What, When and How to Introduce Allergenic Foods: What does the research say

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Timeline of feeding guidelines

Early 2000s 2008 2015 2020
Feeding recommendations by AAP

No evidence of benefit for delaying the introduction of allergenic foods beyond 4-6 months of age
Ok to introduce peanuts, eggs and fish

2008

2019

Same recommendation are in place


LEAP
(learning early about peanut allergy)

Early introduction of peanut-based products (before 11 months of age) lead to the prevention of peanut allergy in high-risk infants*

NIAID released feeding updates based on LEAP trial in 2017

Addendum guideline for the prevention of peanut allergy in the US

Summary of Addendum Guidelines

<table>
<thead>
<tr>
<th>Addendum Guideline</th>
<th>Infant Criteria</th>
<th>Recommendations</th>
<th>Earliest Age of Peanut Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe eczema, egg allergy, or both</td>
<td>Strongly consider evaluation with peanut-specific IgE and/or skin prick test; and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods.</td>
<td>4 to 6 months</td>
</tr>
<tr>
<td>2</td>
<td>Mild to moderate eczema</td>
<td>Introduce peanut-containing foods.</td>
<td>Around 6 months</td>
</tr>
<tr>
<td>3</td>
<td>No eczema or any food allergy</td>
<td>Introduce peanut-containing foods.</td>
<td>Age-appropriate and in accordance with family preferences and cultural practices</td>
</tr>
</tbody>
</table>

Enquiring about tolerance (EAT) study

- Randomly assigned to:
  - early introduction of 6 foods (peanuts, cooked egg, cow’s milk, sesame, whitefish and wheat) or
  - standard introduction group (exclusively breast fed until 6 months of age)

- Prevalence of food allergy was significantly lower in early introduction group than standard introduction (2.4% vs. 7.3%)

- Peanut and egg also showed significantly lower allergy with the ingestion of 2g per week of these foods

- Trial failed to showed efficacy of early introduction vs. standard introduction in an-intention-to treat analysis.

- Question if prevention of food allergies by early introduction may be dependent on adherence and dose

Early Egg Introduction

- **HEAP**
  - Enrolled infants in general population without IgE sensitization
  - Early introduction does not prevent egg sensitization or allergy

- **STEP**
  - Evaluated effects of early egg introduction for primary prevention in those with hereditary risk for egg allergy (no eczema)
  - Early introduction does not reduce risk by 12 months of age

- **BEAT**
  - Early introduction in infants with family history of atopy
  - Early introduction can reduce sensitization for those at high risk

Fineman et al, Annals 2018;120, 241-244

Dietary Guidelines 2020-2025

- Follow a healthy dietary pattern at every life stage
- Exclusive breastfeeding for 6 months of life through at least 1st year of life
  - Iron fortified formula if breastmilk unavailable
- Introduce “nutrient dense” foods at 6 months of life including potentially allergenic foods
  - Introduction of allergenic foods could reduce child’s risk of developing a food allergy
    - Peanuts, eggs, cow’s milk products, tree nuts, wheat, soy, shellfish and fish
  - Introduction of peanut containing food at 4-6 months in infants at high risk of peanut allergy

Available at www.dietaryguidelines.gov
Recommendations that are unchanged

- Maternal dietary restrictions during pregnancy and breastfeeding are not recommended

- Use of hydrolyzed formulas do not prevent food allergies or development of food sensitization


A Consensus Approach to the Primary Prevention of Food Allergy Through Nutrition: Guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology

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- David M. Fleischer MD
- Edmond S. Chan MD
- Carina Venter PhD, RD
- Jonathan M. Spengel MD, PhD
- Elissa M. Abrams MD, MPH
- David Stukus MD
- Marion Groetch RD
- Marcus Shaker MD, MS
- Matthew Greenhawt MD, MBA, MSc
Comparison of existing early peanut and/or other potentially allergenic food introduction guidelines

<table>
<thead>
<tr>
<th>NATIONAL INSTITUTES OF ALLERGY AND INFECTIOUS DISEASES</th>
<th>BRITISH SOCIETY FOR ALLERGY AND CLINICAL IMMUNOLOGY</th>
<th>AUSTRALASIAN SOCIETY FOR CLINICAL IMMUNOLOGY AND ALLERGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>— Addendum 1: Infants with severe eczema, egg allergy, or both should have introduction of age-appropriate peanut-containing food as early as age 4 to 6 mo to reduce the risk of peanut allergy.</td>
<td>— Exclusive breastfeeding for around the first 6 mo of life.</td>
<td>— When your infant is ready, at around 4 to 6 mo, start to introduce various solid foods, starting with iron-rich foods, while continuing breast-feeding.</td>
</tr>
<tr>
<td>— Addendum 2: Infants with moderate eczema should have introduction of age-appropriate peanut-containing food around age 6 mo, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy.</td>
<td>— Foods containing peanut and hen’s egg need not be differentiated from other complementary foods and should be introduced in an age-appropriate form. There should be an age of at least 6 mo, alongside continued breast-feeding, at a time and in a manner to suit both the family and infant child.</td>
<td>— All infants should be given allergenic solid foods including peanut butter, cooked egg, dairy, and wheat products in the first year of life. This includes infants at high risk of allergy.</td>
</tr>
<tr>
<td>— Addendum 3: 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.</td>
<td>— The deliberate exclusion of peanut or hen’s egg beyond age 6 to 12 mo may increase the risk of allergy.</td>
<td>— Hydrolysed (partially or extensively) infant formula is not recommended for the prevention of allergic disease.</td>
</tr>
</tbody>
</table>

• Fleischer D. JACI: In Practice 2021; 9(1): 22-43.e4

Risk assessment for development of food allergy among infants

![Risk assessment for development of food allergy among infants](Image)

Fleischer D. JACI: In Practice 2021; 9(1): 22-43.e4
New Recommendations

• Peanut starting at 6 months of age but not before 4 months
• Egg starting at 6 months of age but not before 4 months
  • Screening can be done prior, but not required for peanut and egg
  • Introduction after tolerating complementary foods
• Do not deliberately delay introduction of other allergenic foods
  • No RCT exist to better inform decision making


Early peanut introduction works

• In Australia- early introduction practices led to a 16% decrease in peanut allergy
• Peanut allergy prevalence
  • 2018-2019: 2.6% VS
  • 2007-2011: 3.1%*
    • *After accounting for migration and population changes.
  • 2018-2019: 4.8% in infants that did not consume peanuts until after 12 months of age
• Severe reactions to introducing peanut early were uncommon

Cow’s milk prevention

• The Strategy for Prevention of Milk Allergy by Daily Ingestion of Infant Formula in Early Infancy (SPADE)
  • Enrolled 504 general population infants in Japan
  • Daily cow’s milk formula supplementation with ongoing breastfeeding between 1-2 months
    • OR
  • Cow’s milk avoidance with soy milk supplementation

• Findings:
  • Significant reduction in cow’s milk allergy 0.8% vs 6.8%
  • At least 10ml ingestion per day is required for tolerance

Abrams and Sicherer. Annals 2021; 127 (1): 36-41
Cashew Allergy

- Health Nuts study from Melbourne Australia
- Parent recall of food introduction in 1st year of life
- 4 years of age- f/u questionnaire and assessment if reported food allergy and/or food reaction
- 6 years of age-comprehensive cashew assessment and possible OFC

Findings:
- No child who consumed cashew before age 1 developed a cashew allergy vs 3.6% in those who didn’t consume cashews


Practice Takeaways

- Introduce “nutrient dense” foods at 6 months of life including potentially allergenic foods
- Screening can be done prior, but not required for peanut and egg
Thank you for attending

Questions?
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Consensus Approach to the Primary Prevention of Food Allergy: Practical Applications

Raquel Durban, MS, RD, LD/N
Carolina Asthma & Allergy Center

Objectives

• Identify outcomes associated with delayed introduction
• Explain importance and achievement of diet diversity
• Explore breastfeeding and formula use in the allergic and non allergic population.
Risk Assessment for Development of Food Allergy

![Risk Assessment Diagram](image)

**FIGURE 2.** Ascending gradient of risk assessment for the development of food allergy among infants. The bottom of the pyramid represents standard risk and the peak the highest risk for developing food allergy. Fleischer D. JACI: In Practice 2021; 9(1): 22-43.e4

Working with Caregivers on Food Introduction

- Peanut and egg introduction
  - Engage in shared decision-making with caregivers on all aspects of food introduction
  - Provide flexible, patient-focused care and recommendations
  - Testing to be performed only if warranted
Introduction of Peanut

• Introduce peanut-containing products to infants starting around 6 months of age, but not before 4 months, irrespective of relative risk

• Peanut introduction can occur at home, once infant has demonstrated developmental readiness

• Following peanut introduction, regular ingestion should be maintained.

Introduction of Peanut: Practical Feeding Recommendations

• Peanut-containing product: any age-appropriate peanut item that can be administered alone or mixed in with other baby foods

• Infant-safe forms included diluted peanut butter, peanut-containing powders/flours and snacks (e.g., peanut puffs)

• Thinned, natural peanut butter or peanut flour is preferred early weaning food
Introduction of Egg

• Introduce egg or egg-containing products to infants starting around 6 months of age, but not before 4 months, irrespective of their relative risk
• Use only cooked forms of egg; avoid raw and unpasteurized egg-containing products
• Egg introduction can occur at home, once infant has demonstrated developmental readiness
• Following egg introduction, regular ingestion should be maintained.

Introduction of Egg: Practical Feeding Recommendations

• Egg or egg-containing products should be introduced in well-cooked forms
• Eggs can be mixed into other age-appropriate foods, such as grits
Dosing of Peanut- and Egg-Containing Foods

• No known dose relationship to either peanut allergy or egg allergy outcome

• Caregivers should focus on feeding amounts and types of peanut- or egg-containing foods that child likes and tolerates
  • Recommend reasonable amount and frequency, such as 1-2 tsp of peanut butter or egg at least 1x weekly; may be given in larger amounts if child enjoys the food

• Regular exposure over time is considered more important than focusing on fixed dosing interval or amount

Serving Sizes for Age: Daily Recommendations

<table>
<thead>
<tr>
<th>4-6 Months</th>
<th>6-8 Months</th>
<th>8-10 Months</th>
<th>10-12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4-6 feedings</strong></td>
<td><strong>3-5 feedings</strong></td>
<td><strong>3-4 feedings</strong></td>
<td><strong>3-4 feedings</strong></td>
</tr>
<tr>
<td>4-6 oz. per feeding (22-28 oz/day)</td>
<td>6-8 oz. per feeding (28-34 oz/day)</td>
<td>7-8 oz. per feeding (28-34 oz/day)</td>
<td>7-8 oz. per feeding (28-34 oz/day)</td>
</tr>
<tr>
<td>N/A</td>
<td>2-3 servings of iron-fortified baby cereal (2-4 Tbsp) and other soft cooked breads (½ slice), cereals, and starches (2 crackers)</td>
<td>2-3 servings of iron-fortified baby cereal (2-4 Tbsp) and other soft, cooked breads breads (½ slice), cereals, and starches (3-4 Tbsp pasta, 2 crackers)</td>
<td>4 servings of breads (½ slice), and other soft starches (3-4 Tbsp pasta, 2 crackers). Iron-fortified baby cereal (2-4 Tbsp)</td>
</tr>
<tr>
<td>N/A</td>
<td>Offer plain cooked, mashed, or strained vegetables and fruits (2-3 Tbsp only) Avoid combination meat and veg. dinners</td>
<td>2-3 servings of soft, cut up, and mashed vegetables and fruits daily (serving = 2-3 Tbsp)</td>
<td>4 servings daily of vegetables and fruits (serving = 3-4 Tbsp)</td>
</tr>
<tr>
<td>N/A</td>
<td>Offer plain-cooked, pureed meat and beans (1-2 Tbsp/day) Avoid combination dinners.</td>
<td>Offer well cooked, soft, finely cut or pureed meats, cheese, and casseroles (3-4 Tbsp or ¼ cup 2x/day)</td>
<td>1-2 ounces daily of soft, finely cut or chopped meat or other protein foods (3-4 Tbsp or ¼ cup)</td>
</tr>
</tbody>
</table>
Introducing Other Potentially Allergenic Foods

• Tree Nuts: tree nuts butters are infant-safe form
• Sesame: infant-safe forms include tahini paste or hummus mixed with other pureed foods
• Fish and shellfish: introduce when infant is tolerating other age-appropriate foods

• Once introduced and tolerated, foods should be regularly incorporated into infant’s diet in accordance with family and cultural preferences

Introducing Complementary Foods

• AAP Committee on Nutrition recommends exclusive breastfeeding until age 4-6 months in healthy, term infants

• To balance diet and promote acceptance, caregiver may offer single ingredient food at a time and gradually expand variety and texture of foods offered

• Iron-rich foods (pureed meat, poultry, greens, whole grains) should be included in early complementary food introductions, due to insufficient iron in breast milk
Avoid Delayed Introduction of Potentially Allergenic Foods

• Do not deliberately delay introduction once complementary foods have been introduced

• No RCT suggests benefit from early introduction of these foods, but observational data suggest potential harm from delayed introduction.

Health & Economic Outcomes Associated with Early Allergenic Food Introduction

• For egg and peanut introduction:
  • Universal introduction to all infants (in at-risk and not at-risk populations) dominated (e.g., was associated with superior health benefits and lower costs) the other approaches of either screening or delayed introduction.

• Universal introduction cost less, prevented more cases of the food allergy, and produced more net benefit to the patient (measured by gain in quality-adjusted life-years) than other options
### Cost of Delayed Introduction

<table>
<thead>
<tr>
<th>Infant risk scenario</th>
<th>Cost per patient at risk</th>
<th>QALY per patient at risk</th>
<th>Allergic reactions per patient at risk</th>
<th>Incremental societal cost to screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>No screening, early introduction</td>
<td>$6.557</td>
<td>19.63</td>
<td>0.4</td>
<td>—</td>
</tr>
<tr>
<td>Skin test screening before early introduction</td>
<td>$7.576</td>
<td>19.62</td>
<td>0.35</td>
<td>$654,115,322</td>
</tr>
<tr>
<td>sIgE screening before early introduction</td>
<td>$7.977</td>
<td>19.6</td>
<td>0.38</td>
<td>$911,211,774</td>
</tr>
<tr>
<td><strong>Delayed introduction</strong></td>
<td><strong>$11,708</strong></td>
<td><strong>19.46</strong></td>
<td><strong>0.72</strong></td>
<td></td>
</tr>
<tr>
<td>No screening before introduction</td>
<td>$3.278</td>
<td>19.72</td>
<td>0.2</td>
<td>—</td>
</tr>
<tr>
<td>Skin test screening with challenge before introduction</td>
<td>$3.984</td>
<td>19.72</td>
<td>0.2</td>
<td>Dominated</td>
</tr>
<tr>
<td>No screening, early cooked introduction</td>
<td>$2.235</td>
<td>19.78</td>
<td>0.03</td>
<td>—</td>
</tr>
<tr>
<td>Skin test screening before early cooked introduction</td>
<td>$9.100</td>
<td>19.59</td>
<td>0.12</td>
<td>$2,000,351,175</td>
</tr>
<tr>
<td><strong>Delayed cooked introduction</strong></td>
<td><strong>$10,615</strong></td>
<td><strong>19.53</strong></td>
<td><strong>0.13</strong></td>
<td></td>
</tr>
</tbody>
</table>

QALY, Quality-adjusted life-year.
*Model simulations over 20-y time horizons.

Fleischer D. JACI: In Practice 2021; 9(1): 22-43.e4

### Cost of Infant Milk Substitutes

<table>
<thead>
<tr>
<th></th>
<th>Cost per tin</th>
<th>Monthly cost (~ 800ml/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amino acid</strong></td>
<td>$40-49 per 400g</td>
<td>US: $11.25 - $13.80 (6% ave income)</td>
</tr>
<tr>
<td><strong>Extensively hydrolyzed</strong></td>
<td>$38 per 400g</td>
<td>US: $7.40 (4% ave income)</td>
</tr>
<tr>
<td><strong>Soya formula</strong></td>
<td>$33 per 850g</td>
<td>US: $4 (2.5% ave income)</td>
</tr>
</tbody>
</table>
Diet Diversity

- Following introduction of complementary foods, infants should be fed a diverse diet, which may help foster the prevention of food allergy.

- No RCT has investigated association between diet diversity and prevention of food allergy.

Use of Hydrolyzed Formula (HF)

- Partially HF marketed as having enhanced tolerability and reduced allergenicity, compared to cow’s milk formula.

- Formulas are considered safe for at-risk and not-at-risk infants.

- No data that conclusively and consistently show any protective benefit with HF use in the prevention of food allergy.

- Routine HF prescription or recommendation for specific prevention of food allergy or development of food sensitization is not advised.
Pre/Post-natal Food Exposure and Breastfeeding on Development of Food Allergy

- Breastfeeding is not conclusively associated with prevention of any food allergy
- Role of concurrent breastfeeding while introducing allergens in the development of food allergy is unclear.
- Lack of evidence to support deliberate maternal exclusion of high-risk or common allergens during pregnancy and lactation for purposes of preventing food allergy in infants; exclusion is not recommended

Summary

- Engage in shared decision-making with caregivers on timing and strategy of food introduction
- Introduce infant-safe peanut- and egg-containing foods around 6 months of age, but not earlier than 4 months, once infant shows developmental readiness
- Once tolerance is demonstrated, foods should be included in the diet on a frequent basis and in age-appropriate amounts
- Avoid delayed introduction of potentially allergenic foods; delayed introduction is associated with greater risks and increased costs
- Routine recommendation of hydrolyzed formula is not advised for specific prevention of food allergy
- Breastfeeding and maternal dietary exclusion of allergens are not conclusively associated with prevention of food allergy