PEDIATRICS PERSPECTIVES

The Benefits of New Guidelines to Prevent Peanut Allergy

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Peanut allergy appears to have tripled in prevalence in the United States since 1997 and now affects 1% to 2% of children.[1] The high prevalence, severity, and life-long persistence of peanut allergy have generated intense interest in prevention strategies. Initially, such strategies focused on allergen avoidance, but a key observation, the 10-fold higher rate of peanut allergy among Jewish children in the United Kingdom compared with Israeli children of similar ancestry, suggested an alternative approach.[2] A notable difference between these populations was the almost complete lack of peanut ingestion in the first year of life in the United Kingdom compared with substantial consumption among Israeli infants. Based on this observation, the National Institutes of Health–sponsored Learning Early About Peanut Allergy (LEAP) trial randomized 640 infants between 4 and 11 months of age with severe eczema and/or egg allergy to consume or avoid peanut-containing foods until 60 months of age.[3] The study excluded infants with large (>4 mm) positive skin prick tests (SPTs) to peanut, assuming many were already allergic, and stratified the enrolled infants as having no peanut SPT wheal or having one that was 1 to 4 mm in diameter. In the intention-to-treat population with negative SPT (n = 530), the prevalence of peanut allergy at 60 months of age was 13.7% in the avoidance group versus 1.9% in the consumption group (P < .001; 86.1% relative risk reduction), and among those in the SPT positive group (n = 98), the prevalence of peanut allergy was 35.3% in the avoidance group and 10.6% in the consumption group (P = .004; 70% relative risk reduction).

Since the publication of the LEAP study, follow-up of this study population showed that the effect was durable because a subsequent 12-month period of peanut avoidance was not associated with an increased rate of peanut allergy[4] and safe because it did not affect duration of breastfeeding nor negatively impact growth or nutrition.[5] An additional study evaluating early introduction of allergenic foods in an infant cohort recruited from the general population suggested a prevention effect from early introduction of peanut at lower amounts than achieved in the LEAP trial, providing some evidence that generalizing the approach may be beneficial.[6,7]

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TABLE 1 Summary of Addendum Guidelines

Infant Criteria	Recommendations	Earliest Age of Peanut Introduction
Guideline 1. Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE or SPT and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods.	4–6 mo
Guideline 2. Mild to moderate eczema	Introduce peanut-containing foods.	Around 6 mo
Guideline 3. No eczema or any food allergy	Introduce peanut-containing foods.	Age appropriate and in accordance with family preferences and cultural practices

See Togias et al[7] for full discussion of criteria, screening tests, and modality of introduction of peanut.

In 2010, comprehensive food allergy guidelines were published by a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored expert panel (EP), before there was evidence for preventing peanut allergy.[8] In 2015, based on the results of the LEAP study, the NIAID invited members of the 2010 guidelines coordinating committee and other stakeholders to update the 2010 guidelines with an addendum focused on peanut allergy prevention. The oversight coordinating committee, which included the American Academy of Pediatrics (AAP), established an EP to draft the addendum guidelines. The full process is detailed, along with the resulting recommendations and rationale, in the Addendum Guidelines for the Prevention of Peanut Allergy in the United States, Report of the NIAID-Sponsored Expert Panel (www.niaid.nih.gov/sites/default/files/addendum-peanut-allergy-prevention-guidelines.pdf).[7]

The EP developed 3 addendum guidelines, which have been endorsed by the AAP. Each guideline focuses on a different risk group (Table 1). Guideline 1 addresses the highest risk group, those with severe eczema, egg allergy, or both, and is largely based on the LEAP results. Definitions of severe eczema and egg allergy are delineated in the guideline. Briefly, severe eczema is defined in the guidelines as persistent or frequently recurring eczema with typical morphology and distribution assessed as severe by a health care provider and requiring frequent need for prescription-strength antiinflammatory agents, such as corticosteroids or calcineurin inhibitors, despite appropriate use of emollients. The guideline recommends that these high-risk infants have peanut-containing foods introduced as early as 4 to 6 months of age, after other solid food(s) to ensure that the infant is developmentally ready. Allergy testing is advised before peanut introduction. Testing can include a peanut SPT or may begin with serum food-specific IgE testing (sIgE), which, although not used for screening in the LEAP study, is more widely available and, if negative, may reduce referrals and enable more timely initiation of dietary peanut. Actions are based on the test results, which may include home or physician-supervised feeding or exclusion of peanut-containing foods if the child is peanut allergic. For example, if the peanut sIgE is positive ($\geq$0.35 kU_A/L), referral to a specialist with training and experience to perform and interpret SPT and oral food challenges and to manage their risks is recommended. Performing allergy tests to multiple foods is not recommended because of their poor positive predictive value. The EP considered the quality of evidence for this guideline to be "moderate" rather than "high" because it is based on 1 study and considered the contribution of expert opinion to be significant. However, it is notable that the LEAP study showed a strong effect size and statistical significance (as noted above), was randomized, used gold-standard double-blind, placebo-controlled feeding tests, and had excellent adherence (92%) and retention (98.4%).

The guideline also discusses the manner of peanut introduction according to the test results, whether at home or under physician supervision.

Guidelines 2 and 3 address lower-risk populations, extrapolating evidence from LEAP. Guideline 2 suggests that infants with mild or moderate eczema, a group also at increased risk of peanut allergy, should have peanut introduced "around 6 months of age, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy." These infants may have peanut introduced at home after successful ingestion of other solid food(s), without an in-office evaluation, although some may desire an evaluation. The recommendation considers data from participants in the LEAP study with egg allergy but without severe eczema, as well as the notion that the mechanism of protection (antigen-specific oral tolerance) is likely to be the same across groups. Addendum guideline 3 addresses infants without eczema or food allergy, suggesting that peanut be introduced "freely" into the diet together with other solid foods "in accordance with family preferences and cultural practices." This Guideline recognizes that 14% of children who become peanut allergic lack these risk factors in infancy. Therefore, including this group in early introduction is expected to be safe and contribute on a societal basis to peanut allergy prevention.

The guidelines emphasize using "infant safe" forms of peanut, for example peanut butter thinned with warm water or mixed into pureed fruit or vegetables, because peanuts and peanut butter given alone are choking hazards. Advice is provided regarding the amount to feed weekly, and instructions are provided for home and office introduction.

For addendum guideline 1, we recognize that introduction of solids at 4 to 6 months (not before 4 months) departs from other guidelines that call for exclusive breastfeeding for about 6 months,[9] and this change may engender concerns that pediatricians will need to address. In this regard, guidelines calling for exclusive breastfeeding through 6 months predate the LEAP study results and do not specifically address allergy prevention. Furthermore, infants who either consumed or avoided peanut in the LEAP cohorts did not differ in the duration or frequency of breastfeeding and were indistinguishable in nutritional and metabolic parameters at 12, 30, and 60 months of age.[5] The introduction of dietary peanut at 4 to 6 months under guideline 1 should enable more high-risk infants to benefit because fewer will be sensitized to peanut, and fewer will have evolved to clinical peanut allergy and thus be ineligible for this prevention strategy. The LEAP infants were less likely to benefit from dietary peanut if they had a positive skin test or sIgE to peanut by the time peanut was started.

Under guideline 1, the initiation of dietary peanut at 4 to 6 months coincides with visits for well-baby care and immunizations, allowing time for discussion and decision-making, and clinical follow-up (eg, amount and frequency of peanut consumption, parental concerns). However, at-risk infants beyond 6 months of age should also be started on peanut because they are anticipated to benefit.

Many parents and pediatricians have long-held anxieties about feeding peanut-containing foods to young infants, and we are mindful that this may contribute to the many challenges in implementing new "active" guidance to introduce peanut early. However, we hope that pediatricians will embrace this new opportunity to prevent a serious and potentially chronic and costly disease, and we encourage adoption and promulgation of the new guidelines in clinical practice. Backed by high-level evidence, there is a clear rationale on which this intervention is based[3,10]; this was not the case for the previous AAP recommendations espousing avoidance.[11]

There are potential limitations in extrapolating the results of a single study to the general population. However, the prospect of clinical benefit that emerges from the LEAP study is too strong to ethically justify more randomized studies of peanut consumption versus complete avoidance. There are also potential barriers to immediate and full implementation; for example, fear of a reaction, costs of testing and coverage under health care plans, and availability of specialists. Fears of a reaction may be largely allayed by the observation that in the LEAP study, only 7 of 319 infants randomized to consumption reacted at their initial supervised feeding and the reactions were generally mild, successfully treated with antihistamines, and did not require epinephrine.

Individual health care providers, professional societies, insurers, and other stakeholders will need to monitor progress and address resource needs, but reducing the number of persons with costly life-long peanut allergy is likely to have a high return on investment considering the cost of prevention is "only peanuts." We therefore encourage all health care providers to familiarize themselves with the addendum guidelines and operationalize this intervention in their practices.

ABBREVIATIONS

AAP: American Academy of Pediatrics
EP: expert panel
LEAP: Learning Early About Peanut Allergy
NIAID: National Institute of Allergy and Infectious Diseases
sIgE: serum food-specific IgE antibody
SPT: skin prick test

Diseases (NIAID) expert panel and as the American Academy of Pediatrics representative of the coordinating committee of the updated guidelines discussed in this article; Dr Eichenfield served as a member of the expert panel and as the American Academy of Dermatology representative of the coordinating committee of the updated guidelines discussed in this article; Dr Sampson served as a member of the NIAID expert panel of the updated guidelines discussed in this article; is a consultant to Allertein Therapeutics, developing nanoparticle-based therapy for treating peanut allergy; and is employed by DBV Technologies, developing a patch for epicutaneous treatment of food allergies; and Dr Rotrosen has indicated he has no potential conflicts of interest to disclose.

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