An Overview of Food Allergies in Children

Presented by
Stanley A. Cohen, MD
Pediatric Gastroenterology and Nutrition,
Children's Center for Digestive Health Care
Adjunct Professor, Emory University School of Medicine
Founder, CEO and Chair of the Medical Advisory Board, Nutrition4Kids
Faculty Presenter

Stanley A. Cohen, MD

Pediatric Gastroenterology and Nutrition, Children’s Center for Digestive Health Care
Adjunct Professor, Emory University School of Medicine
Founder, CEO and Chair of the Medical Advisory Board, Nutrition4Kids
Atlanta, Georgia
# Faculty Disclosures

<table>
<thead>
<tr>
<th>Role</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stanley A. Cohen, MD</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Research Support</strong></td>
<td>Takeda, Janssen, Medtronic, Abbvie, AstraZeneca, QOL</td>
</tr>
<tr>
<td></td>
<td><em>clinical area for above: IBD, Disaccharidase deficiencies, capsule endoscopy</em></td>
</tr>
<tr>
<td><strong>Speaker</strong></td>
<td>Janssen, Abbvie, QOL</td>
</tr>
<tr>
<td></td>
<td><em>clinical area for above: IBD, Disaccharidase deficiencies, capsule endoscopy</em></td>
</tr>
<tr>
<td><strong>Consultant</strong></td>
<td>Medtronic, Abbvie, AstraZeneca, Mead Johnson Nutrition</td>
</tr>
<tr>
<td></td>
<td><em>clinical area for above: Capsule endoscopy, IBD, infant and child nutrition</em></td>
</tr>
<tr>
<td><strong>Educational Support</strong></td>
<td>Nutricia</td>
</tr>
<tr>
<td></td>
<td><em>clinical area for above: infant and child nutrition</em></td>
</tr>
</tbody>
</table>
Learning Objectives

Characterize the growing prevalence of food allergy among infants and children

Differentiate IgE-mediated, NON-IgE-mediated and MIXED IgE and NON-IgE-mediated reactions in pediatric patients
INTRODUCTION TO FOOD ALLERGY

- Food allergy epidemiology
- Food allergy burden
- Natural history of atopic conditions
Defining Food Allergies

- A **food** is any substance—whether processed, semiprocessed, or raw—intended or adapted for human consumption.

- A **food allergy** is an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.

- **Food allergens** are specific components of food recognized by allergen-specific cells that elicit specific immune reactions.
Food and Skin Allergies Have Nearly Doubled in the Past 20 Years

- Food allergy: +63.5% increase
- Skin allergy: +82.4% increase

*Data from 2009 included children <17 years of age. †Includes hay fever and respiratory allergies.

Prevalence of Food Allergy Worldwide

Burden of Allergic Diseases

Allergy has a significant impact:

- Up to 50 million Americans are affected
- Allergy is the sixth-leading cause of chronic disease in the United States and appears to be on the rise
- The impact on the US health care system is $18 billion per year
- Improved prevention and diagnostic techniques are needed due to the increased prevalence and its associated cost and social impact
Food Allergies

- In the United States, 3 million children are affected by food allergies
- Food allergy is most common in infants and children
- Eight food groups account for 90% of all food allergies in the United States
Daily Considerations for Families With Food Allergies

- Avoiding **cross-contact at home, restaurants, school, and others’ homes**, which can include the following:
  - Handwashing and cleaning after meal preparation
  - Avoiding airborne allergens (e.g., using powdered milk or wheat flour)
  - Creating allergen-free zones in the home
  - Labeling unsafe foods
  - Separating eating utensils and dishes
  - Communicating allergies with restaurant and school staff
  - Avoiding food sharing/contamination outside the home
- Checking **packaged food labels** for potential allergens
- Preparing a **food allergy and anaphylaxis emergency care plan**
  - Carrying emergency medications at all times
The atopic march describes an association between atopic dermatitis, IgE-mediated food allergy, allergic asthma, and allergic rhinitis, which begins with an atopic family history.
Evidence for the Atopic March

Proportion of infants with cow’s milk allergy who experience other atopic conditions at 5 years of age

- Other food allergies: 75%
- Allergic rhinitis: 43%
- Asthma: 40%
- Atopic dermatitis: 21%

Infants with cow’s milk allergy may become susceptible to other allergies later in life.

References:
Food Allergy Pathology

Intrinsic Properties of Food Allergens

- Genetics
  - Adaptive immunity
  - Innate immunity
  - Intestinal and cutaneous barriers

- Environment
  - Environmental exposure
  - Maternal factors
  - Skin and gut microbiome

Food allergy

Benefits of Human Milk and Allergy Development

- Exclusive breastfeeding up to 4 months of age is associated with reduced risk of eczema, wheezing, and cow's milk allergy later in life
  - Breastfeeding beyond 4 months does not reduce the risk of atopic diseases, but up to 1 year of age may reduce risk of gastrointestinal illnesses
- Most studies on breastfeeding have been too small to study the effect on food allergy development
  - Current evidence is conflicting
  - Variability of human milk composition may account for differences across trials
- There are multiple beneficial components of human breast milk
- Maternal avoidance of foods during pregnancy or breastfeeding is currently not recommended
  - No evidence in limiting allergy development

Early Exposure to Microbes May Mediate Development of Allergy

- Formerly known as the hygiene hypothesis, now better characterized as the **Old Friends Mechanism**
  - Early exposure to nonpathogenic microbes that inhabit the natural environment and human microbiome may **promote tolerance** in the immune system and **prevent the development of allergies**

- **Temporal increases in allergic disease** may be attributable to decreased early exposure to “Old Friends” caused by:
  - Changes in lifestyle
  - Rapid urbanization
  - Altered diet
  - Excessive antibiotic use
  - **Not related to** hygiene/cleanliness

The Microbiome Is Critical to Immune Health

Early-life critical window

Conception
- Maternal to fetal microbial transfer

Birth
- Colonization through birth canal
- Microbiome composition is guided by immune, metabolic, and hormonal development

1 year
- Microbiome maturation

Early childhood

---

1 Microbiome maturation is guided by breastfeeding and diet. Antibiotics can disrupt microbiome maturation.

Microbiome Disruption May Predispose to Allergy

- In an analysis of **166 infants** from the longitudinal CHILD study, infants who developed allergies at 1 year \((n = 12; 7.2\%)\) had the following gut disruptions:
  - **Enterobacteriaceae were overrepresented** and **Bacteroidaceae were underrepresented** at 3 months and 1 year
  - **Lower microbiome richness** at 3 months

- Each quartile increase in microbiota richness at 3 months was associated with a **55% reduction in risk** for food allergy by 1 year

- Each quartile increase in the Enterobacteriaceae-to-Bacteroidaceae ratio resulted in a **2-fold increase in risk** for food allergy by 1 year

CHILD, Canadian Healthy Infant Longitudinal Development.

FOOD ALLERGY CHARACTERIZATION

• Differences between IgE- and non-IgE-mediated food allergies
• Clinical signs and symptoms
• Defining tolerance and intolerance
Symptoms of IgE-Mediated Food Allergy Reactions

**Ocular:** Pruritus, conjunctival erythema, tearing, periorbital edema

**Oral:** Angioedema of the lips, tongue, or palate; oral pruritus; tongue swelling

**Lower respiratory:** Cough, chest tightness, dyspnea, wheezing, intercostal retractions, accessory muscle use

**Gastrointestinal:** Nausea, abdominal pain, reflux, vomiting, diarrhea, irritability and food refusal with weight loss over time

**Upper respiratory:** Nasal congestion, pruritus, rhinorrhea, sneezing, laryngeal edema, hoarseness, dry staccato cough

**Cardiovascular:** Tachycardia (occasionally bradycardia in anaphylaxis), hypotension, dizziness, fainting, loss of consciousness

**Cutaneous:** Erythema, pruritus, urticaria, morbilliform eruption, angioedema, eczematous rash

**Other:** Uterine contractions, sense of “impending doom”

Cow’s Milk Allergy/Hypersensitivity Linked to Gastroesophageal Reflux

- In a study of 81 children with GERD, only 66.7% responded to omeprazole
- The remaining one-third of cases were resolved with the elimination of cow’s milk from the diet
- Cow’s milk allergy may mimic or aggravate GERD

Other Features of IgE-Mediated Allergy

- Quick onset
- Reproducible
- Specific indications
- Specific foods
- Positive tests
- May develop tolerance

Diagnosing IgE-mediated Food Allergy

- Requires thorough clinical history and physical exam
  - Obtain information about the history and severity of reactions

- Diagnosis of IgE-mediated food allergy
  - Skin prick test—measure wheal size
  - In vitro immunoassays—measure serum IgE levels

For more information, see *Diagnosing Food Allergies in Infants and Children* with Jonathan Spergel, MD, PhD.
Defining Tolerance and Intolerance

- Although the words tolerance and intolerance are spelled as if they are opposites, they are **unrelated terms**.

- **Tolerance** is a state in which an individual is symptom-free after consumption of a specific food or upon oral food challenge:
  - Can be short- or long-term.

- **Intolerance** is a non-immunologic adverse reaction to food (e.g., reaction to milk due to lactose intolerance).
Development of Tolerance

- Most children with food allergy will **outgrow** allergies to milk, egg, soy, and wheat.
- **Tolerance can develop at any time**, from early childhood to teenage years.
- Higher levels of serum IgE at diagnosis are associated with a lower rate of tolerance development.
- Tolerance development usually—but not always—correlates with a decrease in serum IgE levels over time.
  - Tolerance development may not correlate with changes in response to skin prick tests, but a reduction in the size of a wheal may be suggestive of tolerance onset.
Common Allergens and Rates of Tolerance Development

- 80% of allergic children become tolerant to milk by age 5 years\(^1\)
- 66% of allergic children become tolerant to eggs by age 7 years\(^1\)
- 65% of allergic children become tolerant to wheat by age 12 years\(^1\)
- 20% of allergic children become tolerant to peanuts\(^2\)

---

Adverse Food Reactions

Nontoxic Reactions

Pharmacologic Reactions
- Caffeine sensitivity

Food Intolerance
- Lactase deficiency
- Sucrase-isomaltase deficiency
- Galactosemia

Food Allergy
- IgE-Mediated
  - Hives
  - Anaphylaxis
- Non-IgE-Mediated
  - Intestinal reactions

Toxic Reactions
- Food poisoning
- Infections

†Toxic reactions are not caused by allergic reactions and are instead caused by the ingestion of toxins (eg, Shiga toxin-producing E coli).

Cow’s Milk Allergy: A Common Food Allergy

- Cow’s milk allergy is an immune reaction to the proteins in cow’s milk\(^1\)
  - Affects 2%-3% of infants\(^1,2\)
  - May be mediated by IgE, non-IgE, or mixed IgE and non-IgE pathways\(^3\)
- Cow’s milk allergy should not be confused with lactose intolerance
  - Lactose intolerance is an inability to digest lactose due to absence of the digestive enzyme lactase—no immune involvement\(^4\)

For more information, see **Cow’s Milk Allergy: Mechanisms, Diagnosis and Treatment** with David Fleischer, MD, and Carina Venter, PhD, RD.

Allergic Disorders

**IgE**
- Pollen-food allergy syndrome
- Immediate GI hypersensitivity

**Mixed**
- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis

**Non-IgE**
- Dietary protein enterocolitis
- FPIES

**Gastrointestinal**

**Cutaneous**
- Acute urticaria & angioedema
- Acute contact urticaria
- Atopic dermatitis
- Dermatitis herpetiformis

**Respiratory**
- Allergic rhinitis
- Acute bronchospasm
- Asthma
- Heiner syndrome

**Systemic**
- Generalized anaphylaxis
- Food-associated anaphylaxis
- Exercise-induced anaphylaxis

FPIES, food protein-induced allergic proctocolitis.

† Food allergy is an uncommon cause of these respiratory syndromes.
## Comparison of IgE- and Non-IgE-mediated Food Allergies

<table>
<thead>
<tr>
<th></th>
<th>IgE-mediated food allergy</th>
<th>Mixed IgE or non-IgE-mediated food allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence in children</strong></td>
<td>More common, about 6%</td>
<td>Rare, &lt;1%</td>
</tr>
<tr>
<td><strong>Typical organ systems involved in symptom presentation</strong></td>
<td>Symptoms across broad range of organs, including oral, respiratory, cardiovascular, cutaneous, and gastrointestinal systems</td>
<td>Symptoms usually isolated to gastrointestinal system</td>
</tr>
<tr>
<td><strong>Timing after oral intake</strong></td>
<td>Usually seconds to minutes (within 2 hours)</td>
<td>Usually hours to days</td>
</tr>
<tr>
<td><strong>Severity</strong></td>
<td>May proceed to anaphylaxis</td>
<td>Variable, life-threatening is rare but can occur (eg, FPIES)</td>
</tr>
<tr>
<td><strong>Pathogenesis</strong></td>
<td>Type 1 immune hypersensitivity (IgE-mediated)</td>
<td>Cell-mediated immune hypersensitivity</td>
</tr>
<tr>
<td><strong>Examples</strong></td>
<td>Peanuts, tree nuts, seafood, milk</td>
<td>Eosinophilic esophagitis, food protein-induced enterocolitis syndrome</td>
</tr>
</tbody>
</table>
Food Protein-Induced Enterocolitis (FPIES)

- Age of onset is usually less than 12 months with a <1% prevalence rate
- Milk and soy are most common triggers, but rice, chicken, oat, egg, fish, vegetables, or peanuts may be causative as well
  - Patients often react to more than one food
- FPIES will test negative on skin prick tests and blood tests

For more information, see
Guidelines for Diagnosis and Management of Food Protein-Induced Enterocolitis Syndrome
with Anna Nowak-Węgryzn, MD, PhD.
Eosinophilic Esophagitis (EoE)

- Prevalence of 1 in 2000 children, most commonly in boys (3:1 ratio)
- Symptoms vary with age
  - **Infants and toddlers** – reflux symptoms (vomiting, regurgitation, heartburn, epigastric pain, growth concerns)
  - **School-age children** – abdominal pain
  - **Adolescents and adults** – dysphagia (symptoms are often intermittent)

For more information on EoE, see *Eosinophilic Esophagitis: Practical Diagnosis and Management of Pediatric Patients with EoE* with Mirna Chehade MD, MPH.
FOOD ALLERGY AND NUTRITION
Historically, People Were 100% Breast-fed

- Existence of mankind dependent upon our ability to reproduce and feed our young
- Foods were introduced at 1 year of age
  - Both timing and food introduced were dependent on culture
- Today, infants are often introduced to cow's milk and other foods at earlier ages

Benefits of Breastfeeding

1. No mixing errors
2. Travels well
3. Price is right
4. Don’t have to sterilize nipples
5. Maternal bonding
6. Easy to digest/absorb
7. Decreased infections (otitis and diarrheal)
8. Optimal growth and neurodevelopment
9. You can’t trust cows
10. Reduced allergy
Choosing Infant Formulas

- Most infants will respond well to routine cow’s milk-based formula.
- Soy formula can be an option for infants with cow’s milk allergy, but many infants allergic to milk protein will also be allergic to soy.
- Protein hydrolysate formulas can be helpful for infants with GI bleeding on cow’s milk-based or soy formulas.

For more information, see Optimizing Nutrition in Infants at High-Risk for Developing Allergy with Tatyana Hofmekler, MD, MSc.
Complementary Foods and Growth

• Breast milk is the gold standard to supply nutrients that support optimal growth and development for the first 6 months\(^1\)

• After starting complementary foods, mothers should continue to breastfeed or use infant formula through the first year or beyond as desired\(^1,2\)

• Earlier introduction of complementary foods has not been shown to improve growth before 6 months\(^2\)

AAP Recommends Gradually Adding Complementary Foods at 4 to 6 Months of Age

- Preference is to wait until 4 to 6 months
- However, unique needs or feeding behaviors of the infant may warrant the addition of safe and nutritious complementary foods between 4 and 8 months
- Before 6 months of age, complementary foods may be a less nutritious substitute for human milk or infant formula
- By 6 months, most infants will have reached developmental milestones that allow for the first introduction of complementary foods

Developmental Milestones for Complementary Feeding

- Renal, GI function can metabolize nutrients from complementary foods
- GI maturation driven by ingested foods
- Oral motor function developed for semisolid, solid foods
- Chew and swallow lumpier foods
- Sit up with support
- Sweep food from spoon with upper lip
- Able to feed themselves
- Drink from standard cup
- Eat bite-sized pieces of family foods

Food Consistency During Complementary Feeding

- Renal, GI function can metabolize nutrients from complementary foods
- GI maturation driven by ingested foods
- Aspiration risk of solid foods

- Sit up with support
- Sweep food from spoon with upper lip
- Pureed, mashed, semisolid foods
- Chew and swallow lumpier foods
- Finger foods that child can eat without help

- Critical window to introduce lumpy foods at 10 months
- Family foods in bite-sized pieces

- Oral motor function developed for semisolid, solid foods
- Able to feed themselves
- Drink from standard cup
- Eat bite-sized pieces of family foods

180-degree Change in Prevention Rationale

American Academy of Pediatrics Guidelines on Preventing Food Allergy

**2000**
- Wait to introduce allergenic foods:
  - Milk: 1 year
  - Eggs: 2 years
  - Nuts and fish: 3 years

**2008**
- No evidence for delaying introduction of allergenic foods:
  - Milk, eggs, nuts, and fish: 4-6 months

**2015**
- No evidence for delaying introduction of allergenic foods:

**2019**
- Early introduction of peanuts may be beneficial for infants at high risk for allergy:
  - Milk, eggs, tree nuts, and fish: 4-6 months
  - Peanuts: 4-6 months

---
# How Does Culture Affect the Types of Complementary Foods Offered?

<table>
<thead>
<tr>
<th></th>
<th>4-5 months</th>
<th>6-11 months</th>
<th>12-24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hispanic, %</td>
<td>Non-Hispanic, %</td>
<td>Hispanic, %</td>
</tr>
<tr>
<td>Noninfant cereal</td>
<td>18.5 †</td>
<td>29.2</td>
<td>45.3</td>
</tr>
<tr>
<td>Rice</td>
<td>15.9 *</td>
<td>4.7</td>
<td>26.9 †</td>
</tr>
<tr>
<td>Grains in mixed dishes</td>
<td>15.9</td>
<td>13.0</td>
<td>38.8 †</td>
</tr>
<tr>
<td>Pizza</td>
<td></td>
<td>1.4</td>
<td>1.0 †</td>
</tr>
<tr>
<td>Canned fruit</td>
<td>2.3</td>
<td>8.8</td>
<td>12.1 *</td>
</tr>
<tr>
<td>Fresh fruit</td>
<td>9.1 †</td>
<td>30.0 *</td>
<td>59.3</td>
</tr>
<tr>
<td>Beans and peas</td>
<td>1.4</td>
<td>5.8</td>
<td>19.1 †</td>
</tr>
<tr>
<td>Soup</td>
<td>16.3 *</td>
<td>5.1</td>
<td>23.4 †</td>
</tr>
<tr>
<td>Baby cookies</td>
<td>1.3</td>
<td>1.1</td>
<td>24.8 †</td>
</tr>
<tr>
<td>Sweetened drinks</td>
<td></td>
<td>13.9</td>
<td>53.5 †</td>
</tr>
</tbody>
</table>

*P < .05 vs non-Hispanics; †P < .01 vs non-Hispanics.

Which Foods Should Be Avoided?

- High fat
- High sugar
- Cow’s milk
- Honey
- Choking hazard

1 Before infant is aged 4 to 6 months.
2 Examples are whole nuts or grapes, raw carrots, hot dogs, candy, popcorn.
3 Avoid honey and corn syrup, as they may contain botulism spores.

Encourage Responsive Feeding

Optimal infant feeding depends on what + how + when + where + by whom

Responsive Feeding

- Feed infants directly; assist older children
- Talk to children during feeding; use eye contact
- Be responsive to hunger and satiety cues
- Feed slowly with patience, encouragement; no force feeding
- Experiment with taste, texture, different foods
- Minimize distractions at mealtime
- Feeding involves learning and love

Development of Taste and Food Preferences Influenced by Many Factors

- Innate preference for sweet, salty
- Innate dislike of sour, bitter
- Parental influence
- Cultural influence
- Learned favorites
- Flavor exposure in utero
- Flavor exposure from breast milk
- Fear of new foods
- Variety of food offered

And allergies!

# Food Choices for Nutrients That Allergic Children May Lack

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Lost nutrients</th>
<th>Suggested alternatives (if not allergic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>Protein, fat, calcium, riboflavin, phosphorous, vitamins A, D, B12</td>
<td>Meat, fish, poultry, legumes, eggs, fortified milk substitutes, calcium-fortified foods or drinks</td>
</tr>
<tr>
<td>Eggs</td>
<td>Protein, iron, biotin, folacin, riboflavin, vitamins A, D, E, B12, selenium</td>
<td>Meats, fish, poultry, legumes, dairy, leafy greens, enriched grains</td>
</tr>
<tr>
<td>Soy</td>
<td>Protein, thiamin, riboflavin, iron, calcium, zinc, vitamin B6</td>
<td>Meats, fish, poultry, legumes, eggs, dairy, fruit, vegetables, leafy greens, enriched grains</td>
</tr>
<tr>
<td>Wheat</td>
<td>Thiamin, niacin, riboflavin, folate, iron, fiber</td>
<td>Meats (iron), whole and fortified alternate grain products (oats, buckwheat, amaranth, millet, quinoa, teff, sorghum), seeds, legumes</td>
</tr>
<tr>
<td>Peanuts and tree nuts</td>
<td>Protein, vitamins, minerals</td>
<td>Meats, fish, poultry, eggs, dairy, fruit, vegetables, enriched grains, seeds</td>
</tr>
</tbody>
</table>

For more information, see

**Clinical Recommendations for Reducing and Preventing Food Allergies**

with Hugh Sampson, MD, and Marion Groetch, MS, RDN.