Early Allergen Introduction to Decrease Food Allergy Risk

New Guidelines, Research, and At-Home Implementation

Jonathan Spergel, MD, PhD
Board-Certified Pediatric & Adult Allergist/Immunologist
Professor of Pediatrics at the University of Pennsylvania School of Medicine
Chief of Allergy Section at Children’s Hospital of Philadelphia

Katie Marks-Cogan, MD, FACAAI, FAAAAI
Board-Certified Pediatric & Adult Allergist/Immunologist
Clear Allergy, Culver City, CA
Welcome!

Today’s webinar is powered by Ready, Set, Food!

While FARE does not endorse products, we support and appreciate enterprises and organizations that are committed to serving the food allergy community. FARE’s ability to make an impact is strengthened by partnering with like-minded companies to help raise food allergy awareness and provide more options to all those living with food allergy.
Disclaimer

This presentation is for food allergy education, information and training purposes only. While every effort has been made to ensure the information in this presentation is accurate and up to date for food allergy management, this presentation is not intended to be a substitute for professional legal advice, medical advice, or diagnosis or treatment, and the information in this presentation does not supersede or replace existing state or federal laws and regulations.

FOOD ALLERGY RESEARCH & EDUCATION ("FARE"), ITS REPRESENTATIVES, PARTNERS, EMPLOYEES AND VOLUNTEERS CANNOT GUARANTEE ABSOLUTE PREVENTION OF A FOOD ALLERGY REACTION OR EMERGENCY IN YOUR FACILITY AND HEREBY DISCLAIM ANY AND ALL LIABILITY ASSOCIATED WITH ANY FOOD ALLERGY REACTION ON YOUR PREMISES OR IN CONJUNCTION WITH FOLLOWING THE GUIDELINES SET FORTH IN THIS PRESENTATION OR ANY ADVICE BY FARE.
Jonathan Spergel, MD, PhD
Board-Certified Pediatric & Adult Allergist/Immunologist
Professor of Pediatrics at the University of Pennsylvania
School of Medicine
Chief of Allergy Section
at Children’s Hospital of Philadelphia

Disclosures:
Medical Advisor for Ready, Set, Food!
Speaker: Rockpointe, Medscape
Grants: Alimmune Therapeutics, DBV Technologies, FARE, NIH
Consultant: Regeneron, DBV Technologies, Ready, Set, Food!
Scientific Advisory Board: DBV Technologies

Katie Marks-Cogan, MD, FACAAI, FAAAAI
Board-Certified Pediatric & Adult Allergist/Immunologist
Clear Allergy, Culver City, CA

Disclosures:
Medical Advisor for Ready, Set, Food!
Chief Allergist Ready, Set, Food!
Overview

- Childhood food allergy and recent trends
- Current understanding of prevention
- Studies on early introduction
- Changes to practice guidelines
- Patient compliance challenges and implementation
Epidemiology of Food Allergy in Children

- Prevalence: 8% of children and 10% of infants
- Increase rates in last two decades
- Tripling of peanut allergy


www.foodallergy.org
Managing Food Allergies

- Avoidance - management strategy, not treatment
- Epinephrine - treatment of severe allergic reactions
- Immunotherapy - desensitization strategy
- No true “cure”
Food Allergies in Children

- Food allergy is a major public health concern that affects approximately 8% of children
  - Approximately 40% of children with food allergy reported multiple food allergies

- Food allergy-related emergencies
  - 19.0% reported ≥1 food allergy-related emergency department visit in the previous year
  - 42.0% reported ≥1 lifetime food allergy-related emergency department visit
  - 40.7% had a current epinephrine autoinjector prescription

- Prevalence of specific food allergies in children
  - Peanut (2.2%)
  - Milk (1.9%)
  - When treated as single allergens:
    - Shellfish (1.3%)
    - Tree nut (1.2%)
  - Egg (0.9%)
  - Fin fish (0.6%)
  - Sesame (0.2%)

Quality of Life Impacts

- Milk and egg hardest to avoid
- Milk most common cause of reactions at school
- Peanut most feared, with incidence of anaphylaxis
- Studies have shown activity avoidance, bullying
- Family impacts and decreased productivity

$4,200+ annually food allergy costs per child

Risk Factors

- Atopic dermatitis, family history, male sex
- Most children diagnosed with food allergy do not have a family history
- Among siblings of food allergic children, only 13% are clinically reactive
- Why are food allergies increasing?
  - Vitamin D hypothesis
  - Hygiene hypothesis - diminished microbial diversity
  - Dual allergen exposure hypothesis
  - Impact of avoidance

What Has NOT Been Proven to Reduce the Risk of Developing Food Allergies?

- Avoidance of allergens in the infant’s diet
- Maternal diets prior to birth
- Maternal diets during breastfeeding
- Hydrolyzed infant formulas
- More studies are needed on:
  - Prebiotics and probiotics
  - Vitamin D
  - Moisturizers in infancy


www.foodallergy.org
Allergen Exposure and Infancy

- The nature of food allergen exposure during infancy primes the immune system towards either tolerance or allergy.
- Skin exposure promotes sensitization.
- Gut exposure induces tolerance.

Chinthrajah RS, Hernandez JD, Boyd SD, Galli SJ, Nadeau KC. Molecular and cellular mechanisms of food allergy and food tolerance. Journal of Allergy and Clinical Immunology. 2016 Apr 1;137(4):984-97.
Compared a population of school-age Jewish children in Israel versus the UK and found a 10-fold higher rate of peanut allergy in the UK.

Peanut was introduced at an earlier age and consumed in larger quantities in Israeli infants: 7.1 g of peanut protein per month compared with no exposure (0 g) to peanut protein in children in the UK.

This data suggested that early oral exposure of allergen exposure might be protective against food allergy.
Safety and Early Introduction

- Substantial evidence for lower severity of allergic reactions in infants
  - A survey of U.S. and UK national health registries showed the absence of severe anaphylaxis in children under the age of 1
- Increasing evidence for harm in delaying exposure, including while waiting for testing or allergist evaluation
  - Early exposure to peanut and egg was found to have superior health and economic benefits

Clinical Trials

**The NEW ENGLAND JOURNAL of MEDICINE**

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy


**EAT Trial**

**THE LANCET**

Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial

OSAMU NATSUHE, SHIGENORI KABASHIMA, JUNKO NAKAZATO, KIYOOKO YAMAMOTO-HANADA, MASAMI NOIRITA, MAI KONDO, MAYAKO SAITO, AI KISHINO, TETSUYA TAKIMOTO, EISUKE IMAI, JULIAN TANG, HIROSHI KIDO, GARY W. K. WONG, KENJI MATSUMOTO, HIROHSI SAI TAO, YUKIHIRO OHYA, FOR THE PETIT STUDY TEAM

www.foodallergy.org
Clinical Trial Results

- **Learning Early About Peanut Allergy (LEAP)**
  - Feeding peanut to high-risk infants early and often could prevent them from developing a peanut allergy.
    - It reduced their risk by 81 percent, compared to a control group who avoided peanuts completely for the same five years.
    - High adherence rate (92%) required on average 104 phone calls

- **Learning Early About Peanut Allergy Persistence of Oral Tolerance to Peanut (LEAP-On)**
  - Follow up study demonstrated that early peanut introduction continues to protect children from peanut allergy, even without daily peanut exposure
  - Suggests protection is long-lasting
Clinical Trial Results, Continued

**PETIT**
79% reduction in egg allergy prevalence

**EAT**
In per-protocol analysis, 67% reduction in food allergy prevalence

But only 43% of participants in the early-introduction group were able to adhere to the protocol
Takeaways From Clinical Trials

- No serious reactions in these trials
- Breastfeeding was not impacted
- Growth was not impacted
- Timing matters
- Amount matters
- Sustaining exposure is important
- Compliance was poor
Timeline of Studies and Guidelines

- **2015**
  - LEAP Study: 80% reduction of peanut allergies

- **2016**
  - EAT Study: 67% reduction of peanut, egg, & milk allergies

- **2017**
  - NIH & AAP: New guidelines recommend *early peanut introduction*
  - British BSACI: New guidelines recommend *introducing egg and peanut earlier*
  - CA Pediatric Society: Approves claim *early introduction can help reduce allergies*

- **2018**
  - PETIT Study: 79% reduction of egg allergies
  - FDA: Approves claim *early introduction reduces peanut allergies*

- **2019**
  - Australia ASCIA: Recommends *early allergen exposure in first year of life*
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>AAP reverses previous position on avoidance in high risk infants</td>
</tr>
<tr>
<td>2010</td>
<td>NIAID recommends against delay of food introduction</td>
</tr>
<tr>
<td>Early 2017</td>
<td>NIAID further recommends early age-appropriate peanut introduction for all infants</td>
</tr>
<tr>
<td>Late 2017</td>
<td>FDA issues first qualified health claim on early introduction of peanuts to high-risk infants</td>
</tr>
<tr>
<td>March 2019</td>
<td>AAP releases clinical report updating and replacing 2008 guidance on roles of maternal and early infant diet in preventing food allergies and other atopic conditions</td>
</tr>
</tbody>
</table>
Recommendations on the prevention of peanut allergy are based primarily on LEAP trial

- Ground peanuts and other infant-safe forms of peanuts may be added to babies’ diets after other solid foods are tolerated
  - Whole peanuts are a choking hazard to children under 4

- Evidence does not currently support restricting a mother's diet during pregnancy or breastfeeding, nor the use of hydrolyzed formulas as methods of allergy prevention

- Exclusive breastfeeding for the first 3 to 4 months helps protect against eczema during a child’s first two years of life
Based on LEAP, an NIAID-sponsored expert panel applied the study results to high and moderate-risk infants

Ask your doctor if you are unsure about your child’s risk level

- **High risk (child has severe eczema, egg allergy or both):**
  - Introduce age-appropriate peanut-containing foods between 4 and 6 months.
  - Have your child professionally tested for peanut allergy first (using either a skin prick test or blood test)
  - This will help you and your healthcare provider decide whether to introduce peanut at home or in a healthcare setting

- **Moderate risk (child has mild or moderate eczema alone):**
  - Introduce age-appropriate peanut-containing foods at around 6 months.
  - See your doctor if you have any specific concerns

- **Low risk (child has neither eczema nor food allergy):**
  - Introduce peanut-containing foods depending on your family’s preferences and cultural practices
  - This is considered safe and should lead to a lower rate of peanut allergy, compared with previous recommendations to avoid peanut

Recommendations from International Societies

Australasian Society of Clinical Immunology and Allergy (ASCIA), May 2016
“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.”

The British Society for Allergy and Clinical Immunology (BSACI), May 2018
“In babies at higher risk of food allergy, studies have shown that starting egg and peanut earlier - from 4 months of age - can help prevent food allergy to egg and peanut.”

Canadian Paediatric Society (CPS), January 2019
“There is emerging evidence that early food introduction, between 4 to 6 months of age, may have a role in preventing food allergy, particularly for egg and peanut, in high-risk infants.”

American Academy of Pediatrics (AAP), March 2019
▪ “There is no evidence that delaying the introduction of allergenic foods, including peanuts, eggs, and fish, beyond 4 to 6 months prevents atopic disease.”
▪ “There is now evidence that early introduction of peanuts may prevent peanut allergy.”
▪ “There is now evidence that early introduction in infant-safe forms of peanuts reduces the risk of peanut allergies. Data area less clear for timing of introduction of eggs.”

Lessons From Early Introduction

- Safe and achievable for children with low risk of developing food allergy
- No effects on breastfeeding rates or later nutrition
- Allergen-specific: Early consumption of peanut has no effect on development of other food allergies
- Many children are sensitized even early in infancy
- Don’t delay introduction
- Exposure needs to be sustained


www.foodallergy.org
Remember, anyone can develop a food allergy

It’s no one’s fault when someone develops a peanut or other food allergy. Don’t feel guilty if it happens to you, your child or another family member.
Common Questions

▪ When to start? (Is 4-6 months early enough?)

▪ What food amounts to use? Can too low exposure amounts and frequency cause allergic responses?

▪ Sustained exposure is critical, but how long to continue? Months or years?

▪ Does it last? Is tolerance sustainable?
Infant Feeding in the Real World

Fantasy

Reality

www.foodallergy.org
Introducing Allergens

- Discuss questions with your child’s physician
- Risk levels
- Food allergic sibling and concerns around allergen cross-contact
- Challenges to feeding an infant
- Dosing and level of exposure
- Real-world experience
- Bottle introduction
Introducing Allergens: NIAID Feeding Guidelines

- Let your baby try other foods before you introduce anything with peanut

- Ensure your baby is ready for solid foods

- Never give infants and small children whole peanuts or straight peanut butter, as these foods are choking hazards

- Safe forms of peanut are described in the NIAID feeding guidelines:
  - Peanut butter-flavored corn puffs softened with water for younger babies
  - Smooth peanut butter thinned with water
  - Smooth peanut butter mixed with pureed fruits or vegetables
  - Peanut butter powder or peanut flour mixed with pureed fruits or vegetables


www.foodallergy.org
Progressive delay in timing of exposure to solid foods

- **1960s**: Average age 2 months
- **1970s**: Guidelines recommended delay until after 4 months
- **1990s**: Guidelines recommended delay until after 6 months
- **2000s (until 2008)**: For children at high food allergy risk, guidelines recommended delay until after 1 year for milk, 2 years for egg and 3 years for peanuts
- **2019**: AAP published new clinical report in March 2019
  - Still concludes that there is no evidence that delaying introduction of allergens beyond 4 to 6 months of age prevents atopic disease
  - Evidence supports early introduction of infant-safe forms of peanut
  - More data are needed to understand the impact of the timing of introduction of other foods such as egg on food allergy outcomes as limited evidence is less clear compared to peanut

Future Directions

- Perinatal interventions: pre-natal diet, lactation, etc.
- Environmental role
- Ongoing trials: earlier introduction
  - PreventADALL: Scandinavian study on early introduction of egg, milk, peanut, and wheat BY 4 months of age
  - HealthNuts and SchoolNuts Trials
Conclusion

▪ Food allergies are on the rise
▪ We still have a lot to learn – more research is needed
▪ There is strong evidence for early and sustained allergen introduction in reducing the risk
▪ Medical guidelines now broadly recommend the practice
▪ Parents struggle to adhere to early allergen feeding guidelines
▪ Key: start early and keep going!
Questions?