

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, 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.¹

In February 2015, the *New England Journal of Medicine* published the results of the Learning Early about Peanut Allergy (LEAP) trial.² 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% 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.

In the Division of Allergy, Immunology, and Transplantation at the National Institute of Allergy and Infectious Diseases in Bethesda, Md., **Alkis Togias** is the chief of the Allergy, Asthma, and Airway Biology Branch (AAABB), **Susan F. Cooper** is a health specialist in the Office of Program Planning and Scientific Information, **Marshall Plaut** is the chief of the Food Allergy, Atopic Dermatitis and Allergic Mechanisms Section in AAABB, and **Daniel Rotrosen** is division director. The affiliations of the other authors are listed in **Table 2**. The authors have disclosed no potential conflicts of interest, financial or otherwise. This work was written by employees of the National Institutes of Health and the expert panelists reviewed, edited, and approved the work, which is in the public domain in the United States.

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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

Coordinating committee The NIAID established a coordinating committee (**Table 1**) 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 committee members represented 26 professional organizations, advocacy groups, and federal agencies.

Expert panel In June 2015, the coordinating committee convened an expert panel chaired by Joshua Boyce, MD. The 26 panel members, listed in **Table 2**, were specialists from a variety of relevant clinical, scientific, and public health areas. Panel members were nominated by the coordinating committee organizations, and the composition of the panel received unanimous approval by these member organizations.

The charge to the expert panel was to use the literature review prepared by the NIAID, in conjunction with consensus expert opinion and expert panel-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: Prevention of Food Allergy.¹

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 two 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 expert panel 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 coordinating committee members, open to public comment, revised accordingly, and approved by the expert panel and the coordinating committee.

DEFINING THE STRENGTH OF EACH CLINICAL GUIDELINE

The expert panel 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 expert panel strongly recommended for or against a particular course of action.
- *Suggest* is used when the expert panel weakly recommended for or against a particular course of action.

ADDENDUM GUIDELINES

The expert panel came to consensus on the following three definitions used throughout the addendum guidelines.

TABLE 1. Coordinating committee member organizations and representatives

Academy of Nutrition and Dietetics www.eatright.org Alison Steiber, PhD, RD	American College of Gastroenterology http://gi.org Steven J. Czinn, MD, FACP	National Heart, Lung, and Blood Institute www.nhlbi.nih.gov Janet M. de Jesus, MS, RD
Allergy & Asthma Network Mothers of Asthmatics www.allergyasthmanetwork.org/main Tonya A. Winders, MBA	American Partnership for Eosinophilic Disorders http://apfed.org Wendy Book, MD	National Institute of Allergy and Infectious Diseases www.niaid.nih.gov Daniel Rotrosen, MD Alkis Togias, MD Marshall Plaut, MD
American Academy of Allergy, Asthma & Immunology https://www.aaaai.org/home.aspx Hugh A. Sampson, MD David Fleischer, MD	American Society for Nutrition www.nutrition.org George J. Fuchs, III, MD	National Institute of Arthritis and Musculoskeletal and Skin Diseases www.niams.nih.gov Ricardo Cibotti, PhD
American Academy of Family Physicians www.aafp.org/home.html Jason Matuszak, MD	Asthma and Allergy Foundation of America www.aafa.org Meryl Bloomrosen, MBA, MBI David R. Stukus, MD	National Institute of Diabetes and Digestive and Kidney Diseases www.niddk.nih.gov Frank Hamilton, MD, MPH Margaret A. McDowell, PhD, MPH, RD (retired) Rachel Fisher, MS, MPH, RD
American Academy of Dermatology https://www.aad.org Lawrence F. Eichenfield, MD, FAAD Jon Hanifin, MD	Canadian Society of Allergy and Clinical Immunology www.csaci.ca Edmond Chan, MD, FRCPC	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition www.naspghan.org Glenn Furuta, MD
American Academy of Emergency Medicine www.aaem.org Joseph P. Wood, MD, JD	Eunice Kennedy Shriver National Institute of Child Health & Human Development https://www.nichd.nih.gov Gilman Grave, MD	Society of Pediatric Nurses www.pedsnurses.org Michele Habich, DNP, APN/ CNS, CPN
American Academy of Pediatrics https://www.aap.org Scott H. Sicherer, MD, FAAP	European Academy of Allergy and Clinical Immunology www.eaaci.org Antonella Muraro, MD, PhD	US Department of Agriculture www.usda.gov Soheila J. Maleki, PhD
American Academy of PAs https://www.aapa.org Gabriel Ortiz, MPAS, PA-C, DFAAPA	Food Allergy Research & Education www.foodallergy.org James R. Baker, MD Mary Jane Marchisotto	World Allergy Organization www.worldallergy.org Lanny J. Rosenwasser, MD
American College of Allergy, Asthma and Immunology http://acaai.org/ Amal Assa'ad, MD	National Eczema Association http://nationaleczema.org Julie Block	

TABLE 2. Expert panel, June 2015

Chair

Joshua A. Boyce, professor in the Departments of Medicine and Pediatrics at Harvard Medical School in Boston, Mass., and director of the inflammation and allergy research section and the Jeff and Penny Vinik Center for Allergic Disease Research. Specialty: allergy, pediatric pulmonology

Panelists

- **Maria L. Acebal**, member of the board of directors of Food Allergy Research & Education in McLean, Va., member of the NIAID Advisory Council, and a former chief executive officer of the Food Allergy & Anaphylaxis Network. Specialty: advocacy
- **Amal Assa'ad**, professor of pediatrics, director of the FARE Center of Excellence in Food Allergy, director of clinical services and associate director of the Division of Allergy and Immunology at Cincinnati Children's Hospital Medical Center at the University of Cincinnati in Ohio. Specialty: allergy, pediatrics
- **James R. Baker, Jr.**, chief executive officer and chief medical officer of Food Allergy Research & Education, founding director of the Mary H. Weiser Food Allergy Center at the University of Michigan, and professor of internal medicine in the Division of Allergy and Clinical Immunology at the University of Michigan Health System in Ann Arbor, Mich. Specialty: allergy, advocacy, education
- **Lisa A. Beck**, professor in the Department of Dermatology at the University of Rochester (N.Y.) Medical Center. Specialty: dermatology
- **Julie Block**, president and chief executive officer of the National Eczema Association in San Rafael, Calif. Specialty: advocacy, education
- **Carol Byrd-Bredbenner**, professor of nutrition and extension specialist in the School of Environmental and Biological Sciences at Rutgers University in New Brunswick, N.J. Specialty: nutrition, health communications, behavioral science
- **Edmond S. Chann**, clinical associate professor and head of the Division of Allergy and Immunology in the Department of Pediatrics at BC Children's Hospital, part of the University of British Columbia in Vancouver, Canada. Specialty: allergy, pediatrics
- **Lawrence F. Eichenfield**, professor of pediatrics and dermatology at the University of California, San Diego, School of Medicine and chief of pediatric and adolescent dermatology at Rady Children's Hospital in San Diego, Calif. Specialty: dermatology, pediatrics
- **David M. Fleischer**, associate professor of pediatrics at Children's Hospital Colorado and the University of Colorado Denver School of Medicine in Aurora, Colo. Specialty: allergy, pediatrics
- **George J. Fuchs III**, professor of pediatrics at the University of Kentucky College of Medicine and chief of gastroenterology, hepatology, and nutrition at Kentucky Children's Hospital in Lexington. Specialty: gastroenterology, pediatrics
- **Glenn T. Furuta**, professor of pediatrics and director of the gastrointestinal eosinophilic diseases program at Children's

Hospital Colorado and the University of Colorado School of Medicine in Aurora, Colo. Specialty: gastroenterology, pediatrics

- **Matthew J. Greenhawt**, assistant professor of pediatrics, allergy section, at Children's Hospital Colorado and the University of Colorado School of Medicine in Aurora, Colo. Specialty: allergy, pediatrics
- **Ruchi S. Gupta**, associate professor of pediatrics and medicine and director of the food allergy outcomes research program at the Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine in Chicago, Ill. Specialty: pediatrics
- **Michele Habich**, advanced practice nurse at Central DuPage Hospital in Winfield, Ill. Specialty: nursing, pediatrics, education
- **Stacie M. Jones**, professor of pediatrics at the University of Arkansas for Medical Sciences and chief of allergy and immunology at Arkansas Children's Hospital in Little Rock. Specialty: allergy, pediatrics
- **Kari Keaton**, facilitator at Metro DC Food Allergy Support Group in Rockville, Md. Specialty: advocacy, education
- **Antonella Muraro**, president of the European Academy of Allergy and Clinical Immunology, professor of allergy and pediatric allergy at University Hospital of Padua, and head of the Veneto Region Food Allergy Centre of Excellence for Research and Treatment in Padua, Italy. Specialty: allergy, pediatrics
- **Lanny J. Rosenwasser**, immediate past president of the World Allergy Organization and professor of medicine at the University of Missouri-Kansas City School of Medicine in Kansas City, Mo. Specialty: allergy, pediatrics
- **Hugh A. Sampson**, professor of pediatrics, allergy, and immunology at the Icahn School of Medicine at Mount Sinai and director of the Jaffe Food Allergy Institute in New York, N.Y. Specialty: allergy, pediatrics
- **Lynda C. Schneider**, professor of pediatrics at Harvard Medical School in Cambridge, Mass., and director of the allergy program at Boston (Mass.) Children's Hospital. Specialty: allergy, pediatrics
- **Scott H. Sicherer**, professor of pediatrics, allergy, and immunology and chief of pediatric allergy and immunology at the Icahn School of Medicine at Mount Sinai in New York, N.Y. Specialty: allergy, pediatrics
- **Robert Sidbury**, professor of pediatrics and chief of dermatology at Seattle Children's Hospital, University of Washington School of Medicine in Seattle, Wash. Specialty: dermatology, pediatrics
- **Jonathan Spergel**, Stuart Starr professor of pediatrics, chief of allergy, and director of the Center for Pediatric Eosinophilic Disorders at the Children's Hospital of Philadelphia, Perelman School of Medicine at University of Pennsylvania in Philadelphia, Pa. Specialty: allergy, pediatrics
- **David R. Stukus**, assistant professor of pediatrics in the Section of Allergy and Immunology at Nationwide Children's Hospital in Columbus, Ohio. Specialty: allergy, pediatrics
- **Carina Venter**, allergy specialist and dietitian at Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine in Cincinnati, Ohio. Specialty: allergy, diet, pediatrics

TABLE 3. 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 skin-prick test and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods.	4 to 6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	About 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age-appropriate and in accordance with family preferences and cultural practices

• *Severe eczema* is defined as persistent or frequently recurring eczema with typical morphology and distribution assessed as severe by a healthcare 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 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 healthcare provider with the training and experience to perform and interpret skin-prick tests and oral food challenges and know and manage their risks. Such persons must have appropriate medications and equipment on site.

The addendum guidelines are summarized in **Table 3**.

Addendum guideline 1 The expert panel recommends that infants with severe eczema, egg allergy, or both have introduction of age-appropriate peanut-containing food as early as age 4 to 6 months 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 expert panel recommends that evaluation with peanut-specific IgE (peanut sIgE) measurement, skin-prick tests (**Table 4**), or both be strongly considered before introduction of peanut to determine if peanut should be introduced and, if so, the preferred method of introduction (**Figure 1**). 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 healthcare settings, such as family medicine, pediatrics, or dermatology practices, in which skin-prick test-

ing is not routine. Alternatively, referral for assessment by a specialist may be an option if desired by the healthcare provider and when available in a timely manner.

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 6 to 7 g over three 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 oral food challenge. 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:

Breastfeeding recommendations: The expert panel recognizes that early introduction of peanut may seem to depart from recommendations for exclusive breastfeeding through age 6 months. 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 breastfeeding, and did not influence growth or nutrition.

Age of peanut introduction: For children with severe eczema, egg allergy, or both, the expert panel recommends that introduction of solid foods begins at ages 4 to 6 months, starting with solid food other than peanut. However, it is important to note that the infants in the LEAP trial were enrolled between ages 4 and 11 months 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.

Considerations for family members with established peanut allergy: The expert panel recognizes that many infants eligible for early peanut introduction under this guideline will have older siblings or caregivers with established peanut allergy. The expert panel recommends that

TABLE 4. Important considerations for skin-prick testing

Skin-prick testing reagents, testing devices, and methodology can differ significantly among healthcare providers in the United States or elsewhere. The expert panel recommends that specialists should adjust their skin-prick testing categorization criteria according to their own training and experience. Healthcare providers conducting oral food challenges in infants with 3 mm or greater skin-prick test responses should be aware that the probability of a positive challenge increases with wheal size.

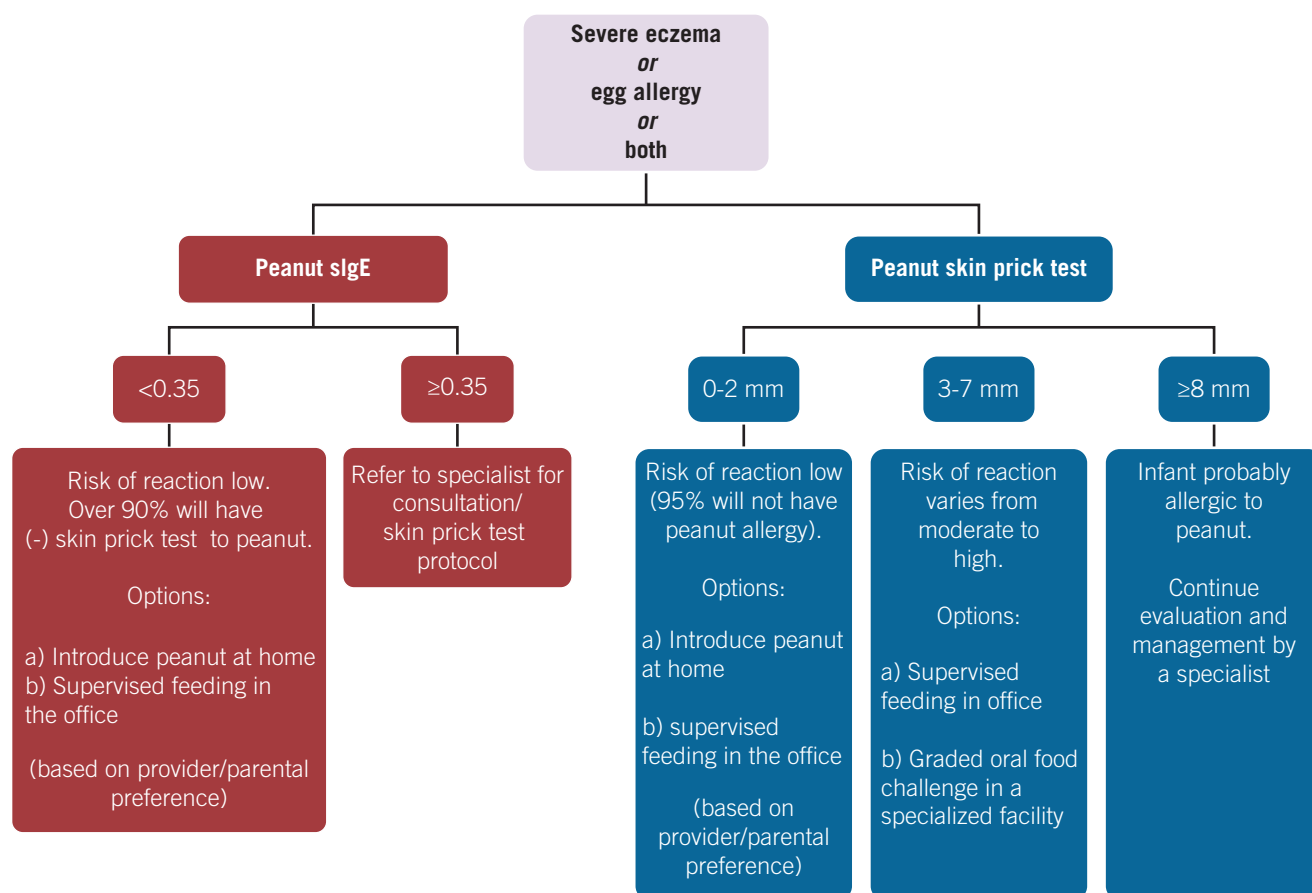


FIGURE 1. Recommended approaches for evaluation of children with severe eczema and/or egg allergy before peanut introduction. To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain healthcare settings.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

in this situation caregivers discuss with their healthcare 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.

Children identified as allergic to peanut: For children who have been identified as allergic to peanut, the expert panel recommends strict peanut avoidance. This may include those children who fail the supervised peanut feeding or the oral food challenge, 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 expert panel suggests that infants with mild-to-moderate eczema should have introduction of age-appropriate peanut-containing food around age 6 months, 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 expert panel recommends that infants in this category may have dietary peanut introduced at home without an in-office

evaluation. However, the expert panel recognizes that some caregivers and healthcare 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 expert panel 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. **JAAPA**

REFERENCES

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