Food for thought: the growing problem of food allergy

In the past decade in Westernized countries, the prevalence of allergies to foods has more than doubled, such that 6 to 8% of infants and 2 to 4% of adults now have food allergies. The threat of severe life-threatening reactions (e.g., anaphylaxis) causes anxiety in patients, parents, teachers, and restaurant owners, particularly because even trace amounts of an offending food—often transferred to or unintentionally introduced into a meal—can trigger severe reactions. This puzzle of increasing prevalence, which no one yet understands, has been variously attributed to a Western lifestyle, changes in microbial exposures due to improved hygiene, widespread antibiotic use, an increase in obesity, and changes in the diet.[1,2]

Immunologically, the reactions are caused by exposure to the culprit food, which results in the rapid activation of mast cells armed with food-specific immunoglobulin E (IgE) antibodies produced inappropriately at an earlier time. Although it is clear that at the molecular level IgE production results from isotype switch to IgE in B cells, in response to interleukin 4 (IL-4) and IL-13 produced by T helper 2 (Th2) cells, why these reactions are so much more common today than several decades ago—and why only a few foods, such as chicken eggs, cow's milk, wheat, soy, peanuts, and nuts cause 90% of reactions—is not understood at all. Furthermore, the precise immunological pathways that lead to allergen sensitization in allergic individuals, but to tolerance in nonallergic individuals, are also not understood. Recent provocative studies suggest that potent allergens have protease activity that is sensed by basophils that secrete thymic stromal lymphopoetin and IL-4, which in turn help to induce Th2 immune responses.[3] Others suggest that commensal intestinal bacteria, which can be eliminated by broad-spectrum antibiotics, activate innate immune protective mechanisms, including Toll-like receptor signaling, which can reduce allergen sensitization.[4,5] A predisposition of the neonatal immune system toward Th2 immunity is thought to drive the greater frequency of food sensitivity in infants, but it is not yet known how commensal intestinal flora or infections induce maturation of the intestine and enhance the development of tolerance to foods.

However, prospects for the future of this growing problem are bright, now that the field of mucosal immunology is rapidly advancing, as highlighted by the creation of this journal. Increasing knowledge about immune tolerance and immunology of the intestinal tract should greatly enhance the chances of improving approaches to the prevention and treatment of food allergy. For example, current dietary recommendations for pregnant mothers, whose children may be at risk for developing food allergy, or regarding breast feeding or the timing of solid-food introduction to prevent the development of food allergy in high-risk infants, are confusing at best,[6] in large part because it is not clear whether early exposure to foods sensitizes or tolerizes young infants and neonates. These fundamental issues are only now being addressed—for example, in studies in infants of avoidance versus early oral exposure to food allergens to induce oral tolerance[7] or of breast milk–mediated transfer of antigen, which induces oral tolerance.[8] The results of such experimental studies of the mucosa (intestinal, respiratory, and skin) will eventually have profound implications for clinical practice, leading to new therapies for food-allergic individuals, including oral and sublingual desensitization protocols to induce food-specific tolerance and the development of allergen-specific regulatory T cells or deletion of allergen-specific effector cells, using food antigens with adjuvants, bacterial products,[9] or probiotics[10] that stimulate innate immune system activation. Thus, the results of studies in mucosal immunology and oral tolerance induction are highly anticipated not only by scientists but also by food-allergic patients and their physicians.

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