

# Consensus Communication on Early Peanut Introduction and Prevention of Peanut Allergy in High-Risk Infants

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**Abstract:** The purpose of this brief communication is to highlight emerging evidence regarding potential benefits of supporting early rather than delayed peanut introduction during the period of complementary food introduction in infants. This document should be considered as interim guidance based on consensus among the following organizations: American Academy of Allergy, Asthma, and Immunology, American Academy of Pediatrics, American College of Allergy, Asthma, and Immunology, Australasian Society of Clinical Immunology and Allergy, Canadian Society of Allergy and Clinical Immunology, European Academy of Allergy and Clinical Immunology, Israel Association of Allergy and Clinical Immunology, Japanese Society for Allergology, Society for Pediatric Dermatology, and World Allergy Organization. More formal guidelines regarding early-life, complementary feeding practices and the risk of allergy development will follow in the next year from the National Institute of Allergy and Infectious Diseases—sponsored Working Group and the European Academy of Allergy and Clinical Immunology.

Peanut allergy is an increasingly troubling global health problem, affecting 1% to 3% of children in many westernized countries. Although multiple methods of measurement have been used, and specific estimates differ, there appears to be a sudden increase in the number of cases in the past 10 to 15 years, such that the prevalence may have tripled in some countries, such as the United States. Extrapolating the currently estimated prevalence, this means nearly 100,000 new cases annually (in the United States and United Kingdom), affecting approximately 1 in 50 primary school-age children in the United States, Canada, United Kingdom, and Australia. A similar increase in incidence is now being noted in developing countries, such as Ghana (1–6).

The purpose of this brief communication is to highlight emerging evidence regarding potential benefits of supporting early rather than delayed peanut introduction during the period of complementary food introduction in infants. A recent study, “Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy (Learning Early about Peanut Allergy —LEAP Trial),” demonstrated an 11% to 25% absolute reduction in the risk of developing peanut allergy in high-risk infants (and a relative risk reduction of up to 80%) when peanuts were introduced between 4 and 11 months of age (7). In light of the significance of these findings, this document serves to better inform the decision-making process for health care providers regarding the potential benefits of early peanut introduction. More formal guidelines regarding early life complementary feeding practices and the risk of allergy development will follow in the next year from a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored Working group and the European Academy of Allergy and Clinical Immunology (EAACI), and thus this document should be considered as interim guidance.

## **Summary of new evidence**

In the LEAP trial, 640 high-risk UK infants (Box 1) ages 4 to 11 months were randomized to consume peanut products at least three times per week (6 g of peanut protein; equivalent to 24 g of peanuts or 3 teaspoons of peanut butter per week) or to completely avoid peanut products for the first 5 years of life. This included 542 infants found to have negative skin prick tests (SPTs) to peanut at study entry and 98 infants with SPT wheal diameters to peanut of 1 to 4 mm (minimally SPT positive) at study entry. An additional 76 children were excluded from study entry before randomization based on an SPT of 5 mm or greater. These children were assumed to have a very high likelihood of reacting to a peanut challenge. In an intention-to-treat analysis, 17.2% in the peanut avoidance group and 3.2% in the peanut consumption group developed food challenge–proven peanut allergy by the age of 5 years, corresponding to a 14% absolute risk reduction, a number needed to treat (NNT; number of persons needed to be treated for one to receive benefit) of 7.1, and a relative risk reduction of 81% (7).

When examined in further detail, the isolated beneficial effects for the primary and secondary prevention of peanut allergy translated to an NNT of 8.5 in the SPT-negative infants and an NNT of 4 in the minimally SPT-positive infants. Secondary analyses showed similar levels of prevention in white, black, and South Asian (Indian and Pakistani) children. Overall, the risk of early introduction in this group was low; 7 of the 319 children randomized to the consumption group reacted to peanut at the baseline food challenge, suggesting that peanut food challenge and introduction, even in minimally SPT-positive infants, is safe and feasible. Six children in the consumption group developed peanut allergy during the study, indicating that peanut allergy can still develop despite attempts at primary and secondary prevention. Finally, the LEAP trial included only high-risk infants with a minimal or negative SPT to peanut and therefore does not address a strategy for those without these risk factors for developing peanut allergy (7).

## **How does the LEAP trial affect present guidance for early complementary feeding practices?**

Existing guidelines pertaining to the early introduction of complementary foods have indicated that the introduction of highly allergenic foods, such as peanuts, need not be delayed past 4 or 6 months of age, although they do not actively recommend introduction of peanuts between 4 and 6 months of age in high-risk infants, and some of these guidelines specify that certain infants considered at high risk for the development of allergic disease should first consult an expert (8–14).

The LEAP data provide level 1 evidence that the practice of early peanut introduction is safe and effective in selected high-risk infants. This study is the first prospective randomized trial of early peanut intervention and informs provider decision making regarding high-risk infants, including those who already have a positive peanut SPT but are not yet clinically reactive, receiving the benefits noted in the LEAP trial, which may reduce the risk of developing peanut allergy up to 81%.

Because children with less severe risk factors for peanut allergy were excluded from enrollment in the LEAP trial, there are no prospective, randomized data investigating the benefit or risk of early peanut introduction in the general population or those at low risk. Consequently this communication's guidance is limited to integrating the findings learned in the LEAP trial to other similar high-risk children in more diverse settings around the world, although multiple guidelines have not recommended delaying allergen introduction in general and low-risk populations.

### **Interim guidance regarding early peanut introduction**

Based on data generated in the LEAP trial and existing guidelines, the following interim guidance is suggested to assist the clinical decision making of health care providers.

There is now scientific evidence (level 1 evidence from a randomized controlled trial) that health care providers should recommend introducing peanut-containing products into the diet of "high-risk" infants early in life (4–11 mos old) in countries where peanut allergy is prevalent, because delaying the introduction of peanuts may be associated with greater risk of developing peanut allergy.

Infants with early onset atopic disease, such as severe eczema, or egg allergy in the first 4 to 6 months of life (see Box 1 for LEAP criteria) may benefit from evaluation by an allergist or physician trained in the management of allergic diseases in this age group regarding the appropriateness of early peanut introduction. Evaluation of such patients may consist of performing peanut skin testing or in-office observed peanut ingestion as deemed appropriate after discussion with the family. The clinician may perform an observed peanut challenge for those with evidence of a positive peanut skin test to determine whether they are clinically reactive before initiating at-home peanut introduction. Both such strategies were used in the LEAP trial protocol.

Adherence in the LEAP trial was excellent (92%), with infants randomized to consume peanuts ingesting a median of 7.7 g of peanut protein (interquartile range 6.7–8.8 g) per week during the first 2 years of the trial, compared with a median of 0 g in the avoidance group (see Box 2 for examples of peanut-containing foods used in the LEAP trial). Although the outcome of the LEAP regimen was excellent, the study does not address the use of alternative doses of peanut protein, minimal length

of treatment necessary to induce the tolerogenic effect, or potential risks of premature discontinuation or sporadic feeding of peanuts.

### **Rationale for evaluating and applying this policy to a high-risk population**

The LEAP trial demonstrates that peanuts can be successfully introduced early in a high-risk population (e.g., the population defined in the LEAP trial). However, without intervention by health care providers, there is the potential that the introduction of allergenic foods into the diet of high-risk infants will be delayed because of the widespread belief that such foods may exacerbate eczema.

There will be more extensive guidelines in the near future from the NIAID Working Group and EAACI Guidelines Group and their multidisciplinary stakeholders. These groups will consider all the available data and determine whether there is sufficient evidence to apply prevention strategies to the general population. Engagement of the primary care, allergy, and dermatology communities to implement these findings rapidly and change the culture of early feeding practices is essential, and the forthcoming NIAID Working Group and EAACI Guidelines Group documents will clarify a best practices approach.

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## Figures

### Box 1

#### *Enrollment Criteria Used in the LEAP Trial*

Infants considered at “high risk” as defined by the LEAP trial criteria:

*Egg allergy*: Children with either

1. An SPT wheal diameter  $\geq 6$  mm from exposure to raw hen’s egg white and no history of previous egg tolerance, or

2. An SPT wheal diameter  $\geq 3$  mm from exposure to pasteurized hen's egg white and allergic symptoms related to exposure to hen's egg.

*Severe eczema:* An eczematous rash that

1. Requires the application of topical creams or ointments containing corticosteroids or calcineurin inhibitors and, if the participant is  $< 6$  months of age, lasted for at least 12 out of 30 days on two occasions or, if  $> 6$  months of age, lasted for at least 12 out of 30 days on two occasions in the last 6 months, or
2. Is currently or was previously graded  $\geq 40$  using the modified SCORAD evaluation.

Example of method of SPT: used in the LEAP trial

- SPT to peanut extract done in the presence of a negative control and a positive histamine control.
- SPT should be performed in duplicate and the maximum wheal diameter of the two SPTs should be calculated and rounded up to the greatest whole millimeter.

In the LEAP trial, the measurement of IgE reaction to peanut resulted in considerably higher rates of sensitization than skin testing, which could lead to numerous unnecessary oral peanut challenges.

SPT = skin prick test.

## **Box 2**

*Examples of Peanut-Containing Foods Used in the LEAP Trial*

- Smooth peanut butter (1 teaspoon) mixed with milk or with mashed or pureed fruit
- Bamba snack\* (Osem; 25-g bag, 21 sticks)—for young infants ( $< 7$  mos), softened with 20 to 30 mL of water or milk and mixed with milk or with mashed or pureed fruit or vegetables
- Peanut soup
- Finely ground peanuts mixed into other foods, such as yogurt

\*Other foods more customary to particular nations or cultures may be substituted.

Whole peanuts are not recommended for introduction because they are a choking hazard in children younger than 4 years.