

Early Introduction of Peanut: New Horizons in Preventing Food Allergy

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Food allergy is a serious healthcare concern, with over 7% of Canadians self-reporting at least one food allergy (1). Common food allergies include egg (affecting 1% of Canadian children), milk (<1%), fish (1%), wheat (<1%), and tree nuts (1.6%) (1). Peanut allergy in particular affects 1-2% of children in westernized countries, and its prevalence has doubled in the past 10 years (2). Peanut allergy is unique in that it is unlikely to be outgrown, persisting in 80% of allergic children into adulthood (3), and it accounts for the majority of fatal reactions to foods (4).

Food allergy impacts the daily habits of food-allergic individuals and their families, as well as the community at large. Bans on allergenic foods, such as peanut, are becoming more common in schools and community locales. The prevention of food allergy is an important medical priority, particularly since there is a marked lack of disease-modifying therapies available for food-allergic individuals. This commentary will discuss the findings from a recent study that may significantly impact the clinical approach to preventing severe food allergies.

Older clinical guidelines recommended the avoidance of common allergenic foods in infancy and early childhood as a means of preventing food allergy. These guidelines were in place in Canada until as recently as 2013 and were largely based on consensus rather than direct evidence (5).

Over the past decade, evidence began to emerge that cast doubt on the protective benefit of delayed introduction of allergenic foods. One such study observed that the prevalence of peanut allergy in Jewish children in the United Kingdom was 10-fold higher when compared to Israeli Jewish children of similar ancestry. This discordance in peanut allergy prevalence correlated with differences in timing of peanut introduction into the diet: children in the U.K. generally did not consume peanuts in the first year of life, while Israeli children were routinely eating peanuts

starting at 7 months of age (6).

The Learning Early About Peanut Allergy (LEAP) Study, lead by Dr. Gideon Lack, was established in 2006 to investigate whether early dietary introduction of peanut could prevent peanut allergy. The results of this landmark study were published in the February 2015 edition of the *New England Journal of Medicine* (7).

The LEAP Study enrolled 640 infants aged 4 – 11 months who were considered at risk for peanut allergy due to the presence of severe eczema, egg allergy, or both. Participants were randomized to either avoid or regularly consume peanuts until 60 months of age. They were also stratified into separate cohorts according to the presence or absence of a preexisting sensitivity to peanut as defined by skin prick test: sensitized children had a wheal size of 1-4 mm and unsensitized children had no measurable wheal size. The primary outcome of the study was the proportion of participants with clinical peanut allergy at 60 months of age, as defined by oral food challenge.

The results of the LEAP Study were remarkable. In the unsensitized cohort, 13.7% of children who had been randomized to avoid peanut had clinical peanut allergy at 60 months compared with 1.9% of unsensitized children who had been randomized to consume peanut ($p < 0.001$). This represented an 86.1% relative reduction in the prevalence of peanut allergy. In the peanut-sensitized cohort, 35.3% of children in the avoidance group and 10.6% of children in the consumption group had peanut allergy at 60 months ($p = 0.004$). This represented a 70% relative reduction in the prevalence of peanut allergy. Peanut-specific serum antibodies were also measured over the course of the study. Children who consumed peanut had increased peanut-specific IgG4, while children who avoided peanut had elevated titers of peanut-specific IgE and a lower ratio of peanut-specific IgG4:IgE. IgE antibodies coat

the surface of allergic effector cells and activate these cells upon allergen binding, while IgG4 antibodies are thought to be protective in allergy due to their ability to bind allergen in circulation and block its IgE-binding capacity (8). The LEAP Study authors concluded that in infants at high risk of developing peanut allergy, peanut consumption in the first year of life significantly reduced the prevalence of peanut allergy by five years of age.

The concept of oral tolerance has been known since 1946, when Merrill Chase demonstrated that feeding guinea pigs the contact sensitizing agent 2-dinitrochlorobenzene rendered them hyporesponsive to subsequent intracutaneous exposures to the drug (9). The LEAP Study is the first randomized control trial to directly demonstrate the ability of early oral exposure to prevent clinical food allergy in both sensitized and unsensitized children. Subsequent clinical studies are evaluating the feasibility of extending this early exposure regimen to other food allergens and cohorts of low risk children (10). A recent study led by McMaster University investigator Maxwell Tran has found that early introduction of eggs and milk is protective against the development of allergies to these foods (11). These findings may help shape future clinical guidelines and food allergy prevention strategies

Beyond these clinical implications, the LEAP Study findings lend credence to the theory that route of initial antigen exposure can dictate the nature of the antigen-specific immune response, be it tolerance or allergy. There is mounting evidence that early exposure to peanut through the skin may lead to allergic sensitization (12, 13), and the LEAP study has demonstrated that early oral exposure can lead to tolerance. Further research in this area will lead to a greater understanding of the biological mechanisms driving allergic sensitization and immune tolerance. ■

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