

# An Overview of Food Allergies in Children



ANNENBERG CENTER FOR HEALTH SCIENCES  
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*Imparting knowledge. Improving patient care.*

*Presented by*

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# Faculty Disclosures

## Stanley A. Cohen, MD

### Research Support

Takeda, Janssen, Medtronic, Abbvie, AstraZeneca, QOL

*clinical area for above: IBD, Disaccharidase deficiencies, capsule endoscopy*

### Speaker

Janssen, Abbvie, QOL

*clinical area for above: IBD, Disaccharidase deficiencies, capsule endoscopy*

### Consultant

Medtronic, Abbvie, AstraZeneca, Mead Johnson Nutrition

*clinical area for above: Capsule endoscopy, IBD, infant and child nutrition*

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*clinical area for above: infant and child nutrition*



# 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

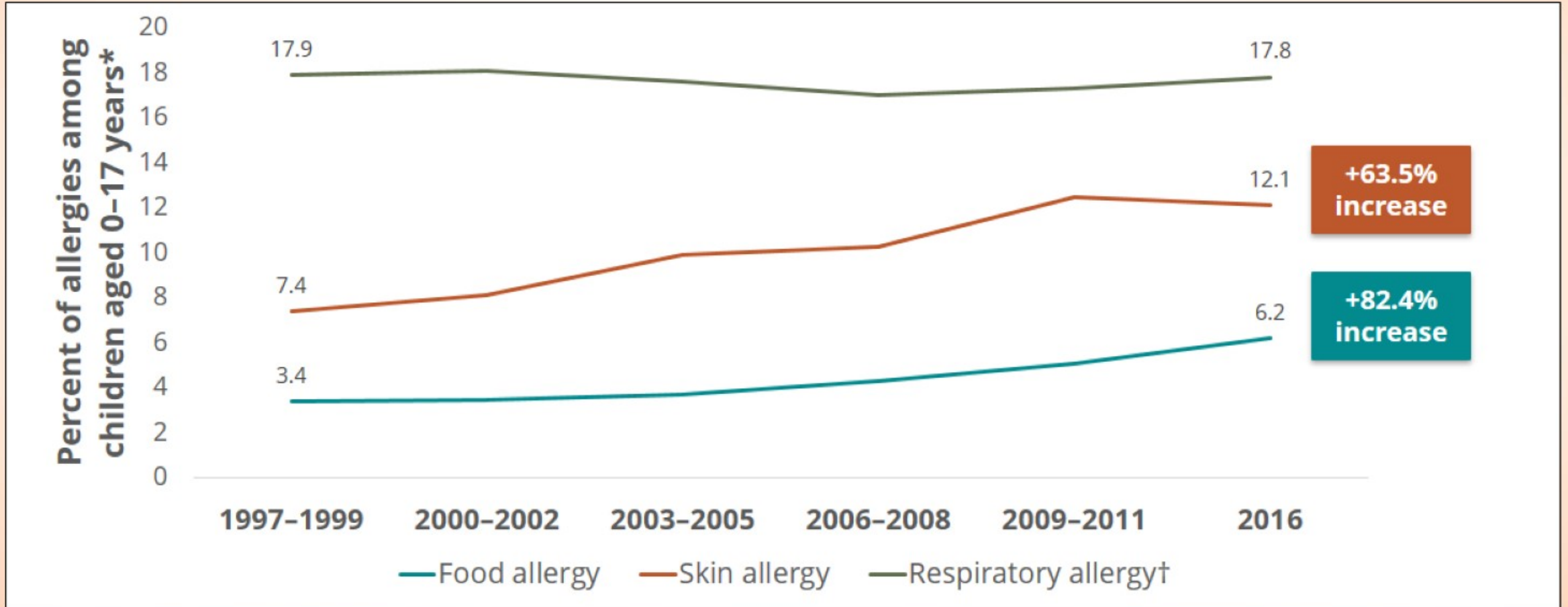


# Defining Food Allergies

- 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



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

Image adapted from Jackson KD, et al. *NCHS Data Brief*. 2013;(121):1-8.  
Black LI, Benson V. Tables of Summary Health Statistics for US Children: 2016 National Health Interview Survey.  
[https://ftp.cdc.gov/pub/Health\\_Statistics/NCHS/NHIS/SHS/2016\\_SHS\\_Table\\_C-12.pdf](https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2016_SHS_Table_C-12.pdf). Published 2018. Accessed June 10, 2019.



# Prevalence of Food Allergy Worldwide

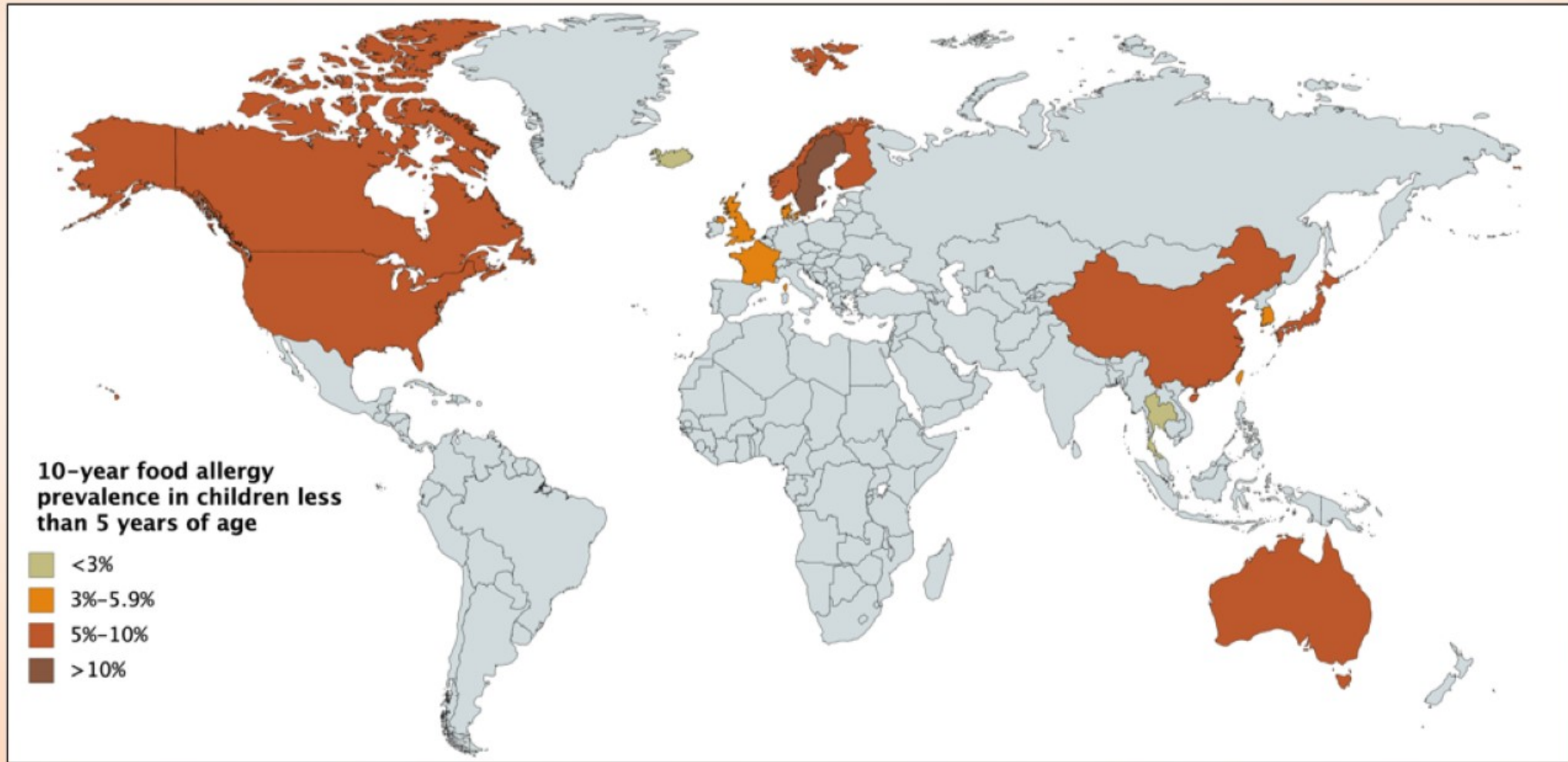


Image adapted from Renz H, et al. *Nat Rev Dis Primers*. 2018;4:17098.





# 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



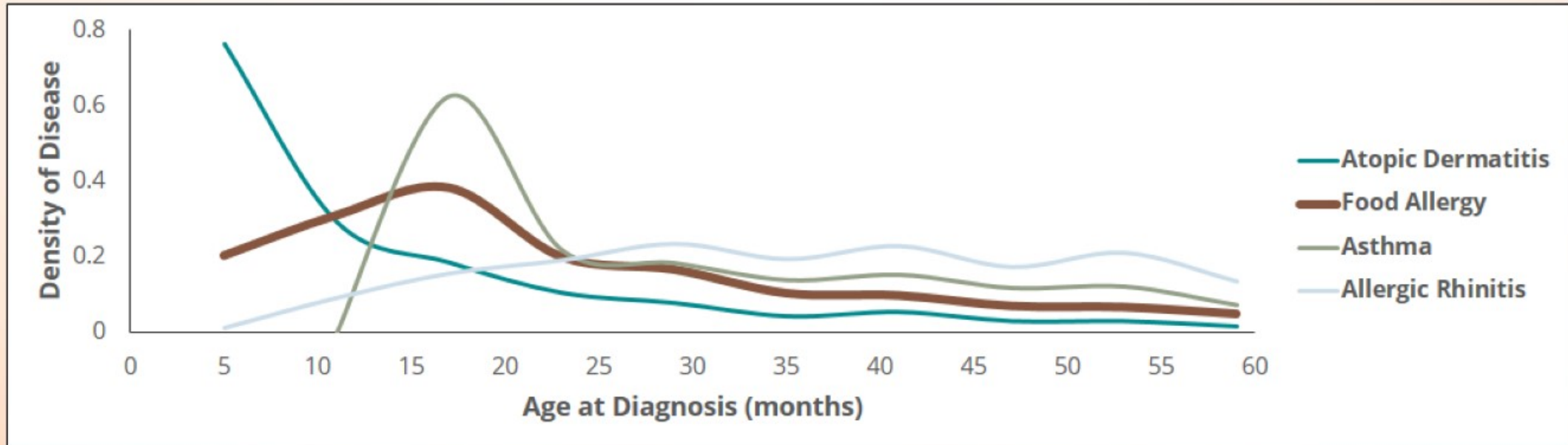
# Daily Considerations for Families With Food Allergies

- Avoiding **cross-contact at home, restaurants, school, and others' homes**, which can include the following:
  - Handwashing and cleaning after meal preparation
  - Avoiding airborne allergens (eg, 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

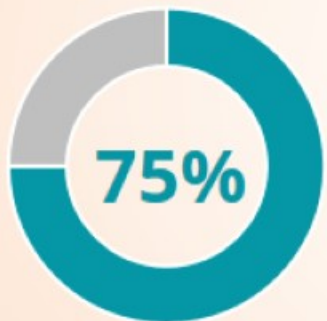
The atopic march describes an association between atopic dermatitis, IgE-mediated food allergy, allergic asthma, and allergic rhinitis, which begins with an atopic family history.



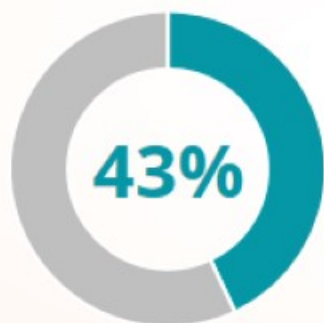
# Evidence for the Atopic March

Proportion of infants with cow's milk allergy who experience other atopic conditions at 5 years of age<sup>1</sup>

Other food allergies



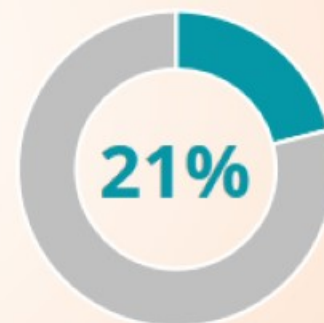
Allergic rhinitis



Asthma



Atopic dermatitis

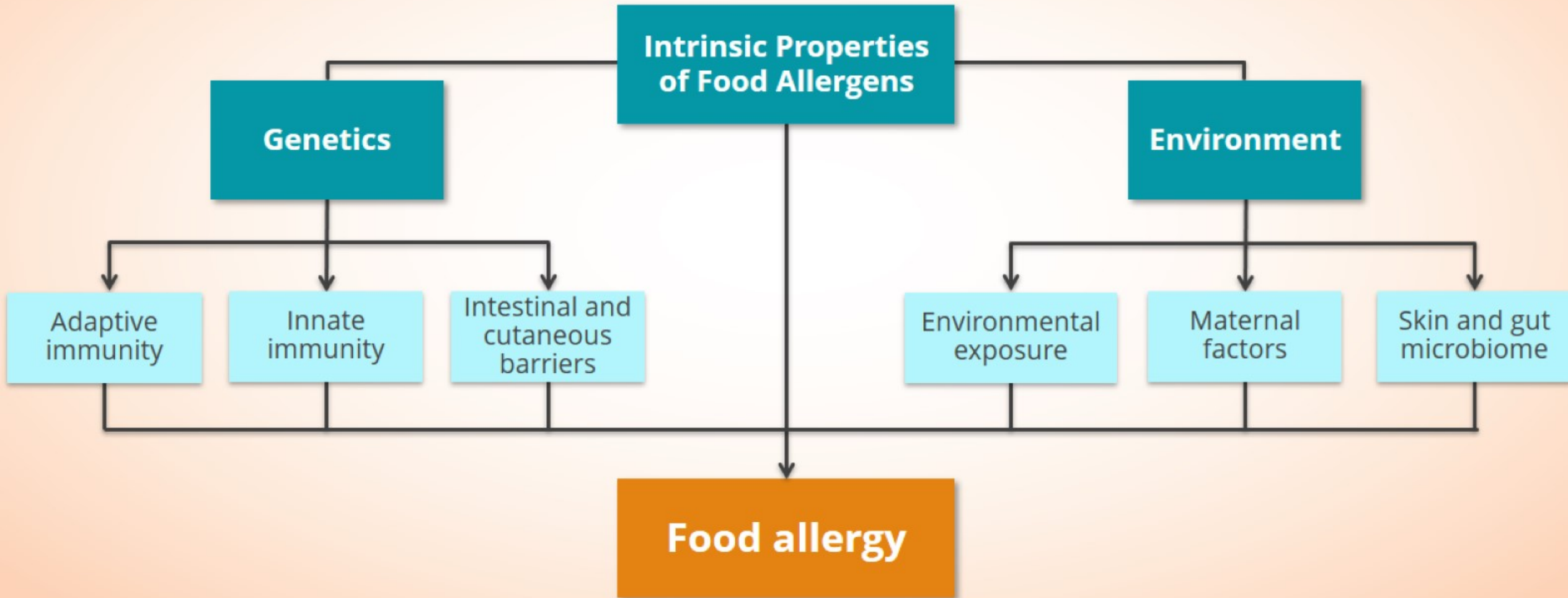


Infants with cow's milk allergy may become susceptible to other allergies later in life.



1. Bishop JM, et al. *J Pediatr*. 1990;116(6):862-867.
2. Høst A, et al. *Allergy*. 1990;45(8):587-596.
3. Wood RA, et al. *J Allergy Clin Immunol*. 2013;131(3):805-812.
4. Thomsen SF. *Eur Clin Respir J*. 2015;2.

# Food Allergy Pathology



Adapted from Otsu K, Dreskin SC. *Discov Med*. 2011;12(65):319-328.



# 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<sup>†</sup>



**1 year**

Microbiome  
maturation



**Early childhood**

<sup>†</sup>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.

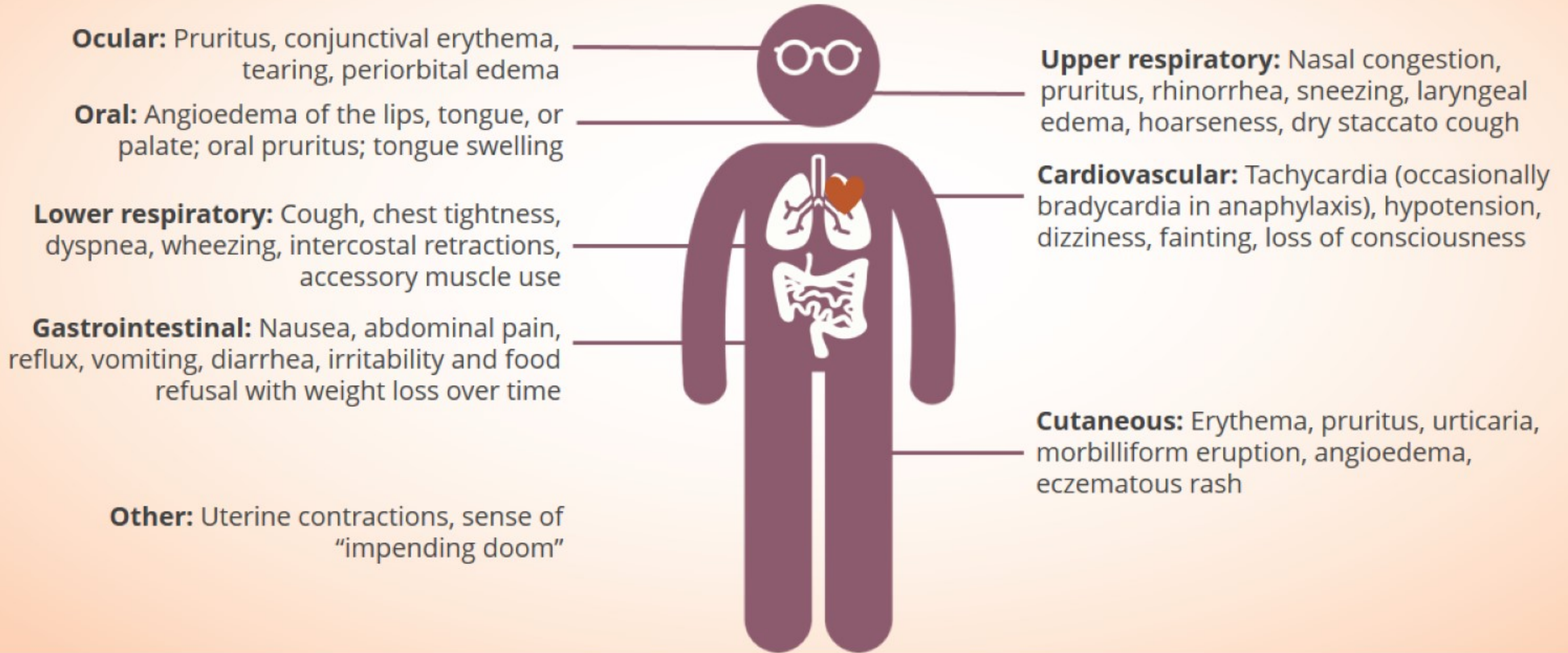


# FOOD ALLERGY CHARACTERIZATION

- Differences between IgE- and non-IgE-mediated food allergies
- Clinical signs and symptoms
- Defining tolerance and intolerance



# Symptoms of IgE-Mediated Food Allergy Reactions



# 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



Credit: yavdat/Bigstock

1. Burks AW, et al. *J Allergy Clin Immunol*. 2012;129(4):906-920.
2. Burks AW, et al. *Pediatrics*. 2011;128(5):955-965.
3. Sicherer SH, et al. *Pediatrics*. 2012;129(1):193-197.



# 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 (eg, 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**<sup>1</sup>



**66%** of allergic children become tolerant to **eggs** by age **7 years**<sup>1</sup>



**65%** of allergic children become tolerant to **wheat** by age **12 years**<sup>1</sup>

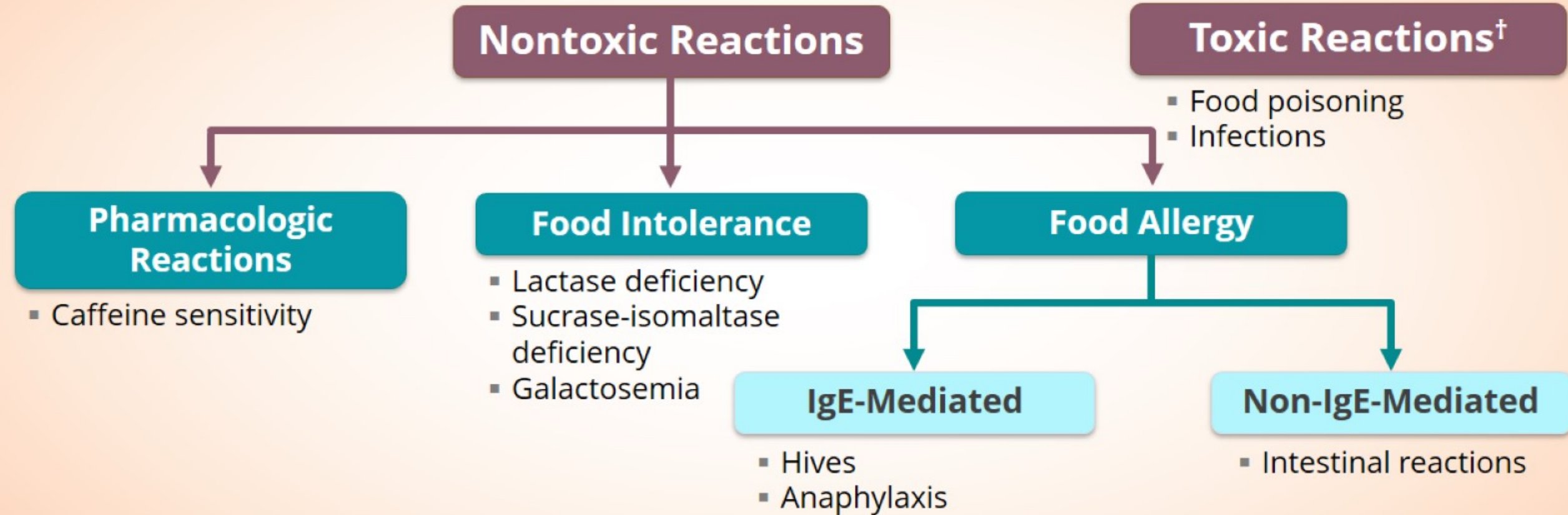


**20%** of allergic children become tolerant to **peanuts**<sup>2</sup>

1. NIAID-Sponsored Expert Panel. *J Allergy Clin Immunol.* 2010;126(6 Suppl):S1-S58.  
2. Peters RL, et al. *J Allergy Clin Immunol.* 2015;135(5):1257-66.e1-2.



# Adverse Food Reactions



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

Adapted from Cianferoni A, Spergel JM. *Allergol Int.* 2009;58(4):457-466.



# Cow's Milk Allergy: A Common Food Allergy

- Cow's milk allergy is an immune reaction to the proteins in cow's milk<sup>1</sup>
  - Affects 2%–3% of infants<sup>1,2</sup>
  - May be mediated by IgE, non-IgE, or mixed IgE and non-IgE pathways<sup>3</sup>
- 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<sup>4</sup>

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

1. Caffarelli C et al. *J Pediatr*. 2010;36:5.

2. Høst A. *Ann Allergy Asthma Immunol*. 2002;89(6 Suppl 1):33-37.

3. NIAID-Sponsored Expert Panel. *J Allergy Clin Immunol*. 2010;126(6 Suppl):S1–S58.

4. du Toit G et al. *Arch Dis Child*. 2010;95:134-144.



# Allergic Disorders



Gastrointestinal

Pollen-food allergy syndrome  
Immediate GI hypersensitivity

Eosinophilic esophagitis  
Eosinophilic gastritis  
Eosinophilic gastroenteritis

Dietary protein enterocolitis  
FPIES



Cutaneous

Acute urticaria & angioedema  
Acute contact urticaria

Atopic dermatitis

Dermatitis herpetiformis



Respiratory

Allergic rhinitis<sup>†</sup>  
Acute bronchospasm<sup>†</sup>

Asthma<sup>†</sup>

Heiner syndrome



Systemic

Generalized anaphylaxis  
Food-associated anaphylaxis  
Exercise-induced anaphylaxis

FPIES, food protein-induced allergic proctocolitis.

<sup>†</sup>Food allergy is an uncommon cause of these respiratory syndromes.



# Comparison of IgE- and Non-IgE-mediated Food Allergies

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



# 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-Węgrzyn, 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 diarrhea)
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<sup>1</sup>
- After starting complementary foods, mothers should continue to breastfeed or use infant formula through the first year or beyond as desired<sup>1,2</sup>
- Earlier introduction of complementary foods has not been shown to improve growth before 6 months<sup>2</sup>

1. American Academy of Pediatrics. *Pediatrics*. 2005;115:496-506.  
2. Agostoni C, et al. *JPGN*. 2008;46:99-110.

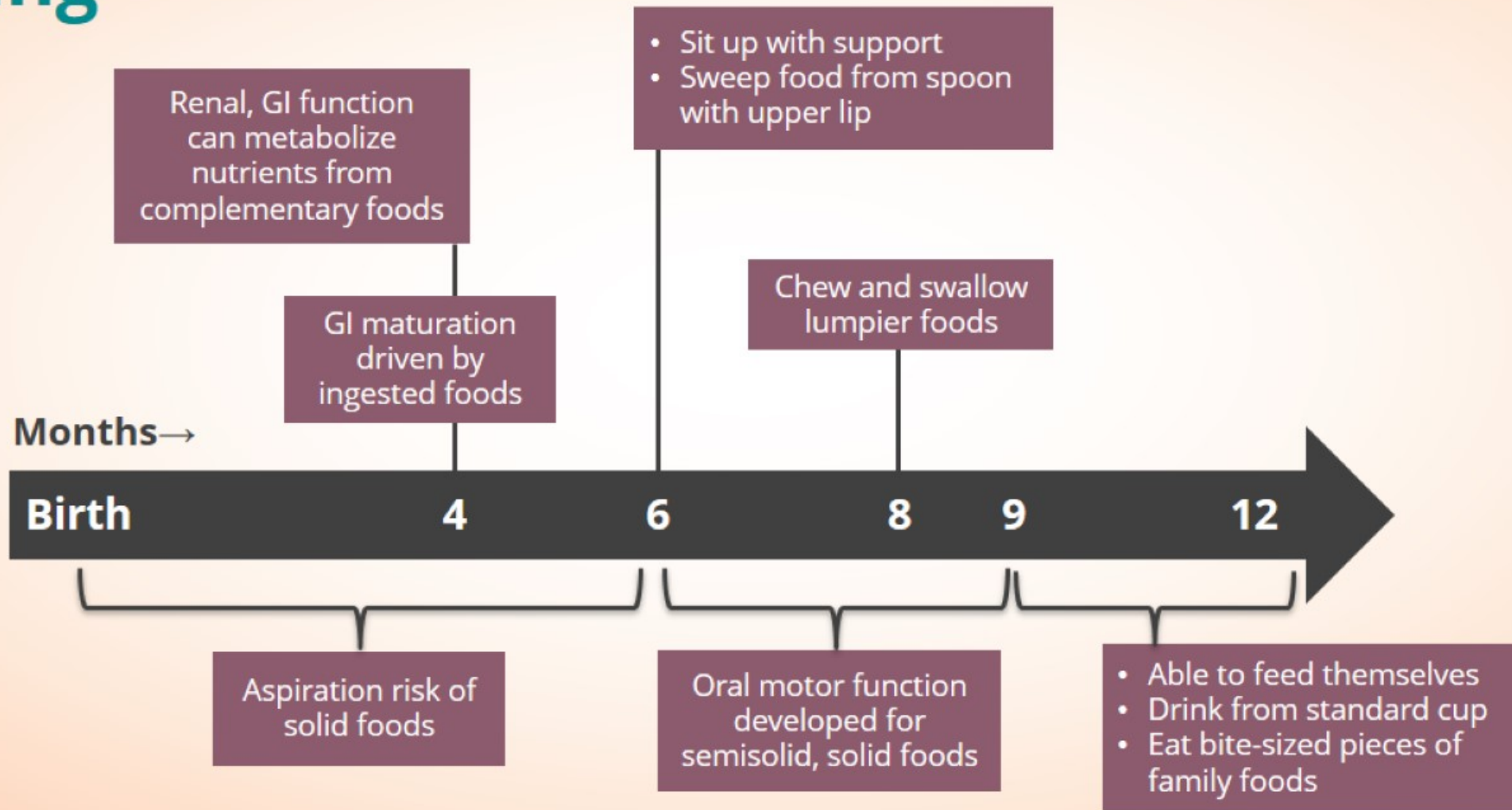


# AAP Recommends Gradually Adding Complementary Foods at 4 to 6 Months of Age

- 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



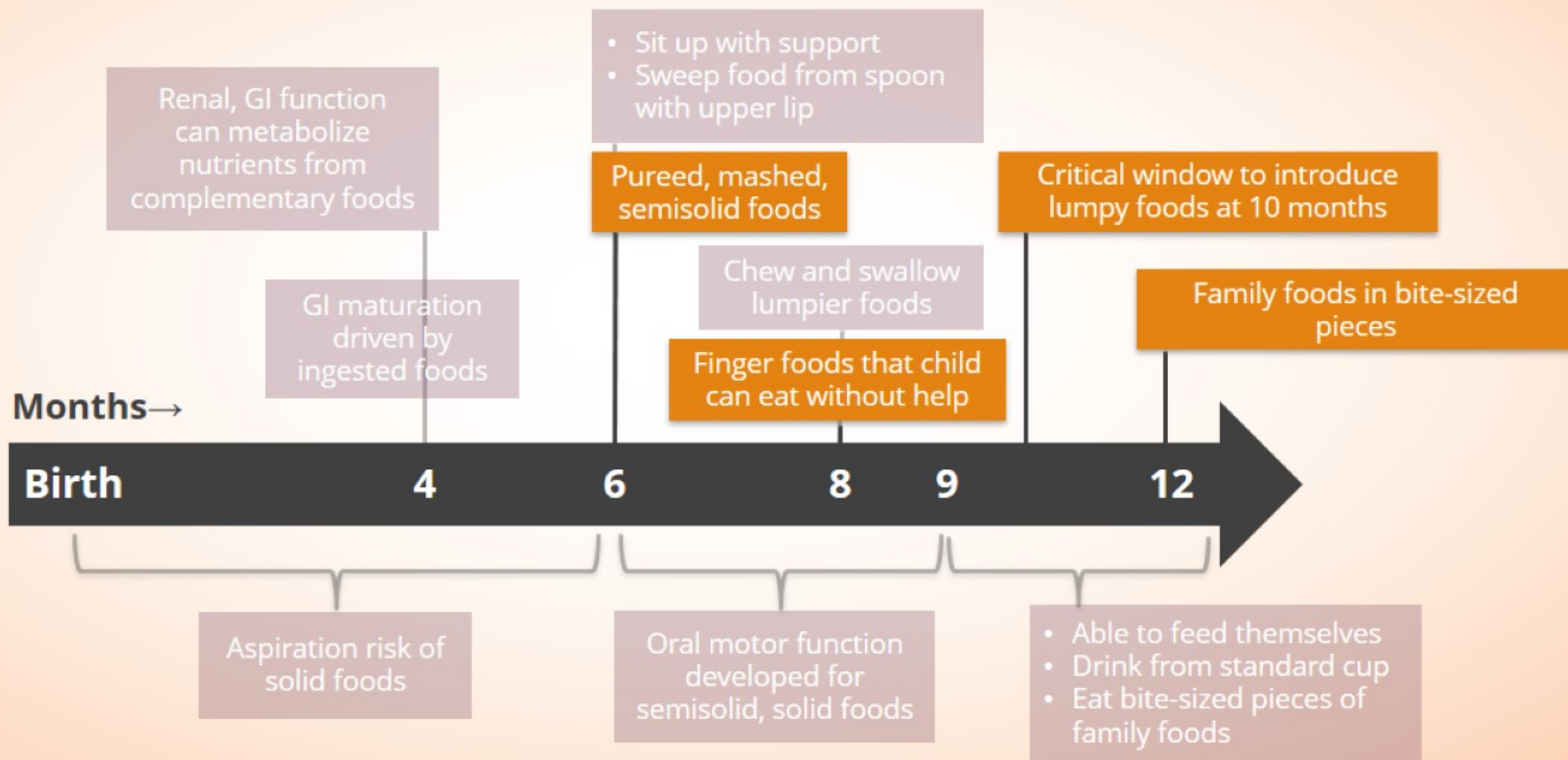
# Developmental Milestones for Complementary Feeding



1. Naylor AJ, Morrow AL. Washington, DC: Wellstart International and the LINKAGES Project/Academy for Educational Development; 2001. [www.pronutrition.org/files/Developmental%20Readiness.pdf](http://www.pronutrition.org/files/Developmental%20Readiness.pdf). Accessed February 16, 2012.
2. ESPGHAN Committee on Nutrition: Agostoni C, et al. *JPGN*. 2008;46:99-110.



# Food Consistency During Complementary Feeding



1. Naylor AJ, Morrow AL. Washington, DC: Wellstart International and the LINKAGES Project/Academy for Educational Development; 2001. [www.pronutrition.org/files/Developmental%20Readiness.pdf](http://www.pronutrition.org/files/Developmental%20Readiness.pdf). Accessed February 16, 2012.
2. ESPGHAN Committee on Nutrition: Agostoni C, et al. *JPGN*. 2008;46:99-110.



# 180-degree Change in Prevention Rationale

## American Academy of Pediatrics Guidelines on Preventing Food Allergy

2000<sup>1</sup>

Wait to introduce allergenic foods:



Milk: 1 year



Eggs: 2 years



Nuts and fish: 3 years

2008<sup>2</sup>

No evidence for delaying introduction of allergenic foods:



Milk, eggs, nuts, and fish: 4-6 months

2015

LEAP study

2019<sup>3</sup>

No evidence for delaying introduction of allergenic foods:



Milk, eggs, tree nuts, and fish: 4-6 months

Early introduction of peanuts may be beneficial for infants at high risk for allergy:



Peanuts: 4-6 months

1. Zeiger RS. *Pediatrics*. 2003;111(6 Pt 3):1662-1671.
2. Greer FR, et al. *Pediatrics*. 2008;121(1):183-191.
3. Greer FR, et al. *Pediatrics*. 2019;143(4). pii:e20190281.





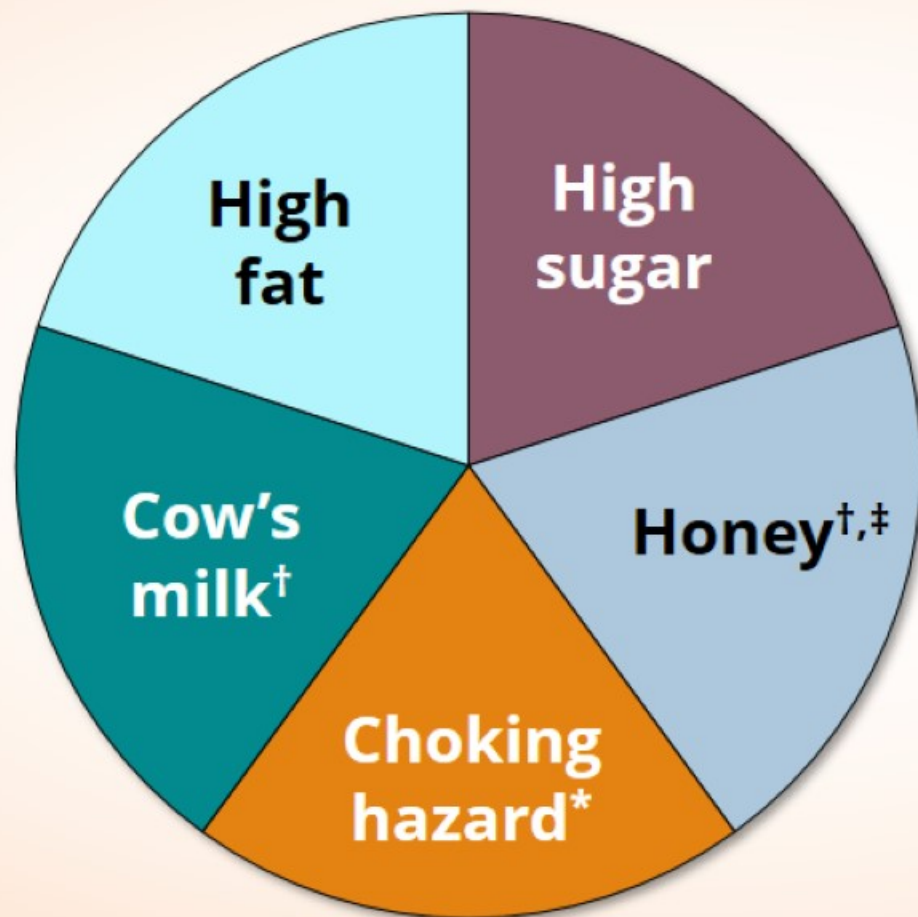
# How Does Culture Affect the Types of Complementary Foods Offered?

	4-5 months		6-11 months		12-24 months	
	Hispanic, %	Non-Hispanic, %	Hispanic, %	Non-Hispanic, %	Hispanic, %	Non-Hispanic, %
Noninfant cereal			18.5 <sup>†</sup>	29.2	45.3	57.8
Rice			15.9 <sup>*</sup>	4.7	26.9 <sup>†</sup>	13.0
Grains in mixed dishes			15.9	13.0	38.8 <sup>†</sup>	54.4
Pizza				1.4	1.0 <sup>*</sup>	9.7
Canned fruit	2.3		8.8	13.7	12.1 <sup>*</sup>	26.2
Fresh fruit	9.1 <sup>†</sup>		30.0 <sup>*</sup>	17.7	59.3	53.1
Beans and peas	1.4		5.8	1.8	19.1 <sup>†</sup>	6.5
Soup			16.3 <sup>*</sup>	5.1	23.4 <sup>†</sup>	10.7
Baby cookies	1.3	1.1	24.8 <sup>†</sup>	14.5	9.1	13.4
Sweetened drinks			13.9	6.7	53.5 <sup>†</sup>	35.8

<sup>†</sup> $P < .05$  vs non-Hispanics; <sup>\*</sup> $P < .01$  vs non-Hispanics.



# Which Foods Should Be Avoided?



<sup>†</sup>Before infant is aged 4 to 6 months.

\*Examples are whole nuts or grapes, raw carrots, hot dogs, candy, popcorn.

<sup>‡</sup>Avoid honey and corn syrup, as they may contain botulism spores.

ESPGHAN Committee on Nutrition. *JPGN*. 2008;46:99-110.

Feeding Infants and Young Toddlers: Using the Latest Evidence in Child-Care Settings. [https://healthyeatingresearch.org/wp-content/uploads/2017/05/her\\_ece\\_051817-FINAL.pdf](https://healthyeatingresearch.org/wp-content/uploads/2017/05/her_ece_051817-FINAL.pdf). Published May 2017. Accessed June 10, 2019.



# Encourage Responsive Feeding

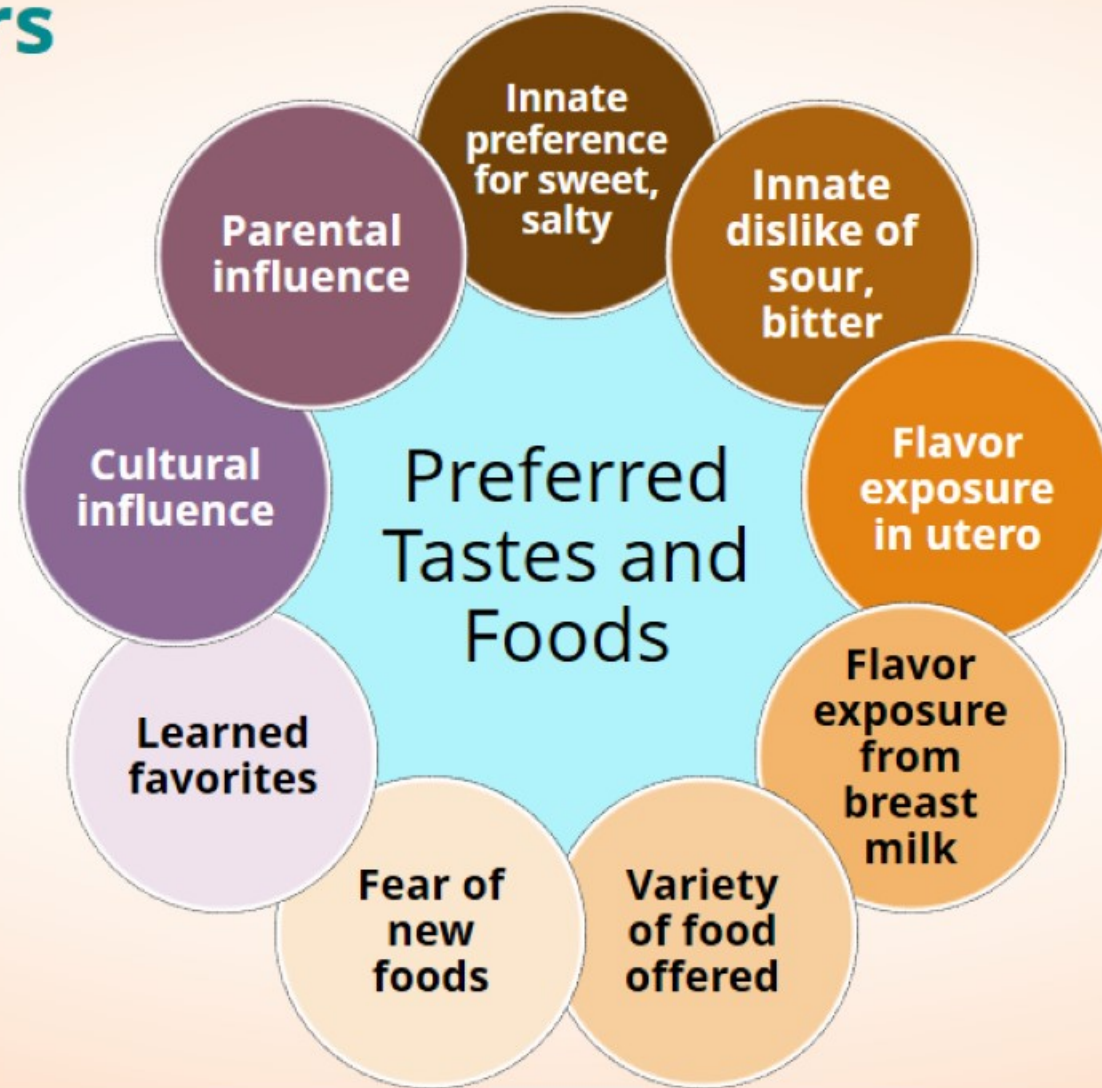
**Optimal infant feeding depends on  
what + how + when + where + by whom**

**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



**And allergies!**



# Food Choices for Nutrients That Allergic Children May Lack

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

For more information, see  
***Clinical Recommendations for Reducing and Preventing Food Allergies***  
with Hugh Sampson, MD, and Marion Groetch, MS, RDN.

