

Good News for Toddlers with Peanut Allergy

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In this issue of the *Journal*, Greenhawt and colleagues report the findings of the EPITOPE (Epicutaneous Immunotherapy in Toddlers with Peanut Allergy) trial, a phase 3, multinational, double-blind, randomized, placebo-controlled trial of Viaskin Peanut 250 μ g, a patch that delivers peanut protein to the skin to desensitize young children with peanut allergy.¹ The trial, which involved toddlers 1 to 3 years of age, met its clinical end points, and the product, if approved, could eventually be used in this population. The primary finding is that after receiving treatment with the peanut patch for a year, 67.0% of the toddlers in the intervention group could safely ingest the peanut-protein equivalent of approximately three to four peanuts or approximately one peanut, depending on how sensitive to peanut they were at baseline. In the placebo group, 33.5% of the children reached this end point.

Food allergy is common in most areas of the world, and its prevalence seems to be increasing. Peanut allergy, one of the most common food allergies, develops primarily in the early years of life and, in 70 to 80% of cases, remains a problem into adulthood. For many decades, avoidance has been the standard approach for the management of food allergies, but accidental exposures with potentially serious systemic allergic reactions (i.e., anaphylaxis) can occur. In 2020, the Food and Drug Administration approved the use of an oral form of peanut allergen immunotherapy for patients 4 to 17 years of age.² This is the only approved treatment for any form of food allergy; however, published studies suggest that oral immunotherapy with other foods, such as egg and milk, may also be effective. As a result, many practitioners have been using orally delivered foods for the same purpose for approximately a decade.

The peanut patch offers an epicutaneous immunotherapy approach. Here, peanut allergens are delivered to the skin and appear to induce some of the same immunologic effects as other forms of allergen immunotherapy, such as suppressing the levels of allergen-specific IgE anti-

bodies and increasing the production of IgG4, which is postulated to inhibit allergic reactions. Animal models of epicutaneous immunotherapy suggest that cutaneous dendritic cells play a role in initiating the immunologic effects, but much remains to be learned about the operative mechanisms of this approach in humans.

Peanut allergy can be very substantially reduced if peanut is introduced into the diet as early as 4 to 6 months of age.³ Early dietary introduction to prevent peanut allergy in children is now part of practice guidelines around the world, but the implementation is lagging. In addition, questions have arisen regarding the effectiveness of early dietary introduction of peanut in real life.⁴ This uncertainty is to some extent due to the lack of knowledge regarding the appropriate range of the peanut-protein dose, the age at introduction, and the frequency and duration of peanut consumption needed to induce long-term tolerance. Even after the appropriate prevention approaches are applied, the eradication of peanut allergy is unlikely, and the need for effective treatments will remain. Toddlers are of particular interest since their immune systems have plasticity that can theoretically allow for higher efficacy and longer-lasting benefits from allergen immunotherapy after therapy is discontinued.

It is important to consider the pros and cons of epicutaneous and oral peanut immunotherapy, since the parents and clinicians of children with peanut allergy may eventually need to choose between these two treatments. A trial of peanut oral immunotherapy that did not involve the use of the commercially available product was recently conducted among children 1 to 3 years of age (the Oral Immunotherapy for Induction of Tolerance and Desensitization in Peanut-Allergic Children Trial [IMPACT]).⁵ The characteristics of the participants in the IMPACT population were similar to those in the EPITOPE trial except that the median age was approximately 10 months older and the median peanut-specific serum IgE level at baseline was higher in the IMPACT population than in the EPITOPE population. Although

the results from two separate trials cannot be directly compared, the data suggest that oral immunotherapy may have a stronger protective effect than the effect reported in the EPITOPE trial. For example, an outcome that was evaluated in both trials was the percentage of participants who had received the highest cumulative dose of peanut at the end of the trial, amounting to at least 10 peanuts, without having an allergic reaction. In the EPITOPE trial, 37% of the children in the intervention group and 10% of those in the placebo group had this result, as compared with 71% and 2%, respectively, in the IMPACT trial. These results should be considered cautiously, because the outcome was determined after 2 years of intervention in the IMPACT trial and after only 1 year in the EPITOPE trial. On the other hand, epicutaneous immunotherapy appears to have a better safety profile than oral immunotherapy. For example, allergic reactions that resulted in the administration of epinephrine occurred in 10% of the children in the intervention group in the EPITOPE trial and in 22% of those in the IMPACT trial. Also, eosinophilic esophagitis was seen in 3% of the children in the IMPACT trial who had received oral peanut immunotherapy.

Many patients, whether children or adults, have multiple food allergies, and the development of treatment should take this fact into account. Successful studies of multifoed oral immunotherapy have been conducted, so the development of multifoed skin patches may also

be possible. Simpler approaches, such as targeting IgE, the culprit behind all food allergies, or targeting the mast cell, the ultimate effector cell, are also being evaluated. New concepts that use various immunomodulators together with allergen immunotherapy are being considered. The EPITOPE trial results are very good news for toddlers and their families as the next step toward a future with more treatments for food allergies.

The opinions expressed in this editorial do not necessarily represent the views of the National Institute of Allergy and Infectious Diseases, the National Institutes of Health, or any other agency of the United States government.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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