Food Allergy Therapy: Is a Cure Within Reach?

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• Food allergy • Immunotherapy • Oral immunotherapy
• Oral desensitization • Milk allergy • Peanut allergy
• Egg allergy • Food allergy therapy

Food allergy is a growing public health problem.[1] In the United States, it is estimated that 3.9% of general population under 18 years of age is affected by food allergies; the prevalence increased by 18% from 1997 to 2007.[2] Currently, the only treatment of food allergy relies on strict food avoidance, dietary management to avoid nutritional deficiencies, and prompt emergency treatment of acute reactions. There is an unmet medical need for an effective food allergy therapy; thus, development of therapeutic interventions for food allergy is a top research priority. Studies concentrate on the foods most commonly implicated in severe IgE-mediated anaphylactic reactions (peanut, tree nuts, and shellfish) and the most common food allergens, such as cow's milk and hen's egg.[3] The promising therapies under investigation can be classified as food allergen-nonspecific and food allergen-specific.[4] The food allergen-nonspecific therapies for food-induced anaphylaxis include monoclonal anti-IgE antibodies, which increase the threshold dose for peanut in peanut-allergic individuals, and Chinese herbs, which prevent peanut anaphylaxis in an animal model and are currently being evaluated in human studies (**Table 1**). The food allergen-specific therapies include oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and epicutaneous immunotherapy (EPIT) with native food allergens (**Table 2**) and mutated recombinant proteins, which have decreased IgE-binding activity, coadministered within heat-killed *Escherichia coli* to generate maximum immune response (**Table 3**).

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Table 1
Allergen-nonspecific therapy for food allergy

Therapy	Mechanism of Action	Effects	Comments
Monoclonal anti-IgE	Binds to circulating IgE, prevents IgE deposition on mast cells, and blocks degranulation. Interferes with the facilitated antigen presentation by B-cell and dendritic cells.	Improves symptoms of asthma and allergic rhinitis; provides protection against peanut anaphylaxis in 75% of treated patients.	Subcutaneous at monthly or 2-week intervals, unknown long-term consequences of IgE elimination; food nonspecific; ongoing studies of combined anti-IgE and milk OIT in children
Traditional TCM	Down-regulation of T_H2 cytokines (IL-4, IL-5, and IL-13), up-regulation of T_H1 cytokines (IFN-γ and IL-12), decreased allergen IgE, decreased T-cell proliferation to peanut.	Reverses allergic inflammation in the airways, affords prolonged protection from peanut anaphylaxis (for ~half of mouse lifespan).	Oral, generally safe and well tolerated; current studies focus on identification of the crucial active herbal components in the multiherb formulas and establishing optimal dosing in phase I and II clinical trials

WHO NEEDS FOOD ALLERGY THERAPY?

Subjects at high risk for severe anaphylaxis and those unlikely to outgrow food allergy spontaneously are most in need of food allergy therapy. Traditional allergy tests (measurement of food allergen-specific IgE antibodies in serum or skin prick test) do not reliably predict the severity of future reactions or the spontaneous development of tolerance. The severity of food-allergic reactions may relate to the diversity of the immune response to IgE-binding epitopes on food allergens (**Fig. 1**). In a peptide microarray-based immunoassay, children with severe reactions to peanut and milk had IgE antibodies that bound to higher number of epitopes than children with mild reactions.[5–7] Persistent milk-allergic children had increased epitope diversity compared with those who outgrew their allergy.[7] Using a competitive peptide microarray assay, allergic patients demonstrated a combination of high-affinity and low-affinity IgE binding whereas those who had outgrown their milk allergy had primarily low-affinity binding.[7] Similarly, persistent egg allergy was associated with recognition of the sequential epitopes on ovomucoid, the major egg white allergen. Subjects who generated IgE antibody responses against both the conformational and sequential epitopes of ovomucoid were likely to have persistent egg allergy. In contrast, subjects who generated IgE antibody responses predominantly against the conformational epitopes of ovomucoid were more likely to have transient egg allergy.[8] Recognition of the specific casein epitopes might identify children at risk for more persistent milk allergy.[9] Persistence of food allergy might be related to high lifetime peak values of food-specific serum IgE antibodies. Two reports describing the natural history of milk and egg allergy in children with multiple food allergies observed that few children with peak milk-specific or egg white–specific IgE antibody levels greater than or equal to 50 kilounits of antibody (kU_A)/L (UniCAP, Phadia, Uppsala, Sweden) outgrew their respective allergy by teenage years.[10,11]