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9. Food allergy

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Food allergy, defined as an adverse immune response to food proteins, affects as many as 6% of young children and 3% to 4% of adults. Food-induced allergic reactions are responsible for a variety of symptoms involving the skin, gastrointestinal tract, and respiratory tract and might be caused by IgE-mediated and non–IgE-mediated (cellular) mechanisms. Our understanding of how food allergy represents an abrogation of normal oral tolerance is evolving. Although any food can provoke a reaction, relatively few foods are responsible for the vast majority of significant food-induced allergic reactions: milk, egg, peanuts, tree nuts, fish, and shellfish. A systematic approach to diagnosis includes a careful history, followed by laboratory studies, elimination diets, and often food challenges to confirm a diagnosis. Many food allergens have been characterized at a molecular level, which has increased our understanding of the immunopathogenesis of food allergy and might soon lead to novel diagnostic and therapeutic approaches. Currently, management of food allergies consists

of educating the patient to avoid ingesting the responsible allergen and to initiate therapy in case of an unintended ingestion. (J Allergy Clin Immunol 2006;117:S470-5.)

Key words: *Food allergy, food hypersensitivity, oral tolerance, gastrointestinal food hypersensitivity, food allergens, anaphylaxis*

Approximately 20% of the population alters their diet for a perceived adverse reaction to food, the cause of which might include a verifiable adverse immune response to a food protein (eg, food allergy), a host-specific metabolic disorder (eg, lactose intolerance), a response to a pharmacologically active (eg, caffeine) or toxic (eg, food poisoning) food component, or nonreproducible adverse reactions, such as food aversions (Table I).[1-4] Food-induced allergic disorders result from immunologic pathways that include activation of effector cells through food-specific IgE antibodies, cell-mediated reactions resulting in subacute or chronic inflammation, or combined pathways. Approximately 6% of young children and 3.7% of adults in the United States have a food allergy.[1,5] In young children the most common causal foods are cow's milk (2.5%), egg (1.3%), peanut (0.8%), wheat (approximately 0.4%), soy (approximately 0.4%), tree nuts (0.2%), fish (0.1%), and shellfish (0.1%). Early childhood allergies to milk, egg, soy, and wheat usually resolve by school age (approximately 80%).[6] Although peanut, tree nut, and seafood allergies are generally considered permanent, 20% of young children with peanut allergy experience resolution by age 5 years (recurrence is also possible).[7,8] Adults are therefore more likely to have allergies to shellfish (2%), peanut (0.6%), tree nuts (0.5%), and fish (0.4%). Reactions to fruits and vegetables are common (approximately 5%) but usually not severe. Allergy to seeds (eg, sesame) is being increasingly reported.[9] Genetic risk factors include a family history of atopic disorders, but environmental factors modulate the expression of food allergy, as evidenced by a recent doubling of the rate of peanut allergy in children.[10]

PATHOGENESIS

Food allergy might result from a breach in oral tolerance to foods while they are being ingested (class 1 food allergy) or might result from sensitization to allergens apart from their exposure to the gastrointestinal tract, recognized instead during respiratory exposure (class 2 food allergy).[11,12] Class 1 food allergy typically occurs to food proteins that are generally stable to digestion that are encountered by infants or children during a presumed window of immunologic immaturity. In contrast, class 2 food allergy is typically the result of sensitization to labile proteins encountered through the respiratory route, such as pollens resulting in IgE antibodies that recognize homologous epitopes on food proteins of plant origin (eg, pollen-food related syndrome). Murine studies[13] and evidence from human epidemiologic studies[14] indicate that class 1 allergens, such as egg and peanut, might evade oral tolerance by initial sensitizing exposure through the skin.

Abbreviation used
SPT: Skin prick test

Gut barrier

The gastrointestinal mucosal barrier is a complex physical (mucus, epithelial cell tight junctions, acid, and enzymes) and immunologic structure.[12] Abrogation of the barrier might promote food allergy; studies neutralizing stomach pH showed increased ability to promote allergic sensitization.[15] Similarly, developmental immaturity of components of the gut barrier (enzymatic activity and sIgA) might account for the increased prevalence of food allergy in infancy. However, a small amount of ingested food antigens is normally absorbed and transported throughout the body in an immunologically intact form, and oral tolerance prevails.[1,12]

Oral tolerance induction

Antigen-presenting cells, especially intestinal epithelial cells and dendritic cells, and regulatory T cells play a central role in oral tolerance.[12,16] Five regulatory T cells have been identified in conjunction with intestinal immunity: T_H3 cells, a population of $CD4^+$ cells that secrete TGF-β; T_R1 cells, $CD4^+$ cells that secrete IL-10; $CD4^+CD25^+$ regulatory T cells; $CD8^+$ suppressor T cells; and γδ T cells. Intestinal epithelial cells process luminal antigen and present it to T cells on an MHC class II complex but lack a second signal, thus suggesting their potential to play a role in tolerance induction.[12] Dendritic cells residing within the lamina propria and noninflammatory environment of Peyer's patches express IL-10 and IL-4, which favor the generation of tolerance.[12,17] Properties of antigens, dose, and frequency of exposure influence tolerance induction. High-dose tolerance involves deletion of effector T cells, whereas low-dose tolerance is mediated by activation of regulatory T cells with suppressor functions.[12]

Commensal gut flora might also influence the mucosal immune response. Gut flora is largely established in the first 24 hours after birth and is dependent on maternal flora and local environment. Studies feeding lactating mothers and their offspring *Lactobacillus GG* suggest that probiotics might be of benefit in preventing atopic dermatitis,[18] possibly by enhancing a T_H1 cytokine response (IFN-γ),[19] but whether they will be useful for preventing food allergy remains to be demonstrated.

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0091-6749/$32.00

doi:10.1016/j.jaci.2005.05.048