associated with food sensitization (OR 3.0; 95% CI, 1.0-8.7; $P = .043$). This result supports the hypothesis of a barrier defect being a risk for sensitization, but after adjustment for risk of clinical food allergy among those sensitized, there was no further influence of *FLG* mutations, suggesting this mutation is not playing a role in progression of sensitization to clinical allergy. Although these various studies add pieces to the risk factor puzzle, it is clear that multiple and likely interacting genetic and environmental factors affect risk, and more studies are needed to unravel the relative effect of these factors.

Reducing allergy risk by dietary and other means is a logical response to the apparent increase in food allergy and atopic disease.[6] The influence of maternal pregnancy diets was addressed by examining a large (n = 61,980) Danish birth cohort database.[12] Although food allergy was not investigated, children of mothers with frequent intake of peanut during pregnancy, as compared with those without, were less likely (OR, 0.66; 95% CI, 0.44-0.98) to have children with asthma at 18 months of age, with a similar finding for tree nut consumption. Whether this reflects a generally "healthier" diet or is a study result affected by reverse causation remains to be determined in controlled studies.

Probiotics might present an active means to combat potential adversities attributed to increased hygiene. Jensen et al[13] presented a 5-year follow-up on a randomized postnatal study of 6 months of treatment with *Lactobacillus acidophilus*, with results that continued to show no protective effect for any physician-diagnosed allergic disease, but earlier findings of increased risk for sensitization in treated children were no longer cumulatively significant. Additional long-term studies of different types of probiotics and varying treatment regimens are needed.

Gastrointestinal food allergy

Better treatments for eosinophilic esophagitis (EoE), which might be currently underdiagnosed because of indistinct symptoms and patchy inflammation that might be missed on biopsy, are sorely needed.[14,15] Identification of an accurate and noninvasive biomarker would be a significant advance for diagnosis and management. Lu et al[16] profiled the expression of microRNAs (miRNAs), regulators of mRNA expression and translation, in esophageal biopsy specimens of patients with and without EoE and with glucocorticoid-treated disease and also in plasma. Differentially expressed miRNAs were identified and were largely reversible in patients undergoing successful treatment. They identified 21 upregulated and 11 downregulated miRNAs providing a signature that was distinct for active EoE, that corresponded with tissue eosinophilia, and that corresponded to or elucidated pathways involved in allergic inflammation. Importantly, a single miRNA was detected that marked disease remission and has implications for understanding the pathogenesis of disease remission and elucidating a possible role of epigenetic reprogramming. Three miRNAs were identified in the plasma that could potentially be used as biomarkers, which, if confirmed in further studies, would be a remarkable advance to reduce the need for endoscopy and biopsy to monitor this disease during various interventions.

The current primary treatments for EoE are diet or off-label use of inhaled steroids. Schroeder et al[17] presented a case series of 4

children who responded to swallowing inhaler-actuated ciclesonide meant for asthma treatment, which the authors argue might have advantages over fluticasone or budesonide, as used in prior reports, because of the low oral bioavailability and other characteristics of ciclesonide. However, diet is a mainstay of therapy. Unfortunately, data regarding identification of causal foods and diet efficacy are few, but several studies in the *Journal* provide important insights on dietary management.

Henderson et al[18] provided a retrospective report concerning their dietary approach with 98 children with EoE not treated with glucocorticoids, defining success as histologic remission. The success rate was 96% among 49 patients treated with an elemental diet, 81% for 26 patients on a 6-food elimination diet (2 variations were used, with avoidance of milk, egg, wheat, soy, peanuts, tree nuts, fish, and shellfish for all, and 15 avoided additional foods that were tested positive), and 65% for 23 patients whose diet was determined based on results of skin prick tests (SPTs), atopy patch tests (APTs), or both. After 116 single-food reintroductions, the negative predictive value of skin testing for remission was only 40% to 67%.

Spergel et al[19] reported slightly different results in a retrospective review of 941 patients of whom 319 had definitive food-responsive disease diagnosed by biopsy. Regarding testing, the negative predictive value for the combination of SPTs and APTs averaged 92%, with the exception of milk at 44%, and the positive predictive value averaged 44%. An empiric 6-food elimination diet or removal of positive foods on testing had a success rate of 53%, although test-directed diets resulted in an average of only 3 foods removed. Milk, egg, wheat, and soy were the most common culprits. Removal of foods identified on skin testing with empiric elimination of milk led to resolution in 77% of patients, milk alone had a 30% response, and milk, egg, wheat, soy, and meats had a 77% response rate.

Molina-Infante et al[20] prospectively treated 22 adults with EoE using SPTs (including raw foods) and APTs but found low efficacy (26%) of the approach, although it remains clear that adults and not just children have food-responsive EoE.[21] Overall, dietary approaches to EoE require a consideration of patient-specific preferences, but these new data provide important insights on the likely effectiveness of the many options.

Medical therapy of EoE, without the stress, social, and nutritional issues associated with food elimination, might be preferable for many patients, and therapies other than steroids are being sought. Spergel et al[22] reported a clinical trial of reslizumab, an antibody that neutralizes IL-5, in children and adolescents and found a significant reduction in esophageal eosinophil values on therapy (67% in subjects receiving 2 mg/kg vs 24% in placebo-treated subjects, $P < .0001$), although clinical outcomes based on symptom scores were not significant and were not associated with changes in eosinophilia. The safety profile was very good, and additional studies will be needed to further evaluate the treatment.

EoE is just one of a number of gastrointestinal food allergy–related disorders.[2] Food protein–induced enterocolitis syndrome is a non–IgE-mediated food allergy characterized by delayed severe vomiting and possible hypotension that typically is described to affect infants and young children.[23,24] Fernandes et al[25] describe a 53-year-old with this disorder triggered by scallops, expanding the age spectrum of this disorder. Food protein–induced enterocolitis is likely underrecognized in adults because symptoms could be attributed to "food poisoning" and allergy test results are characteristically negative. Food protein–induced proctocolitis is another non–IgE-mediated disorder of infants characterized by mucus and blood in stools often attributed to cow's milk. Ohtsuka et al[26] evaluated the transcriptome of mucosal biopsy specimens of affected infants and did not confirm an allergic signature, which is in line with some studies suggesting that symptoms can be from infection in some patients and dietary exclusion is not needed.

Pathophysiology

Elucidating the pathophysiology of food allergy is necessary for developing better diagnostic, treatment, and prevention strategies. Ruiter and Shreffler[27] reviewed the role of dendritic cells in food allergy, exploring evidence that food allergens can interact directly with dendritic cells or with cells with innate immune functions to induce T_H2 skewing. Three murine studies elucidated additional mechanisms.

Tunis et al[28] evaluated the role of mast cells in tolerance induction because prior studies have indicated their role in activating regulatory T cells and a role in peripheral tolerance. However, they found that oral tolerance was successfully induced to ovalbumin and peanut in control and mast cell–deficient mice, that regulatory T cell development was not mast cell dependent, and that histamine blockade and mast cell IgE activation did not impair tolerance induction.

Kucuk et al[29] sought to determine the mechanisms underlying and possibly distinguishing food-induced anaphylaxis compared with gastrointestinal reactions (diarrhea) using a murine model. Passive immunization with IgE anti-trinitrophenyl (anti-TNP) followed by ingestion of BSA-TNP caused systemic reactions but not diarrhea, whereas both systemic reactions and diarrhea were induced in mice presensitized with intraperitoneal ovalbumin plus oral ovalbumin. More BSA-TNP was needed to induce shock than diarrhea in presensitized mice, and treatment with IgG anti-TNP, which does not enter the gut, was protective of both outcomes. In these and additional experiments, the investigators showed that the allergen had to be absorbed to induce symptoms. The results suggest that immunotherapies that induce systemic IgG can suppress local and systemic food-induced allergic reactions.

Wang et al[30] embarked on a series of experiments to investigate the role of Pim1 kinase in patients with food allergy. They investigated this kinase because data suggest that $CD4^+$ T cells play an important role in food allergy and because Pim1 kinase, which regulates the transcription factor Runx, has been implicated in cytokine-dependent signaling and T-cell proliferation and was upregulated in murine models of lung allergen challenge. Among a series of experiments, the allergic inflammatory response to peanut was reversed with Pim1 kinase inhibition, and *in vitro* inhibition of Pim1 kinase attenuated T_H2 and T_H17 cell differentiation and expansion, suggesting this pathway might be a viable new target for therapy.

Additional studies have identified potential factors or mechanisms involved in causing sensitization and eliciting food-induced allergic reactions. The Mexico City Childhood Asthma Study (n = 492 with asthma) evaluated candidate genes associated with positive skin test results to at least 1 food through analysis of trios (162 trios included a sensitized asthmatic proband).[31] They found that signal transducer and activator of transcription 6 *(STAT6)* and low-density lipoprotein

receptor–related protein 1 *(LRP1)* polymorphisms were associated with food sensitization, but only the former has clear biologic correlates, with prior associations for food allergy, asthma, and EoE.

Regarding reaction severity, Menikou et al[32] followed up on an observation from a murine model showing peanut could activate complement and hypothesized that this might relate to reaction severity in human subjects. Therefore they evaluated genetic variations in complement activation in relation to peanut allergy severity. They studied 82 patients with peanut allergy, and although they confirmed past observations that asthma was a risk factor for more severe reactions, they could not identify an association with genetic variations in complement activation. The murine response might not generalize to human subjects.

Delayed anaphylaxis to meats has been attributed to IgE reactivity toward galactose-α-1,3-galactose (α-Gal), a novel observation that a carbohydrate determinant is responsible for a severe allergic reaction. Mullins et al[33] noted that some patients with meat allergy also reacted to bovine or porcine gelatin. They explored this association further and tested patients referred for suspected allergy to medications, venoms, foods, or idiopathic reactions. They found that 40 of 1335 subjects had positive gelatin test results and 30 of the 40 had a red meat allergy (among these were 12 with gelatin reactions). Two patients with reactions to gelatin colloid had positive test results to gelatin, and the remaining 8 positive test results were among patients with idiopathic anaphylaxis or drug-induced allergic reactions. They detected α-Gal in bovine gelatin colloids and also noted positive test results for IgE to this determinant in 20 of 24 with meat allergy and 20 of 22 with positive gelatin skin test results. These data clearly suggest that α-Gal might be a target of reactivity to meat-derived gelatin and that a subset of those with meat allergy might react. Another study suggested allergic reactions to a carbohydrate moiety. Some cow's milk formula has been supplemented with short-chain galacto-oligosaccharides as a prebiotic. Chiang et al[34] report 5 children who tolerate cow's milk protein but had anaphylaxis that was attributed (through challenge or testing) to this additive. Although tick bites have been hypothesized to be the sensitizing exposure for α-Gal reactivity, the sensitizing route for the children in this case series from Singapore is unknown.

Diagnosis

Studies to improve diagnosis include correlation of oral food challenge (OFC) outcomes to standard serum IgE results, testing of allergen components, epitope binding, basophil activation, and bioinformatics approaches.[2,35-42] Several studies focused on egg allergy,[38,43,44] particularly whether diagnostic testing could determine when extensively heated egg (baked into wheat-based foods) would be tolerated in subjects with egg allergy. Lieberman et al[44] reported the results of 100 OFCs to baked egg in children, with a 66% rate of tolerance. Serum IgE measurement to egg white (ImmunoCAP; Thermo Fisher Scientific, Portage, Mich) and SPTs were performed. The skin test wheal size was not informative for predicting outcomes, but an egg white–specific IgE level of 2.5 kU_A/L had a negative predictive value of 0.89, and a level of 10 kU_A/L had a positive predictive value of 0.60. The median level for those who reacted was 5.85 kU_A/L compared with 2.81 kU_A/L in those who were tolerant. Caubet et al[43] related outcomes of baked egg OFCs to levels of specific IgE and IgG_4 to ovomucoid and ovalbumin, establishing whether IgE/IgG_4 ratios were additionally informative. The rationale for this approach is that IgG_4 levels increase during successful immunotherapy. Indeed, baked egg–reactive children had higher ratios, and inclusion of IgG_4 levels in logistic regression models was more informative than IgE levels alone. It remains unclear whether the specific IgG_4 occurs from occult exposure or through another means because these children tested were ostensibly avoiding egg in any form.

Improved diagnosis of peanut allergy is a significant concern.[39] Dang et al[45] compared 5 strategies for diagnosing peanut allergy by evaluating test parameters in 200 Australian children with a median age of 14 months; the test population was derived from a population-based study (randomly selected from among those with peanut sensitization), and peanut allergy was proved by OFCs. They considered using high/low diagnostic values of peanut IgE of greater than 15 kU_A/L or less than 0.35 kU_A/L, SPT wheal responses of greater than 8 mm or less than 3 mm, or Ara h 2 levels of greater than 1.0 kU_A/L or less than 0.01 kU_A/L because prior studies suggested good diagnostic values at these decision points. Using peanut IgE alone would have resulted in 95 OFCs, using SPT responses alone would have resulted in 50 OFCs, and using Ara h 2 alone would have resulted in the need for 44 OFCs. However, a stepped approach of testing peanut IgE followed by Ara h 2 would have reduced the need for OFCs to 32, and SPTs followed by Ara h 2 measurement would have reduced the need for OFCs to only 21. Thus a stepped approach, which is similar to considering retesting after determination of a post-test probability, favored skin testing and then component testing for their population. Component testing to peanut is increasingly being studied. Presumably, many persons only sensitized to Ara h 8, a birch-related protein, can consume heated peanut. In evaluation of 144 Swedish children only sensitized to Ara h 8, all but one could tolerate peanut ingestion as reported from natural ingestion or during OFCs to roasted peanut.[46] The 1 patient who reacted was re-evaluated and showed an increase in peanut-specific IgE levels from 1.5 to 8.8 kU_A/L and detectable Ara h 6 (0.45 kU_A/L), which is a stable peanut allergen not included on some panels. Additional diagnostic value can be obtained from identification of IgE binding to specific "informative" epitopes on peanut proteins. Lin et al[47] used microarray immunoassays to map epitopes on the major peanut proteins and then used a bioinformatics approach to identify patterns that were most informative. This approach performed significantly better than standard methods.

The OFC remains the primary means to diagnose food allergy, and yet a survey answered by 670 members of the American Academy of Allergy, Asthma & Immunology revealed that barriers exist that impede their use of the test, including lack of time (55%), poor reimbursement (54%), risk (52%), lack of staff (44%), and lack of office space (27%).[48] Thus 70% of respondents performed 5 or fewer OFCs each month. This is unfortunate because quality of life is significantly affected, and this test can result in improving this heavy burden.[49-51] Additional insights into OFCs were reported from a study analyzing the outcomes of 1843 OFCs performed on children, showing that gastrointestinal symptoms were more likely with challenges to egg and peanut compared with milk, soy, or wheat and that respiratory symptoms were more likely from peanut compared with milk, egg, soy, or wheat.[52] Sometimes a patient having a negative double-blind, placebo-controlled or open OFC result is noted to react on subsequent ingestion of the food, raising the question of whether the gradual feeding is creating a brief desensitized state for some

patients[53]; the advice is to ensure an adequate test feeding and tolerance of a "meal-sized" portion and to encourage incorporation of the food into the diet. OFCs are also an important component of research studies, but attempts at standardized approaches have not been universally implemented. Koplin et al[54] presented their approach to standardized OFCs with a good safety record, and a consensus report toward standardizing double-blind, placebo-controlled OFCs was published as well.[55]

Treatment

Oral immunotherapy (OIT) and sublingual immunotherapy (SLIT) continue to be a significant focus of food allergy research. Issues that require further study include whether the therapy can induce tolerance that is independent of continued dosing and whether the therapy is safe (eg, acute reactions or chronic disease, such as EoE,[56] induced by treatment being too strong a risk) and whether there is a way to identify who might best benefit or has benefitted while receiving therapy.[57] Several studies have added to our knowledge on these topics. Keet et al[58] randomized children with milk allergy to receive SLIT alone (to a maintenance dose of 7 mg) or SLIT followed by OIT (at 2 maintenance doses of 1000 mg or 2000 mg). They underwent OFCs at 12 and 60 weeks of maintenance, and if they passed the 60-week "desensitization" OFC, they withdrew therapy for 1 and 6 weeks to test for tolerance off therapy. There were 30 subjects randomized to the 3 groups, and at the time of the 8-g milk food challenge, only 1 in the SLIT group, 6 in the lower-dose OIT group, and 8 in the higher-dose OIT groups passed, with the OIT groups doing significantly better ($P = .002$). Of the 15 who passed the challenge, 6 regained reactivity off therapy, 2 after only 1 week. Thus the results from OIT were more robust, but there were more reactions related to dosing in the OIT group, and tolerance was not achieved for many. There is interest in following biomarkers during OIT/SLIT both for monitoring and understanding mechanisms of tolerance. In this milk study skin test results decreased, basophil activation decreased, and milk-specific IgG_4 levels increased in all groups. The study was not powered to evaluate markers of success on an individual basis. Kulis et al[59] postulated that because OIT/SLIT is administered at mucosal surfaces, specific IgA responses can play a role in immune modulation. They tested 10 subjects undergoing a year of therapy with peanut SLIT and 7 receiving placebo for salivary and serum peanut-specific IgA. Salivary and serum peanut-specific IgA levels increased significantly only for those receiving SLIT, although some subjects showed little change. In fact, there was a correlation of salivary but not serum IgA responses to clinical outcomes, indicating its potential promise as a biomarker.

To further elucidate mechanisms of OIT, Leonard et al[60] established a mouse model of egg OIT. They were able to demonstrate desensitization but not tolerance (2 weeks off therapy) and were able to desensitize with extensively heated or native ovomucoid. The OIT induced serum specific IgE and IgA; suppressed IL-4, IL-13, and IFN-γ; and decreased intestinal barrier function, and the authors were unable to show systemic effector cell desensitization. Nonoral challenge of the treated mice showed little protection, indicating a more localized protective response, which the authors also partially characterized by showing changes in gastrointestinal gene expression. Notable in this study was the similar efficacy of extensively heated and raw egg protein for OIT. In a clinical study Leonard et al[61] presented follow-up on children with egg allergy who were successfully challenged to baked egg products and ate them routinely. These children were 14.6 times more likely than comparison control subjects ($P < .0001$) to have tolerance to unheated egg, suggesting a potentially easier form of egg OIT for those who can tolerate it in both the human and murine studies.

Additional modalities of treatment are being explored. Kulis et al[62] used pepsin-digested cashew proteins in a murine model of anaphylaxis to explore whether digestion of the proteins could present a less allergenic but appropriately immunogenic form of immunotherapy. The digested proteins were less able to trigger allergic reactions in the mice but were capable of sensitizing and desensitizing them, presenting the possibility of a simple vaccine approach (rather than creating specific peptides). In another therapeutic approach a randomized trial of Lactobacillus GG for children with milk allergy showed a greater chance of allergy resolution in the treated children at 12 months. Finally, insights on the use of omalizumab were reported in 2 articles[63,64] showing that the treatment resulted in an improved threshold of reactivity to ingest peanut, and yet 60% of the subjects' basophils showed no suppression or an increased response. Additional analysis of *in vitro* and clinical responses suggested that a poorer omalizumab response was associated with more basophil activation (thus the mast cell response is adequate, but the basophil response was contributing to poor clinical response). Increased basophil response was associated with high specific/total IgE ratios and increased intrinsic basophil responses to IgE-mediated stimulation, providing some insight into the varying response to treatment with "anti-IgE antibodies" noted in prior studies.

ANAPHYLAXIS

Anaphylaxis is a clinical diagnosis. Criteria that were proposed by an expert panel convened by the National Institute of Allergy and Infectious Diseases/Food Allergy & Anaphylaxis Network (NIAID/FAAN) were subjected to a validation study.[65] The design was a retrospective cohort study of emergency department patients using allergists' diagnosis as a reference standard. Of 214 patients, 86 (40.2%) met the NIAID/FAAN criteria for anaphylaxis. Allergists gave 61 (28.5%) patients a diagnosis of anaphylaxis, 59 (96.7%) of whom satisfied the anaphylaxis criteria. The expert panel criteria showed 96.7% sensitivity and 82.4% specificity, with a positive predictive value of 68.6% and negative predictive value of 98.4%, indicating usefulness in the emergency department setting.

These criteria are also used in research studies, such that as performed by Huang et al,[66] who evaluated triggers, treatments, and outcomes of anaphylaxis in an inner-city pediatric emergency department in New York City. They identified 213 anaphylactic reactions in 192 children (97 male patients; median age, 8 years). Using the NIAID/FAAN criteria resulted in more diagnoses than were given by the emergency department (ie, 151 reactions had not been coded as anaphylaxis). They found no time trends of anaphylaxis prevalence over the 5-year period analyzed. The triggers included foods (71%), "unidentified" (15%), drugs (9%), and "others" (5%). Epinephrine was administered in 169 (79%) reactions but in only 58 (27%) before arrival to the emergency department. Patients with Medicaid were less likely to receive prehospital epinephrine ($P < .001$), and hospitalization was less likely if epinephrine was administered before arrival in the emergency department. These studies suggest the need for more dissemination and application of the anaphylaxis criteria in practice and better education on prompt administration of epinephrine.

Platelet-activating factor (PAF) is known to be a potent mediator of anaphylaxis, and increased levels were shown to correlate with severity, unlike tryptase or histamine.[67] Vadas et al[67] sought to determine the potential role of treatment with epinephrine in patients with anaphylaxis, considering, in particular, whether timing of administration interacts with the action of PAF. They used human vascular smooth muscle cells and measured the effect of epinephrine on PAF-mediated prostaglandin E_2. They found that preincubation of smooth muscle cells with epinephrine before the addition of PAF suppressed prostaglandin E_2 release, whereas treatment with epinephrine after PAF stimulation at later time points was less effective. These results suggest that epinephrine plays a role in the PAF axis and that, if the *in vitro* model has clinical relevance, this might partly explain why prompt administration of epinephrine is more likely to suppress symptoms than delayed treatment.

The studies above indicate the importance of prompt injection of epinephrine in patients with anaphylaxis to maximize clinical benefits and avoid morbidity/mortality. Simons and Schatz[68] reviewed the approach to anaphylaxis in pregnancy and emphasized addressing diverse causes, confirming causes and ensuring allergen avoidance, positioning the mother on her left side during anaphylaxis to improve venous return to the heart, and confirming the importance of emergency management, including prompt administration of epinephrine for anaphylaxis. Proper dosing of epinephrine is another clinical concern. Rudders et al[69] approached the question of whether obesity is a risk factor for requiring more epinephrine doses, an issue that has been raised for autoinjectors because of fixed doses and possibly insufficient needle length resulting in subcutaneous rather than intramuscular administration. They evaluated outcomes for 321 emergency department patients treated for anaphylaxis and did not find an increased need for greater than 1 dose based on obesity. The topic of appropriate epinephrine self-injector prescribing among allergists was addressed in the context of doing so for patients undergoing allergen immunotherapy. Gupta et al[70] surveyed members of the American Academy of Allergy, Asthma & Immunology and found that among 299 who responded, there was a wide range of prescribing practices, from 13.5% who reported never prescribing to 33.3% who always did, suggesting the need for additional studies, education, and guidance on appropriate practice. Proper training requires the use of autoinjector trainers; Jacobsen et al[71] compared the force needed to activate trainers and live devices, as well as recoil forces, revealing some differences that might be worth noting when instructing patients with trainers. For example, for some devices, it might require more force to activate the trainer than the live device, and live devices generally cause more recoil.

HYPERSENSITIVITY TO STINGING INSECTS

Key research issues for stinging insect hypersensitivity include refined risk assessment, improved diagnosis, and effective therapy. Regarding risk assessment, Stoevesandt et al[72] identified risk factors for severe anaphylaxis in patients with Hymenoptera venom allergy by assessing multiple factors. They analyzed 657 patients for baseline tryptase level, age, sex, preexisting cardiopulmonary conditions, cardiovascular medication, insect type, localization of the sting, time interval to onset of symptoms, and presence of cutaneous involvement. They identified only 4 significant ($P < .001$) risk factors for severe anaphylaxis, including increased baseline tryptase levels, absence of urticaria or angioedema during anaphylaxis, less than 5 minutes from sting to onset of symptoms, and senior age. Interestingly, an absence of skin symptoms was significantly related to the tryptase level, suggesting possible mastocytosis.

Regarding venom diagnostics, Eberlein et al[73] attempted to resolve the possible diagnostic confusion, which occurs about 60% of the time, when positive IgE test results to bee and wasp venom co-occur; this could be due to cross-reactive carbohydrate determinants or true dual allergy. They used a basophil activation test with venoms and bromelain and horseradish peroxidase and also evaluated recombinant allergen–based IgE testing. They tested 22 patients and found double positivity (12 patients), double negativity (1 patient), or single positivity (9 patients) to rApi m 1 and rVes v 5. Further recombinant allergen–based IgE testing in the last patients revealed positive results to the other venom in all cases except one. Basophil activation test results were double positive (6 patients), double negative (2 patients), or single positive (14 patients). Four patients with negative results for specific IgE antibodies to cross-reactive carbohydrate determinants had positive results on basophil activation tests, and these tests with bromelain and horseradish peroxidase showed a sensitivity of 50% and 81% and a specificity of 91% and 90%, respectively. Thus the basophil activation test with horseradish peroxidase was a good means to determine sensitivity to the cross-reactive carbohydrate determinants. The authors concluded, as did others,[74] that component-resolved IgE testing is helpful and here elucidated the pattern of double positivity, showing a majority of true double sensitizations independent of sensitization to cross-reactive carbohydrate determinants and that the basophil activation test might add information about the culprit insect.

Venom immunotherapy is the cornerstone of treatment,[75,76] but there are various options for dosing regimens. Brown et al[77] performed a head-to-head safety comparison of initiation of immunotherapy with semirush (44 patients treated over 10 visits in 9 weeks) or ultrarush (49 patients treated over 3 visits in 2 weeks) schedules for treating jack jumper ant allergy. Objective systemic reactions were more likely during ultrarush initiation (65% vs 29%, $P < .001$), as were severe reactions (12% vs 0%, $P = .029$). Times to maximal increases in venom-specific IgG_4 levels were no different between treatments, whereas the maximal increase in venom-specific IgE levels occurred earlier with ultrarush treatment. One hundred seventy-eight patients were randomized to maintenance doses of either 50 μg (90 patients) or 100 μg (88 patients). The target maintenance dose had no effect on the occurrence of 1 or more systemic reactions, but multiple-failure-per-subject analysis found that the 50-μg dose reduced the likelihood of reactions. Thus the ultrarush initiation increased risks and the lower maintenance dose reduced them, but the effect on treatment efficacy is still under investigation.

There are increasing reports of infestation of bedbugs, *Cimex lectularius*. Price et al[78] analyzed sera from 30 patients reporting bites in New York City and found that 57% were IgE sensitized to bedbug extracts. Additional characterization of the IgE reactivity identified cross-reactivity with cockroach and dust mites but also (for 30%) a protein unique to the bedbug. Thus far, correlation of the sensitization to altered reactivity to bites has not been reported.

DRUG ALLERGY

Misdiagnosis of drug hypersensitivity leads to substantial unnecessary costs and puts patients at risk. For example, Sastre

et al[79] evaluated 71 Spanish patients admitted in 1 day with a diagnosis that included drug hypersensitivity and found that, after careful allergy evaluations, only 26 (37%) had confirmed allergy. However, diagnosis can be challenging, and information on approaches to achieve accurate results is sorely needed. Romano et al[80] evaluated 105 subjects with reported nonimmediate reactions to cephalosporins by using skin prick and intradermal tests (including a late reading at 2 and 3 days) and patch tests with cephalosporins and various β-lactam agents, and those with negative test results were challenged. Only 7 had a final diagnosis of cephalosporin allergy with delayed symptoms (mostly maculopapular reactions after 2 days) and positive test results, but only 1 was challenged (positive), and therefore the significance of a positive test result was not entirely confirmed. The results of the delayed or immediate intradermal tests with the culprit were positive or trace positive in these subjects. However, 86 of the 98 subjects with negative test results were challenged and tolerated the medications. Thus the rate of positive response to delayed intradermal testing was 4.7%, and the test had good sensitivity. Another study reported the accuracy of SPTs and intradermal tests for the diagnosis of immediate hypersensitivity to proton pump inhibitors[81] and the utility of performing multiple serial skin tests to identify those at risk for hypersensitivity reactions to carboplatin.[82]

The underlying immunologic basis of hypersensitivity reactions leading to Stevens-Johnson syndrome remains elusive. However, increasing studies have revealed that HLA alleles are a major genetic determinant. Wei et al[83] expanded carbamazepine-specific cytotoxic T lymphocytes *in vitro* from patients with Stevens-Johnson syndrome or toxic epidermal necrolysis and analyzed the interaction between HLA-B and carbamazepine analogs based on cytotoxic T-cell response, surface plasmon resonance, peptide-binding assay, site-directed mutagenesis, and computer modeling. The endogenous peptide-loaded HLA-B*1502 molecule presented carbamazepine to cytotoxic T cells without the involvement of intracellular drug metabolism or antigen processing. The HLA-B*1502/peptide/β_2-microglobulin protein complex showed binding affinity toward chemicals sharing 5-carboxamide on the tricyclic ring. However, modifications of the ring structure of carbamazepine altered HLA-B*1502 binding and the cytotoxic T-cell response. In addition to HLA-B*1502, other HLA-B75 family members could also present carbamazepine-activated cytotoxic T cells, whereas members of the HLA-B62 and HLA-B72 families could not. Three residues (Asn63, Ile95, and Leu156) in the peptide-binding groove of HLA-B*1502 were involved in presentation and activation. Computer simulations revealed a preferred molecular conformation of the 5-carboxamide group of carbamazepine and the side chain of Arg62 on the B pocket of HLA-B*1502. Thus, for the first time, a direct interaction of HLA with drugs was shown, providing a detailed molecular mechanism of HLA-associated drug hypersensitivity.

Another common concern is adverse or allergic reactions to vaccines, a topic covered in an updated practice parameter.[84] Novel vaccines also pose a concern, as evidenced by allergic reactions noted to a novel antihelminth vaccine.[85] However, the greatest attention recently has been to the administration of influenza vaccines for persons with egg allergy.[86] Des Roches et al[87] combined their results with those of 26 other studies that included more than 25 patients with egg allergy receiving the influenza vaccine. The summary included 4172 patients (513 with severe allergy) receiving a total of 4729 doses without anaphylaxis, indicating a risk of anaphylaxis (95% CI) of 0% to 0.08% (95% CI among those with severe egg allergy, 0% to 0.66%). This finding adds credence to current recommendations,[84] which generally advise that the vaccine (trivalent influenza vaccine) can be administered as a single dose without testing to persons with only hive reactions to egg by a primary care physician with a 30-minute observation (assuming personnel and equipment to manage anaphylaxis are available) and that persons with a history of acute symptoms other than isolated urticaria from egg ingestion are referred to an allergist for essentially the same approach. The approach is different if there is no clear egg allergy or if there has been a previous reaction to the vaccine.

ALLERGIC SKIN DISEASES

Mechanisms underlying atopic dermatitis (AD) and urticaria continue to be actively studied, with the expectation that it will lead to new approaches in the management of these common allergic skin diseases. Advances in the pathobiology and treatment of allergic skin diseases are shown in Table III.

Genetic influences in AD

The association of *FLG* mutations in patients with AD, first described in northern Europe, has been demonstrated in US population studies.[88] *FLG* mutations increase the risk for persistent dry skin,[89] enhance percutaneous immune responses,[90] and are associated with increased expression of IL-1 cytokines in the stratum corneum of patients with AD.[91] The skin barrier abnormality caused by *FLG* mutations is also associated with increased serum 25-hydroxy vitamin D concentrations.[92] Polymorphisms located within the overlapping anoctamin 3 *(ANO3)* and mucin 15 *(MUC15)* genes,[93] as well as the *IL10* gene,[94] have been associated with AD.

Immunologic responses

The development of AD is influenced by multiple factors, including early-life exposures,[95,96] allergen environmental exposures, infection,[97] and autoreactivity.[98] These immunologic triggers result in a complex inflammatory response in atopic skin that is associated with an early T_H2 response followed by a T_H1 and T_H22 response in the chronic phases of AD.[99] Dendritic cells are key skin cells that connect information from the environment with the innate and adaptive immune system.[100] Release of thymic stromal lymphopoietin from a variety of cell sources, such as keratinocytes, plays a critical role in driving early T_H2 cell activation through its action on dendritic cells, including Langerhans cells.[101,102]

The T_H2 response during early AD lesional formation contributes to skin barrier dysfunction[103] and an increase in levels of IL-31, which enhances pruritus and recently has been found to affect keratinocyte differentiation.[104] Defects in epidermal differentiation are further enforced by IL-22 expression in AD skin.[105] The complex cytokine profile that evolves after acute AD lesional formation includes an increase in IFN-γ levels, which induces apoptosis of keratinocytes.[106] However, these effects could be counterbalanced by IL-10, which controls dendritic cell–induced T-cell reactivity in the skin.[107,108] Corticotropin-releasing hormone, which downregulates IL-10 production by adaptive

forkhead box protein 3–negative regulatory T cells,[109] has been recently found to have altered expression in patients with AD.[110]

Although AD is known as a T_H2- and T_H22-mediated inflammatory skin disease, and psoriasis is known as a T_H1/T_H17-mediated skin disease,[111] there might be AD subsets that do not follow this rule. Indeed, IL-17 expression has been reported in mouse models of eczema.[112] Recently, a comparative transcriptomic analysis of AD and psoriasis revealed evidence for increased *IL17* gene expression and shared neutrophilic inflammation in patients with these 2 skin diseases.[113] However, future studies are needed to determine whether IL-17 expression in the T_H2/T_H22 cytokine environment of AD would lead to different biologic responses than seen in the polarized T_H1/IL-17 environment of psoriasis.

Treatment of AD

There remains considerable interest in studying factors that contribute to the atopic march[114] and approaches to prevent AD.[115] The use of probiotic therapy or bacterial lysates early in the course of illness is under active study.[13,116] Allergen immunotherapy in patients triggered by one primary allergen is another approach that has gained renewed interest.[117] In patients whose symptoms are difficult to control with topical anti-inflammatory therapy, consideration should be given to alternative anti-inflammatory therapies, including phototherapy.[118,119] Aside from its anti-inflammatory effects, UV therapy also has a beneficial effect in augmenting serum vitamin D levels.[120] During the past year, there have also been several new insights into potential mechanisms by which pruritus and mast cell activation can be controlled in patients with AD.[121,122]

Urticaria and angioedema

Mortality in patients with hereditary angioedema was often due to laryngeal attacks in previous undiagnosed patients.[123] Generalized urticaria after vaccination with helminth antigens[124] attracted interest this past year. There was also considerable interest in the relationship between autoimmunity and chronic idiopathic urticaria.[125,126] Activation of complement by the complement controller domain of thyroperoxidase was proposed to be an important contributor to the development of urticaria and angioedema in patients with thyroid autoimmunity.[127]

CONCLUSIONS AND SUMMARY

In the year since our last review, numerous exciting advances have been reported in the *Journal*. It is becoming very clear that food allergy has increased in prevalence, and insights about risk factors, including sensitization through an impaired skin barrier, dietary influences, hygiene, and so on, are providing targets for controlled trials and prevention studies. Fascinating insights on EoE diagnosis and management are likely to quickly give way to improved care for patients with this troubling disease. The armamentarium for diagnosing food, insect venom, and drug allergies continues to grow, with some strategies already in the commercial marketplace. Various observational studies provide clinical lessons about daily management of anaphylaxis and food allergy, emphasizing the need to educate patients and ensure a proper diagnosis to enhance care and quality of life. Numerous clinical and preclinical treatment studies provide hope, but caution is needed in discerning risk and benefits and moving toward larger clinical trials. New insights into mechanisms underlying AD and urticaria have also been identified. These advances present information that can improve patient care today and provide insights into how we will improve diagnosis and treatment in the future.

REFERENCES

1. Sicherer SH, Leung DY. Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2011. J Allergy Clin Immunol 2012;129:76-85.
2. Burks AW, Tang M, Sicherer S, Muraro A, Eigenmann PA, Ebisawa M, et al. ICON: food allergy. J Allergy Clin Immunol 2012;129:906-20.
3. Soller L, Ben Shoshan M, Harrington DW, Fragapane J, Joseph L, St Pierre Y, et al. Overall prevalence of self-reported food allergy in Canada. J Allergy Clin Immunol 2012;130:986-8.
4. Keet CA, Wood RA, Matsui EC. Limitations of reliance on specific IgE for epidemiologic surveillance of food allergy. J Allergy Clin Immunol 2012;130:1207-9.e10.
5. Gupta RS, Springston EE, Smith B, Pongracic J, Holl JL, Warrier MR. Parent report of physician diagnosis in pediatric food allergy. J Allergy Clin Immunol 2012 [Epub ahead of print].
6. Lack G. Update on risk factors for food allergy. J Allergy Clin Immunol 2012;129:1187-97.
7. Rinaldi M, Harnack L, Oberg C, Schreiner P, St Sauver J, Travis LL. Peanut allergy diagnoses among children residing in Olmsted County, Minnesota. J Allergy Clin Immunol 2012;130:945-50.
8. Keet CA, Wood RA, Matsui EC. Personal and parental nativity as risk factors for food sensitization. J Allergy Clin Immunol 2012;129:169-75.
9. Savage JH, Matsui EC, Wood RA, Keet CA. Urinary levels of triclosan and parabens are associated with aeroallergen and food sensitization. J Allergy Clin Immunol 2012;130:453-60.
10. Osborne NJ, Ukoumunne OC, Wake M, Allen KJ. Prevalence of eczema and food allergy is associated with latitude in Australia. J Allergy Clin Immunol 2012;129:865-7.
11. Tan HT, Ellis JA, Koplin JJ, Matheson MC, Gurrin LC, Lowe AJ, et al. Filaggrin loss-of-function mutations do not predict food allergy over and above the risk of food sensitization among infants. J Allergy Clin Immunol 2012;130:1211-3.e3.
12. Maslova E, Granstrom C, Hansen S, Petersen SB, Strom M, Willett WC, et al. Peanut and tree nut consumption during pregnancy and allergic disease in children-should mothers decrease their intake? Longitudinal evidence from the Danish National Birth Cohort. J Allergy Clin Immunol 2012;130:724-32.
13. Jensen MP, Meldrum S, Taylor AL, Dunstan JA, Prescott SL. Early probiotic supplementation for allergy prevention: long-term outcomes. J Allergy Clin Immunol 2012;130:1209-11.e5.
14. Fiorentino R, Liu G, Pariser AR, Mulberg AE. Cross-sector sponsorship of research in eosinophilic esophagitis: a collaborative model for rational drug development in rare diseases. J Allergy Clin Immunol 2012;130:613-6.
15. Saffari H, Peterson KA, Fang JC, Teman C, Gleich GJ, Pease LF III. Patchy eosinophil distributions in an esophagectomy specimen from a patient with eosinophilic esophagitis: Implications for endoscopic biopsy. J Allergy Clin Immunol 2012;130:798-800.
16. Lu TX, Sherrill JD, Wen T, Plassard AJ, Besse JA, Abonia JP, et al. MicroRNA signature in patients with eosinophilic esophagitis, reversibility with glucocorticoids, and assessment as disease biomarkers. J Allergy Clin Immunol 2012;129:1064-75.
17. Schroeder S, Fleischer DM, Masterson JC, Gelfand E, Furuta GT, Atkins D. Successful treatment of eosinophilic esophagitis with ciclesonide. J Allergy Clin Immunol 2012;129:1419-21.
18. Henderson CJ, Abonia JP, King EC, Putnam PE, Collins MH, Franciosi JP, et al. Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis. J Allergy Clin Immunol 2012;129:1570-8.
19. Spergel JM, Brown-Whitehorn TF, Cianferoni A, Shuker M, Wang ML, Verma R, et al. Identification of causative foods in children with eosinophilic esophagitis treated with an elimination diet. J Allergy Clin Immunol 2012;130:461-7.
20. Molina-Infante J, Martin-Noguerol E, Alvarado-Arenas M, Porcel-Carreno SL, Jimenez-Timon S, Hernandez-Arbeiza FJ. Selective elimination diet based on skin testing has suboptimal efficacy for adult eosinophilic esophagitis. J Allergy Clin Immunol 2012;130:1200-2.
21. Terrados CS, Antolin-Amerigo D, Foruny JR, Gonzalez AS. Esophageal eosinophilia caused by milk proteins: from suspicion to evidence based on 2 case reports. J Allergy Clin Immunol 2012;129:1416-9.

22. Spergel JM, Rothenberg ME, Collins MH, Furuta GT, Markowitz JE, Fuchs G III, et al. Reslizumab in children and adolescents with eosinophilic esophagitis: results of a double-blind, randomized, placebo-controlled trial. J Allergy Clin Immunol 2012;129:456-63.
23. Tan J, Campbell D, Mehr S. Food protein-induced enterocolitis syndrome in an exclusively breast-fed infant-an uncommon entity. J Allergy Clin Immunol 2012;129:873; author reply 873-4.
24. Hsu P, Mehr S. Egg: a frequent trigger of food protein-induced enterocolitis syndrome. J Allergy Clin Immunol 2012 [Epub ahead of print].
25. Fernandes BN, Boyle RJ, Gore C, Simpson A, Custovic A. Food protein-induced enterocolitis syndrome can occur in adults. J Allergy Clin Immunol 2012;130: 1199-200.
26. Ohtsuka Y, Jimbo K, Inage E, Mori M, Yamakawa Y, Aoyagi Y, et al. Microarray analysis of mucosal biopsy specimens in neonates with rectal bleeding: is it really an allergic disease? J Allergy Clin Immunol 2012;129:1676-8.
27. Ruiter B, Shreffler WG. The role of dendritic cells in food allergy. J Allergy Clin Immunol 2012;129:921-8.
28. Tunis MC, Dawicki W, Carson KR, Wang J, Marshall JS. Mast cells and IgE activation do not alter the development of oral tolerance in a murine model. J Allergy Clin Immunol 2012;130:705-15.
29. Kucuk ZY, Strait R, Khodoun MV, Mahler A, Hogan S, Finkelman FD. Induction and suppression of allergic diarrhea and systemic anaphylaxis in a murine model of food allergy. J Allergy Clin Immunol 2012;129:1343-8.
30. Wang M, Okamoto M, Domenico J, Han J, Ashino S, Shin YS, et al. Inhibition of Pim1 kinase prevents peanut allergy by enhancing Runx3 expression and suppressing T(H)2 and T(H)17 T-cell differentiation. J Allergy Clin Immunol 2012;130:932-44.
31. Hancock DB, Romieu I, Chiu GY, Sienra-Monge JJ, Li H, Estela DR-N, et al. STAT6 and LRP1 polymorphisms are associated with food allergen sensitization in Mexican children. J Allergy Clin Immunol 2012;129:1673-6.
32. Menikou S, Patel MP, Rose KL, Botto M, Warner JO, Pickering MC, et al. Relationship between complotype and reported severity of systemic allergic reactions to peanut. J Allergy Clin Immunol 2012;129:1398-401.
33. Mullins RJ, James H, Platts-Mills TA, Commins S. Relationship between red meat allergy and sensitization to gelatin and galactose-alpha-1,3-galactose. J Allergy Clin Immunol 2012;129:1334-42.
34. Chiang WC, Huang C, Llanora GV, Gerez I, Goh SH, Shek LP, et al. Anaphylaxis to cow's milk formula containing short chain galacto-oligosaccharide (scGOS). J Allergy Clin Immunol 2012 [Epub ahead of print].
35. Fukutomi Y, Sjolander S, Nakazawa T, Borres MP, Ishii T, Nakayama S, et al. Clinical relevance of IgE to recombinant Gly m 4 in the diagnosis of adult soybean allergy. J Allergy Clin Immunol 2012;129:860-3.
36. Javaloyes G, Goikoetxea MJ, Nunez IG, Aranda A, Sanz ML, Blanca M, et al. Pru p 3 acts as a strong sensitizer for peanut allergy in Spain. J Allergy Clin Immunol 2012 [Epub ahead of print].
37. Chinuki Y, Kaneko S, Dekio I, Takahashi H, Tokuda R, Nagao M, et al. CD203c expression-based basophil activation test for diagnosis of wheat-dependent exercise-induced anaphylaxis. J Allergy Clin Immunol 2012;129:1404-6.
38. Haneda Y, Kando N, Yasui M, Kobayashi T, Maeda T, Hino A, et al. Ovomucoids IgE is a better marker than egg white-specific IgE to diagnose boiled egg allergy. J Allergy Clin Immunol 2012;129:1681-2.
39. Klemans RJ, Otte D, Knol M, Knol EF, Meijer Y, Gmelig-Meyling FH, et al. The diagnostic value of specific IgE to Ara h 2 to predict peanut allergy in children is comparable to a validated and updated diagnostic prediction model. J Allergy Clin Immunol 2012 [Epub ahead of print].
40. Gao ZS, Yang ZW, Wu SD, Wang HY, Liu ML, Mao WL, et al. Peach allergy in China: A dominant role for mugwort pollen lipid transfer protein as a primary sensitizer. J Allergy Clin Immunol 2012 [Epub ahead of print].
41. Ford LS, Bloom KA, Nowak-Wegrzyn AH, Shreffler WG, Masilamani M, Sampson HA. Basophil reactivity, wheal size, and immunoglobulin levels distinguish degrees of cow's milk tolerance. J Allergy Clin Immunol 2012 [Epub ahead of print].
42. Caubet JC, Nowak-Wegrzyn A, Moshier E, Godbold J, Wang J, Sampson HA. Utility of casein-specific IgE levels in predicting reactivity to baked milk. J Allergy Clin Immunol 2012 [Epub ahead of print].
43. Caubet JC, Bencharitiwong R, Moshier E, Godbold JH, Sampson HA, Nowak-Wegrzyn A. Significance of ovomucoid- and ovalbumin-specific IgE/IgG(4) ratios in egg allergy. J Allergy Clin Immunol 2012;129:739-47.
44. Lieberman JA, Huang FR, Sampson HA, Nowak-Wegrzyn A. Outcomes of 100 consecutive open, baked-egg oral food challenges in the allergy office. J Allergy Clin Immunol 2012;129:1682-4.
45. Dang TD, Tang M, Choo S, Licciardi PV, Koplin JJ, Martin PE, et al. Increasing the accuracy of peanut allergy diagnosis by using Ara h 2. J Allergy Clin Immunol 2012;129:1056-63.
46. Asarnoj A, Nilsson C, Lidholm J, Glaumann S, Ostblom E, Hedlin G, et al. Peanut component Ara h 8 sensitization and tolerance to peanut. J Allergy Clin Immunol 2012;130:468-72.
47. Lin J, Bruni FM, Fu Z, Maloney J, Bardina L, Boner AL, et al. A bioinformatics approach to identify patients with symptomatic peanut allergy using peptide microarray immunoassay. J Allergy Clin Immunol 2012;129:1321-8.
48. Pongracic JA, Bock SA, Sicherer SH. Oral food challenge practices among allergists in the United States. J Allergy Clin Immunol 2012;129:564-6.
49. van der Velde JL, Flokstra-de Blok BM, de Groot H, Oude-Elberink JN, Kerkhof M, Duiverman EJ, et al. Food allergy-related quality of life after double-blind, placebo-controlled food challenges in adults, adolescents, and children. J Allergy Clin Immunol 2012;130:1136-43.e2.
50. Baptist AP, Dever SI, Greenhawt MJ, Polmear-Swendris N, McMorris MS, Clark NM. A self-regulation intervention can improve quality of life for families with food allergy. J Allergy Clin Immunol 2012;130:263-5.
51. Ben Shoshan M, Sheth S, Harrington D, Soller L, Fragapane J, Joseph L, et al. Effect of precautionary statements on the purchasing practices of Canadians directly and indirectly affected by food allergies. J Allergy Clin Immunol 2012;129:1401-4.
52. Ahrens B, Niggemann B, Wahn U, Beyer K. Organ-specific symptoms during oral food challenge in children with food allergy. J Allergy Clin Immunol 2012;130: 549-51.
53. Niggemann B, Lange L, Finger A, Ziegert M, Muller V, Beyer K. Accurate oral food challenge requires a cumulative dose on a subsequent day. J Allergy Clin Immunol 2012;130:261-3.
54. Koplin JJ, Tang ML, Martin PE, Osborne NJ, Lowe AJ, Ponsonby AL, et al. Predetermined challenge eligibility and cessation criteria for oral food challenges in the HealthNuts population-based study of infants. J Allergy Clin Immunol 2012; 129:1145-7.
55. Sampson HA, van Wijk RG, Bindslev-Jensen C, Sicherer SH, Teuber SS, Burks AW, et al. AAAAI-EAACI PRACTALL standardizing double-blind placebo-controlled oral food challenges. J Allergy Clin Immunol [Epub ahead of print].
56. Sanchez-Garcia S, Rodriguez DR, Escudero C, Martinez-Gomez MJ, Ibanez MD. Possible eosinophilic esophagitis induced by milk oral immunotherapy. J Allergy Clin Immunol 2012;129:1155-7.
57. Beyer K. A European perspective on immunotherapy for food allergies. J Allergy Clin Immunol 2012;129:1179-84.
58. Keet CA, Frischmeyer-Guerrerio PA, Thyagarajan A, Schroeder JT, Hamilton RG, Boden S, et al. The safety and efficacy of sublingual and oral immunotherapy for milk allergy. J Allergy Clin Immunol 2012;129:448-55.
59. Kulis M, Saba K, Kim EH, Bird JA, Kamilaris N, Vickery BP, et al. Increased peanut-specific IgA levels in saliva correlate with food challenge outcomes after peanut sublingual immunotherapy. J Allergy Clin Immunol 2012;129:1159-62.
60. Leonard SA, Martos G, Wang W, Nowak-Wegrzyn A, Berin MC. Oral immunotherapy induces local protective mechanisms in the gastrointestinal mucosa. J Allergy Clin Immunol 2012;129:1579-87.
61. Leonard SA, Sampson HA, Sicherer SH, Noone S, Moshier EL, Godbold J, et al. Dietary baked egg accelerates resolution of egg allergy in children. J Allergy Clin Immunol 2012;130:473-80.
62. Kulis M, Macqueen I, Li Y, Guo R, Zhong XP, Burks AW. Pepsinized cashew proteins are hypoallergenic and immunogenic and provide effective immunotherapy in mice with cashew allergy. J Allergy Clin Immunol 2012;130:716-23.
63. Savage JH, Courneya JP, Sterba PM, MacGlashan DW, Saini SS, Wood RA. Kinetics of mast cell, basophil, and oral food challenge responses in omalizumab-treated adults with peanut allergy. J Allergy Clin Immunol 2012;130:1123-9.e2.
64. Macglashan DW Jr, Savage J, Wood R, Saini S. Suppression of the basophil response to allergen during treatment with omalizumab is dependent on 2 competing factors. J Allergy Clin Immunol 2012;130:1130-5.e5.
65. Campbell RL, Hagan JB, Manivannan V, Decker WW, Kanthala AR, Bellolio MF, et al. Evaluation of national institute of allergy and infectious diseases/food allergy and anaphylaxis network criteria for the diagnosis of anaphylaxis in emergency department patients. J Allergy Clin Immunol 2012;129:748-52.
66. Huang F, Chawla K, Jarvinen KM, Nowak-Wegrzyn A. Anaphylaxis in a New York City pediatric emergency department: triggers, treatments, and outcomes. J Allergy Clin Immunol 2012;129:162-8.
67. Vadas P, Perelman B, Liss G. Platelet-activating factor, histamine, and tryptase levels in human anaphylaxis. J Allergy Clin Immunol 2012 [Epub ahead of print].
68. Simons FE, Schatz M. Anaphylaxis during pregnancy. J Allergy Clin Immunol 2012;130:597-606.
69. Rudders SA, Geyer BC, Banerji A, Phipatanakul W, Clark S, Camargo CA Jr. Obesity is not a risk factor for repeat epinephrine use in the treatment of anaphylaxis. J Allergy Clin Immunol 2012 [Epub ahead of print].
70. Gupta P, Gerrish PK, Silverman B, Schneider A. Current practices among allergists on writing self-injectable epinephrine prescriptions for immunotherapy patients. J Allergy Clin Immunol 2012;129:571-2.

71. Jacobsen RC, Guess TM, Burks AW. Comparing activation and recoil forces generated by epinephrine autoinjectors and their training devices. J Allergy Clin Immunol 2012;129:1143-5.
72. Stoevesandt J, Hain J, Kerstan A, Trautmann A. Over- and underestimated parameters in severe Hymenoptera venom-induced anaphylaxis: cardiovascular medication and absence of urticaria/angioedema. J Allergy Clin Immunol 2012;130: 698-704.
73. Eberlein B, Krischan L, Darsow U, Ollert M, Ring J. Double positivity to bee and wasp venom: improved diagnostic procedure by recombinant allergen-based IgE testing and basophil activation test including data about cross-reactive carbohydrate determinants. J Allergy Clin Immunol 2012;130:155-61.
74. Korosec P, Valenta R, Mittermann I, Celesnik N, Silar M, Zidarn M, et al. High sensitivity of CAP-FEIA rVes v 5 and rVes v 1 for diagnosis of *Vespula* venom allergy. J Allergy Clin Immunol 2012;129:1406-8.
75. Seppala U, Francese S, Turillazzi S, Moneti G, Clench M, Barber D. In situ imaging of honeybee *(Apis mellifera)* venom components from aqueous and aluminum hydroxide-adsorbed venom immunotherapy preparations. J Allergy Clin Immunol 2012;129:1314-20.
76. Varga EM, Kausar F, Aberer W, Zach M, Eber E, Durham SR, et al. Tolerant beekeepers display venom-specific functional IgG(4) antibodies in the absence of specific IgE. J Allergy Clin Immunol 2012 [Epub ahead of print].
77. Brown SG, Wiese MD, van Eeden P, Stone SF, Chuter CL, Gunner J, et al. Ultrarush versus semirush initiation of insect venom immunotherapy: a randomized controlled trial. J Allergy Clin Immunol 2012;130:162-8.
78. Price JB, Divjan A, Montfort WR, Stansfield KH, Freyer GA, Perzanowski MS. IgE against bed bug *(Cimex lectularius)* allergens is common among adults bitten by bed bugs. J Allergy Clin Immunol 2012;129:863-5.
79. Sastre J, Manso L, Sanchez-Garcia S, Fernandez-Nieto M. Medical and economic impact of misdiagnosis of drug hypersensitivity in hospitalized patients. J Allergy Clin Immunol 2012;129:566-7.
80. Romano A, Gaeta F, Valluzzi RL, Caruso C, Alonzi C, Viola M, et al. Diagnosing nonimmediate reactions to cephalosporins. J Allergy Clin Immunol 2012;129: 1166-9.
81. Bonadonna P, Lombardo C, Bortolami O, Bircher A, Scherer K, Barbaud A, et al. Hypersensitivity to proton pump inhibitors: diagnostic accuracy of skin tests compared to oral provocation test. J Allergy Clin Immunol 2012;130:547-9.
82. Patil SU, Long AA, Ling M, Wilson MT, Hesterberg P, Wong JT, et al. A protocol for risk stratification of patients with carboplatin-induced hypersensitivity reactions. J Allergy Clin Immunol 2012;129:443-7.
83. Wei CY, Chung WH, Huang HW, Chen YT, Hung SI. Direct interaction between HLA-B and carbamazepine activates T cells in patients with Stevens-Johnson syndrome. J Allergy Clin Immunol 2012;129:1562-9.
84. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol 2012;130:25-43.
85. Diemert DJ, Pinto AG, Freire J, Jariwala A, Santiago H, Hamilton RG, et al. Generalized urticaria induced by the Na-ASP-2 hookworm vaccine: implications for the development of vaccines against helminths. J Allergy Clin Immunol 2012; 130:169-76.
86. Fung I, Spergel JM. Administration of influenza vaccine to pediatric patients with egg-induced anaphylaxis. J Allergy Clin Immunol 2012;129:1157-9.
87. Des Roches A, Paradis L, Gagnon R, Lemire C, Begin P, Carr S, et al. Egg-allergic patients can be safely vaccinated against influenza. J Allergy Clin Immunol 2012;130:1213-6.e1.
88. Margolis DV, Apter AJ, Gupta J, Hoffstad O, Papadopoulos M, Campbell LE, et al. The persistence of atopic dermatitis and filaggrin (FLG) mutations in a US longitudinal cohort. J Allergy Clin Immunol 2012;130:912-7.
89. Böhme M, Söderhöll C, Kull I, Bergström A, van Hage M, Wahlgren C. Filaggrin mutations increase the risk for persistent dry skin and eczema independent of sensitization. J Allergy Clin Immunol 2012;129:1153-5.
90. Kawasaki H, Nagao K, Kubo A, Hata T, Shimizu A, Mizuno H, et al. Altered stratum corneum barrier and enhanced percutaneous immune responses in filaggrin-null mice. J Allergy Clin Immunol 2012;129:1538-46.
91. Kezic S, O'Regan GM, Lutter R, Jaskasa I, Koster ES, Saunders S, et al. Filaggrin loss-of-function mutations are associated with enhanced expression of IL-1 cytokines in the stratum corneum of patients with atopic dermatitis and in a murine model of filaggrin deficiency. J Allergy Clin Immunol 2012;129:1031-9.
92. Thyssen JP, Thuesen BH, Huth C, Standl M, Carson CG, Heinrich J, et al. Skin barrier abnormality caused by filaggrin (FLG) mutations is associated with increased serum 25-hydroxy vitamin D concentrations. J Allergy Clin Immunol 2012;130:1204-7.e2.
93. Dizier MH, Margaritte-Jeannin P, Madore A, Esparza-Gordillo G, Moffatt M, Corda E, et al. The ANO3/MUC15 locus is associated with eczema in families ascertained through asthma. J Allergy Clin Immunol 2012;129:1547-53.
94. Raedler D, Illi S, Pinto LA, von Mutius E, Illig T, Kabesch M, et al. IL10 polymorphisms influence neonatal immune responses, atopic dermatitis, and wheeze at age 3 years. J Allergy Clin Immunol 2012 [Epub ahead of print].
95. Caroline R, Frei R, Loss G, Büchele G, Weber J, Depner M, et al. Development of atopic dermatitis according to age of onset and association with early-life exposures. J Allergy Clin Immunol 2012;130:130-6.
96. Illi S, Depner M, Genuneit J, Horak E, Loss G, Strunz-Lehner C, et al. Protection from childhood asthma and allergy in Alpine farm environments—the GABRIEL Advanced Studies. 2012;129:1470-7.
97. Bin L, Kim BE, Brauweiler A, Goleva E, Streib J, Ji Y, et al. Staphylococcus aureus a-toxin modulates skin host response to viral infection. J Allergy Clin Immunol 2012;130:683-91.
98. Tang TS, Bieber T, Williams H. Does "autoreactivity" play a role in eczema? J Allergy Clin Immunol 2012;129:1209-15.
99. Guttman-Yassky E, Nograles K. Contrasting pathogenesis of atopic dermatitis and psoriasis—part I: clinical and pathologic concepts. J Allergy Clin Immunol 2011;127:1110-8.
100. Novak N. An update on the role of human dendritic cells in patients with atopic dermatitis. J Allergy Clin Immunol 2012;129:879-86.
101. Ziegler SF. Thymic stromal lymphopoietin and allergic disease. J Allergy Clin Immunol 2012;130:845-52.
102. Nakajima S, Igyártó BZ, Honda T, Egawa G, Otsuka A, Hara-Chikuma M, et al. Langerhans cells are critical in epicutaneous sensitization with protein antigen via thymic stromal lymphopoietin receptor signaling. J Allergy Clin Immunol 2012;129:1048-55.
103. Morizane S, Yamasaki K, Kajita A, Ikeda K, Zhan M, Aoyama Y, et al. TH2 cytokines increase kallikrein 7 expression and function in patients with atopic dermatitis. J Allergy Clin Immunol 2012;130:259-61.
104. Cornelissen C, Marquardt Y, Czaja K, Wenzel J, Lüscher-Firzlaff J, Lüscher B, et al. IL-31 regulates differentiation and filaggrin expression in human organotypic skin models. J Allergy Clin Immunol 2012;129:426-33.
105. Gittler JK, Shemer A, Suárez-Fariñas M, Fuentes-Duculan J, Gulewicz KJ, Wang CQF, et al. Progressive activation of TH2/TH22 cytokines and selective epidermal proteins characterizes acute and chronic atopic dermatitis. J Allergy Clin Immunol 2012 [Epub ahead of print].
106. Rebane A, Zimmermann M, Aab A, Baurecht H, Koreck A, Karelson M, et al. Mechanisms of IFN–induced apoptosis of human skin keratinocytes in patients with atopic dermatitis. J Allergy Clin Immunol 2012;129:1297-306.
107. Boyman O, Werfel T, Akdis CA. The suppressive role of IL-10 in contact and atopic dermatitis. J Allergy Clin Immunol 2012;129:160-1.
108. Girard-Madoux MJ, Kel JM, Reizis B, Clausen BE. IL-10 controls dendritic cell–induced T-cell reactivation in the skin to limit contact hypersensitivity. J Allergy Clin Immunol 2012;129:143-50.
109. Oh SH, Park CO, Wu WH, Kim JY, Jin S, Byamba D, et al. Corticotropin-releasing hormone downregulates IL-10 production by adaptive forkhead box protein 3–negative regulatory T cells in patients with atopic dermatitis. J Allergy Clin Immunol 2012;129:151-9, e1-6.
110. Vasiadi M, Therianou A, Sideri K, Smyrnioti M, Sismanopoulos N, Delivani D, et al. Increased serum CRH levels with decreased skin CRHR-1 gene expression in psoriasis and atopic dermatitis. J Allergy Clin Immunol 2012;129:1410-3.
111. Krueger J, Fretzin S, Suárez-Fariñas M, Haslett P, Phipps K, Cameron G, et al. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. J Allergy Clin Immunol 2012;130:145-54.
112. Oyoshi MK, Wang JYT, Geha RS. Immunization with modified vaccinia virus Ankara prevents eczema vaccinatum in a murine model of atopic dermatitis. J Allergy Clin Immunol 2011;128:890-1.
113. Choy DF, Hsu DK, Seshasayee D, Fung MA, Modrusan Z, Martin F, et al. Comparative transcriptomic analyses of atopic dermatitis and psoriasis reveal shared neutrophilic inflammation. J Allergy Clin Immunol 2012 [Epub ahead of print].
114. Hopper J, Bui QM, Erbas B, Matheson MC, Gurrin LC, Burgess JA, et al. Does eczema in infancy cause hay fever, asthma, or both in childhood? Insights from a novel regression model of sibling data. J Allergy Clin Immunol 2012;130:1117-22.e1.
115. Simpson EL, Keck LE, Chalmers JR, Williams HC. How should an incident case of atopic dermatitis be defined? A systematic review of primary prevention studies. J Allergy Clin Immunol 2012;130:137-44.
116. Lau S, Gerhold K, Zimmermann K, Ockeloen CW, Rossberg S, Wagner P, et al. Oral application of bacterial lysate in infancy decreases the risk of atopic dermatitis in children with 1 atopic parent in a randomized, placebo-controlled trial. J Allergy Clin Immunol 2012;129:1040-7.
117. Novak N, Bieber T, Hoffmann M, Fölster-Holst R, Homey B, Werfel T, et al. Efficacy and safety of subcutaneous allergen-specific immunotherapy with depigmented polymerized mite extract in atopic dermatitis. J Allergy Clin Immunol 2012;130:925-31.
118. Guttman-Yassky E, Nograles KE, Krueger JG. Contrasting pathogenesis of atopic dermatitis and psoriasis—part II: immune cell subsets and therapeutic concepts. J Allergy Clin Immunol 2011;127:1420-32.

119. Tintle S, Shemer A, Suarez-Farinas M, Fujita H, Gilleaudeau P, Sullivan-Whalen M, et al. Reversal of atopic dermatitis with narrow-band UVB phototherapy and biomarkers for therapeutic response. J Allergy Clin Immunol 2011;128:583-93.
120. Milliken SVI, Wassall H, Lewis BJ, Logie J, Barker RN, Macdonald H, et al. Effects of ultraviolet light on human serum 25-hydroxyvitamin D and systemic immune function. J Allergy Clin Immunol 2012;129:1554-61.
121. Murota H, Izumi M, El-Latif MIAA, Nishioka M, Terao M, Tani M, et al. Artemin causes hypersensitivity to warm sensation, mimicking warmth-provoked pruritus in atopic dermatitis. J Allergy Clin Immunol 2012;130:671-82.
122. Sugawara K, Bíró T, Tsuruta D, Tóth BI, Kromminga A, Zákány N, et al. Endocannabinoids limit excessive mast cell maturation and activation in human skin. J Allergy Clin Immunol 2012;129:726-38.
123. Bork K, Hardt J, Witzke G. Fatal laryngeal attacks and mortality in hereditary angioedema due to C1-INH deficiency. J Allergy Clin Immunol 2012;130:692-7.
124. Diemert DJ, Pinto AG, Freire J, Jariwala A, Santiago H, Hamilton RG, et al. Generalized urticaria induced by the Na-ASP-2 hookworm vaccine: implications for the development of vaccines against helminths. J Allergy Clin Immunol 2012; 130:169-76.e6.
125. Confino-Cohen R, Chodick G, Shalev V, Leshno M, Kimhi O, Goldberg A. Chronic urticaria and autoimmunity: associations found in a large population study. J Allergy Clin Immunol 2012;129:1307-13.
126. Posthumus J, Tiñana A, MPH, Mozena JD, Steinke JW, Borish L. Autoimmune mechanisms in chronic idiopathic urticaria. J Allergy Clin Immunol 2012;130:814-6.
127. Kirkpatrick CH. CHA mechanism for urticaria/angioedema in patients with thyroid disease. J Allergy Clin Immunol 2012;130:988-90.