

## EDITORIAL



## Preventing Food Allergy in Infancy — Early Consumption or Avoidance?

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Food allergy among children is common, affecting up to 8% of children younger than 3 years of age.<sup>1</sup> It can be serious, even fatal, with hospital-discharge data from the United States documenting an increasing trend of food-induced anaphylaxis.<sup>2</sup> In order to minimize accidental exposure to foods to which a child could be allergic, many schools in the United States have a “no sharing” policy for food.<sup>3</sup> For decades, we had been trying to stem the rising tide of food allergy by urging parents to avoid exposing their children to foods such as egg, peanut, and fish early in life — a recommendation that was based on the idea that early exposure led to allergic sensitization. A year ago, the compelling results of the Learning Early about Peanut Allergy (LEAP) trial turned this idea on its head by showing that the early consumption of peanut by high-risk infants dramatically decreased their risk of the development of peanut allergy.<sup>4</sup> On the basis of such evidence, a joint consensus communication from 10 national and international medical societies was published, providing guidance on how to introduce peanut in high-risk infants as a primary preventive strategy.<sup>5</sup>

Peanut is just one of the many food allergens. Will the approach from the LEAP trial be effective in the general population? What about allergies to other common foods such as milk, egg, and fish? Perkin et al.<sup>6</sup> now attempt to answer these questions in the *Journal* in their trial, Enquiring about Tolerance (EAT). The investigators studied previously exclusively breast-fed infants from the general population and hypothesized that the early introduction of six allergenic foods into the infant’s diet starting at 3 months would

lead to the prevention of allergy to at least one of these foods.

More than 1300 infants were randomly assigned to the introduction of six allergenic foods (early-introduction group) or to the standard U.K. recommendation of exclusive breast-feeding to approximately 6 months of age (standard-introduction group). The parents of the infants in the early-introduction group were instructed to feed them 3 rounded teaspoons of smooth peanut butter, one small egg, two portions (40 to 60 g) of cow’s milk yogurt, 3 teaspoons of sesame paste, 25 g of white fish, and two wheat-based cereal biscuits every week. All the children were assessed regularly until they reached 3 years of age. In the intention-to-treat analyses, the primary outcome of the percentage of participants with food allergy to one or more of the six foods was 5.6% in the early-introduction group and 7.1% in the standard-introduction group. The difference did not reach statistical significance.

When the study was designed, the investigators were aware that this treatment protocol was very demanding — less than half the participants in the early-introduction group (42.8%) adhered to the trial protocol. However, a per-protocol analysis showed that the primary outcome was significantly lower in the early-introduction group (2.4%) than in the standard-introduction group (7.3%), which suggests that this approach is effective if the parents and infants are able to adhere to the protocol. Although it is easy to assume that the reason the intention-to-treat analysis did not show a difference could be attributed to a lack of adherence to the protocol, I urge caution with this interpretation. It is possible that other

explanations, such as reverse causality, may result in the observed differences between the intention-to-treat analysis and the per-protocol analysis. If the parents and infants did not adhere to the protocol because eating a given food led to subtle avoidance behaviors, the parents would stop trying to feed it to the infants.

Although the trial showed that the early introduction of these allergenic foods was safe, the low rate of adherence that was documented in the trial suggests that the introduction of such a demanding protocol is likely to be even lower in real-life settings, which makes the early-feeding approach ineffective. In the EAT trial, the rate of adherence was the highest for dairy products in the form of yogurt, as opposed to textural food such as egg. This difference may well be due to the rather immature oral motor skills of young infants at 3 to 4 months of age and also to concerns of the parents about choking. If feeding these foods is safe, what is the minimal amount needed for inducing tolerance to these foods? Will the regimen be as effective if we introduce these foods at a later age but early enough before sensitization may occur? How can we improve the preparation of foods to make them easier for parents to administer? These questions must be

addressed before we can hope that an early-feeding strategy will be effective at a population level. In the meantime, evidence is building that early consumption rather than delayed introduction of foods is likely to be more beneficial as a strategy for the primary prevention of food allergy. So feed your children and hope that they will EAT.

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