GUIDELINES

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Addendum guidelines for the prevention of peanut allergy in the United States

Summary of the National Institute of Allergy and Infectious Diseases-sponsored expert panel

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INTRODUCTION

Food allergy is an important public health problem because it affects children and adults, it may be severe and even life-threatening, and it may be increasing in prevalence. Beginning in 2008, the National Institute of Allergy and Infectious Diseases (NIAID), working with other organizations and advocacy groups, led the development of the first clinical guidelines for the diagnosis and management of food allergy. These guidelines (1), which were published in 2010, did not offer strategies for the prevention of food allergy due to a lack of definitive studies at the time.

In February 2015, the *New England Journal of Medicine* published the results of the "Learning Early about Peanut Allergy" (LEAP) trial. This landmark clinical trial showed that introduction of peanut products into the diets of infants at high risk of developing peanut allergy was safe and led to an 81 percent relative reduction in the subsequent development of peanut allergy. The LEAP trial results, combined with other emerging data, strongly suggested that peanut allergy can be prevented through introduction of peanut-containing foods beginning in infancy. This growing body of evidence raised the need for clinical recommendations focusing on peanut allergy prevention.

To achieve this goal and its wide implementation, NIAID invited the members of the 2010 Guidelines Coordinating Committee and other stakeholder organizations to develop this addendum on peanut allergy prevention to the 2010 Guidelines for the Diagnosis and Management of Food Allergy in the United States.

DEVELOPMENT OF THE 2017 ADDENDUM TO THE 2010 GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF FOOD ALLERGY

Coordinating Committee

The NIAID established a Coordinating Committee (CC), whose members are listed in Appendix A, to oversee the development of the addendum; review drafts of the addendum for accuracy, practicality, clarity, and broad utility of the recommendations in clinical practice; review and approve the final addendum; and disseminate the addendum. The CC members represented 26 professional organizations, advocacy groups, and federal agencies.

Expert Panel

In June 2015, the CC convened an Expert Panel (EP) that was chaired by Joshua Boyce, MD. The 26 panel members, listed in Appendix B, were specialists from a variety of relevant clinical, scientific, and public health areas. Panel members were nominated by the CC organizations, and the composition of the panel received unanimous approval by the CC member organizations.

The charge to the EP was to use the literature review prepared by the NIAID, in conjunction with consensus expert opinion and EP-identified supplementary documents, to develop evidence-based recommendations for the early introduction of dietary peanut to prevent peanut allergy. The new guidelines are intended to supplement and modify Guidelines 37 to 40 in Section 5.3.4 of the 2010 Guidelines: (1) "Prevention of Food Allergy."

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Literature Review

NIAID staff conducted a literature search of PubMed, limited to the years 2010 (January) to 2016 (June). Sixty four publications (original research articles, editorials/letters, and systematic reviews) were deemed relevant and placed into 2 tiers: tier 1 contained 18 items, considered highly relevant to the early introduction of peanut or other allergenic foods; and tier 2 contained 46 items on related topics such as food allergy or eczema prevention.

Assessing the Quality of the Body of Evidence

For the tier 1 references, the EP assessed the quality using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Preparation of the Addendum

Draft versions of the addendum were reviewed by the CC members, open to public comment, revised accordingly, and approved by the EP and the CC.

DEFINING THE STRENGTH OF EACH CLINICAL GUIDELINE

The EP has used the verb "recommends" or "suggests" for each clinical recommendation. These words convey the strength of the recommendation, defined as follows:

- *Recommend* is used when the EP strongly recommended for or against a particular course of action.
- *Suggest* is used when the EP weakly recommended for or against a particular course of action.

ADDENDUM GUIDELINES

The EP came to consensus on the following 3 definitions used throughout the addendum guidelines.

- *Severe eczema* is defined 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 topical corticosteroids, calcineurin inhibitors, or other anti-inflammatory agents despite appropriate use of emollients.
- *Egg allergy* is defined as a history of an allergic reaction to egg and a skin prick test (SPT) wheal diameter of 3 mm or greater with egg white extract, or a positive oral egg food challenge result.
- A *specialist* is defined as a health care provider with the training and experience to (1) perform and interpret SPTs and oral food challenges (OFC) and (2) know and manage their risks. Such persons must have appropriate medications and equipment on site.

Table 1 provides a summary of the addendum guidelines to be used as a quick summary.

Addendum Guideline 1

The EP recommends that infants with severe eczema, egg allergy, or both have introduction of age-appropriate peanut-containing food as early as 4 to 6 months of age to reduce the risk of peanut allergy. Other solid foods should be introduced before peanut-containing foods to show that the infant is developmentally ready. The EP recommends that evaluation with peanut-specific IgE (peanut sIgE) measurement, SPTs, or both be strongly considered before introduction of peanut to determine if peanut should be introduced and, if so, the preferred method of introduction. To minimize a delay in peanut introduction for children who may test negative, testing for peanut sIgE may be the preferred initial approach in certain health care settings, such as family medicine, pediatrics, or dermatology practices, in which skin prick testing is not routine. Alternatively, referral for assessment by a specialist may be an option if desired by the health care provider and when available in a timely manner.

TABLE 1. *Summary of Addendum Guidelines 1, 2, and 3*

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

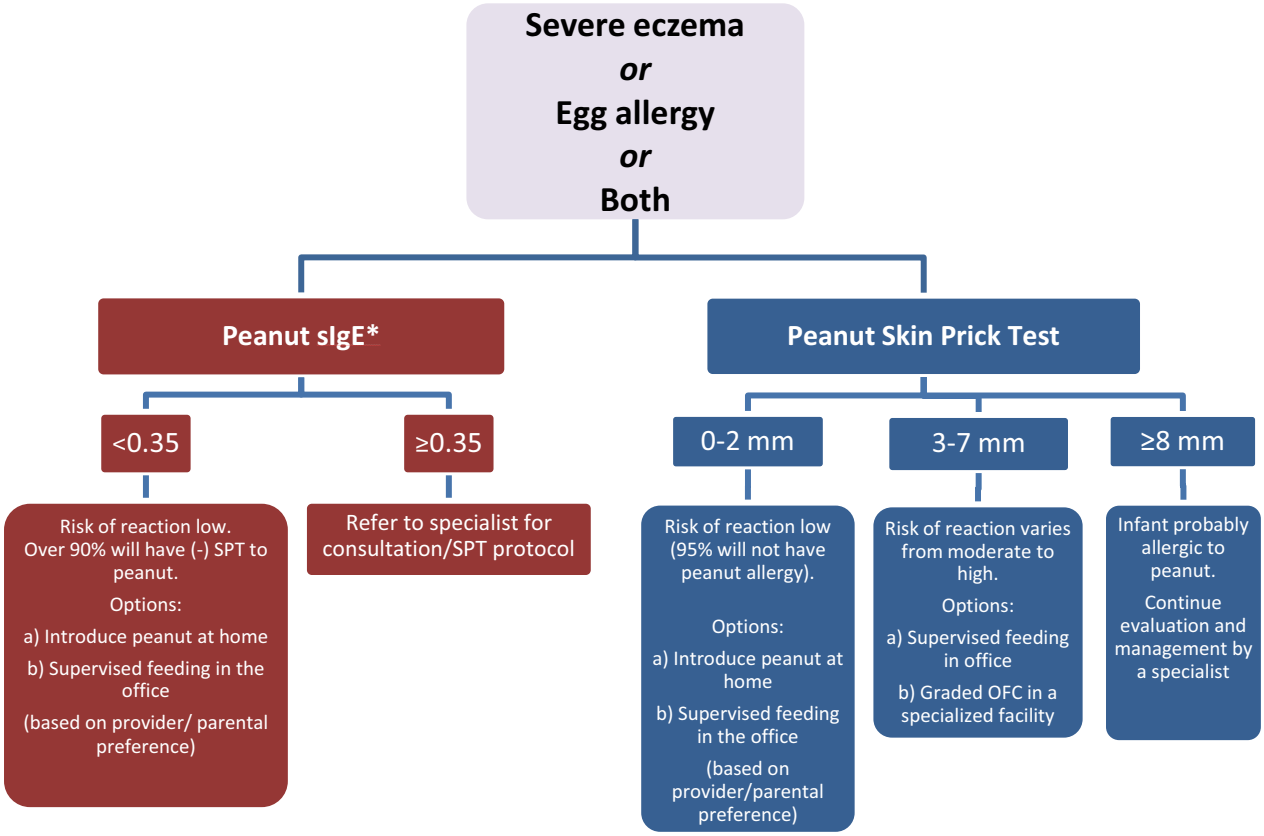

Figure 1. Recommended approaches for evaluation of children with severe eczema and/or egg allergy before peanut introduction. *To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.

Figure 1 provides recommended approaches for evaluation of children with severe eczema, egg allergy, or both before peanut introduction.

Important considerations for skin prick testing

SPT reagents, testing devices, and methodology can differ significantly among health care providers in the United States or elsewhere. The EP recommends that specialists should adjust their SPT categorization criteria according to their own training and experience.

Health care providers conducting oral food challenges in infants with 3 mm or greater SPT responses should be aware that the probability of a positive challenge increases with wheal size.

If the decision is made to introduce dietary peanut based on the recommendations of addendum guideline 1, the total amount of peanut protein to be regularly consumed per week should be approximately 6 to 7 grams over 3 or more feedings.

Quality of evidence. Moderate.

The designation of the quality of evidence as "moderate" (as opposed to "high") is based on the fact that this recommendation derives primarily from a single randomized, open-label study: the LEAP trial. However, it should be noted that the assessment of the LEAP trial's primary outcome was based on a double-blind, placebo-controlled OFC. Furthermore, confidence in this recommendation is bolstered by the large effect size demonstrated in the LEAP trial and prior epidemiological data that peanut allergy is relatively infrequent in Israel, where early childhood consumption of peanut is common.

Contribution of expert opinion. Significant.

Additional comments.

1). *Breast-feeding recommendations*: The EP recognizes that early introduction of peanut may seem to depart from recommendations for exclusive breast-feeding through 6 months of age. However, it should be noted that data from the nutrition analysis of the LEAP cohort indicate that

introduction of peanut did not affect the duration or frequency of breast-feeding, and did not influence growth or nutrition.

2). *Age of peanut introduction*: For children with severe eczema, egg allergy, or both, the EP recommends that introduction of solid foods begins at 4 to 6 months of age, starting with solid food other than peanut. However, it is important to note that the infants in the LEAP trial were enrolled between 4 and 11 months of age and benefitted from peanut consumption regardless of age at entry. Therefore, if the 4- to 6-month time window is missed for any reason, including developmental delay, infants may still benefit from early peanut introduction.

3). *Considerations for family members with established peanut allergy*: The EP recognizes that many infants eligible for early peanut introduction under this guideline will have older siblings or caregivers with established peanut allergy. The EP recommends that in this situation caregivers discuss with their health care providers the overall benefit (reduced risk of peanut allergy in the infant) versus risks (potential for further sensitization and accidental exposure of the family member to peanut) of adding peanut to the infant's diet.

4). *Children identified as allergic to peanut*: For children who have been identified as allergic to peanut, the EP recommends strict peanut avoidance. This may include those children who fail the supervised peanut feeding or the OFC, or those children who, upon further evaluation by a specialist, are confirmed as being allergic to peanut. These children should be under long-term management by a specialist.

Addendum Guideline 2

The EP suggests that infants with mild-to-moderate eczema should have introduction of age-appropriate peanut-containing food around 6 months of age, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy. Other solid foods should be introduced before peanut-containing foods to show that the infant is developmentally ready. The EP recommends that infants in this category may have dietary peanut introduced at home without an in-office evaluation. However, the EP recognizes that some caregivers and health care providers may desire an in-office supervised feeding, evaluation, or both.

Quality of evidence. Low.

The quality of evidence is low because this recommendation is based on extrapolation of data from a single study.

Contribution of expert opinion. Significant.

Addendum Guideline 3

The EP suggests that infants without eczema or any food allergy have age-appropriate peanut-containing foods freely introduced in the diet together with other solid foods and in accordance with family preferences and cultural practices.

Quality of evidence. Low.

Contribution of expert opinion. Significant.

REFERENCE

1. Boyce JA, Assa'ad A, Burks AW et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 2010;126(suppl): S1–S58.

APPENDIX A

COORDINATING COMMITTEE MEMBER ORGANIZATIONS AND REPRESENTATIVES

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Lanny J. Rosenwasser, MD

APPENDIX B

EXPERT PANEL, JUNE 2015

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Director, Inflammation and Allergic Disease Research Section
Director, Jeff and Penny Vinik Center for Allergic Disease Research
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Panelists
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Board of Directors, Food Allergy Research & Education

Member of NIAID Advisory Council
Former CEO of Food Allergy and Anaphylaxis Network
Specialty: Advocacy

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Director, FARE Center of Excellence in Food Allergy
Director of Clinical Services, Division of Allergy and Immunology
Associate Director, Division of Allergy and Immunology
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Food Allergy Research & Education, McLean VA
Founding Director, Mary H. Weiser Food Allergy Center, University of Michigan
Professor of Internal Medicine, Division of Allergy and Clinical Immunology
University of Michigan Health System
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Lisa A. Beck, MD
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University of Rochester Medical Center
School of Medicine and Dentistry
Specialty: Dermatology

Julie Block
President and CEO
National Eczema Association
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Carol Byrd-Bredbenner, PhD, RD, FAND
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Kari Keaton
Facilitator, Metro DC Food Allergy Support Group

Specialty: Advocacy/education

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Head of the Veneto Region Food Allergy Centre of Excellence for Research and Treatment
University Hospital of Padua, Italy
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