Milk and Soy Protein Allergy: Diagnosis and Management in Infants

Sponsored by Neocate from Nutricia North America
Learning Objectives

At the end of the presentation, attendees will be able to:

• Understand the significance of childhood food allergy
• Discuss the clinical aspects of allergy related disorders
• Establish a diagnosis for children with dairy and soy milk protein allergy
• Initiate a treatment plan for children with food allergies
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 U.S. and appears to be on the rise
- The impact on the U.S. Health Care system is $18B/year
- Improved prevention and diagnostic techniques are needed due to the increased prevalence and its associated cost and social impact
Food Allergies

• In the U.S., seven million people are affected by food allergies

• Food allergy is most common in infants and children
  – Occur in 8% of children ≤ 6 years of age

• ~90% childhood food allergy is from six food types:

<table>
<thead>
<tr>
<th>Most Common Childhood Food Allergens</th>
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<tbody>
<tr>
<td>Milk</td>
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<td>Soy</td>
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<td>Egg</td>
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<tr>
<td>Peanut</td>
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<td>Wheat</td>
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<td>Tree Nuts</td>
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</table>

• Most common food allergies (Milk, Soy, and Egg) are also the most likely to be outgrown by age six

Adverse Food Reactions

Reactions to Foods

Toxic Reactions
- Bacterial food poisoning
- Caffeine
- Tyramine

Non-immunologic Reactions
- Lactase deficiency
- Sucrase-Isomaltase deficiency
- Trehalase
- Galactosemia

Immunologic Reactions
- Allergies:
  - Atopic Dermatitis
  - Gastrointestinal
  - Reactive Airway Disease
  - Anaphylaxis
When to Suspect Food Allergy

• **Family History (65%)**

• **Common Potential Symptoms and Prevalence:**
  – Cutaneous or Atopic Dermatitis (50 - 70%)
  – Respiratory (wheezing/coughing/etc.) (20 - 30%)
  – Gastrointestinal
    • Esophageal Reflux or Regurgitation (42%)
    • Stool Irregularities (Diarrhea, Blood in Stool) (50 - 60%)
    • Failure to Thrive (25%)
  – Excessive Crying/severe irritability (27%)

Family History

What is the chance a child will have some form of allergy?
• 50% to 80% if both parents have atopic history…

Potential for Food Allergy Based on Parent Atopic History

Both Parents* (5%)
One Parent* Or Sibling (31%)
Neither Parent* (64%)

Potential for Childhood Allergy Correlates To Parents’ History of Allergy

Approximate numbers in developed countries.  Adapted from
Family History

Is parent atopic history a reliable indicator of allergy?

NO

- 55% of allergy incidence is diagnosed among children whose parents do not have atopic history
Symptom: Atopic Dermatitis

A common chronic skin disease that most often presents prior to 5 to 7 years of age

- **Signs and symptoms**
  - Rash
  - Pruritus
  - Skin dryness, excoriations
  - Irritability

- **Severe atopic dermatitis is associated with food hypersensitivity**

Atopic Dermatitis

Prevalence:

• Incidence of Atopic Dermatitis grew 275% in 50 years
  – From 5% in 1946 to over 19% in 1996

• 17.1% cumulative incidence in first six months

• Certain ethnic groups are at higher risk
  – African American
  – Asian
  – Male gender
  – Children of mothers with eczema

M Moore et al  Pediatrics 2004;113(3):468-474
Symptom: Respiratory-Related

Less common, but may indicate more serious food allergy

- Chronic rhinitis is the most common respiratory tract manifestation of food allergy
- Large tonsillar and adenoid tissues, sometimes with upper airway obstruction, may be caused, or aggravated by, food allergies
- Acute respiratory responses to food are usually present in near-fatal or fatal reactions after food ingestion
- Food allergy in early childhood is a marker indicating an increased risk to develop respiratory allergy

Heiner, Ann Allergy. Dec 1984
James, Pediatrics Vol. 111 No. 6 June 2003
Respiratory

Three main food induced respiratory allergic reactions:

**Rhinitis**
- Nasal symptoms occur in 70% of child respiratory allergic reactions
- No substantiated evidence linking milk and thickening of mucus

**Anaphylaxis**
- 50% of respiratory reactions include trouble breathing, wheezing, throat tightness, and nasal congestion

**Asthma**
- The prevalence of food-related wheezing seems to be highest in the youngest patients with atopic disease
- Most children with asthma have food-induced asthmatic reactions
Symptom: Gastrointestinal

- Regurgitation
  - May be frequent
  - Often occurs after feeding
  - Difficult to distinguish from physiologic GER
  - May have eosinophilic gastritis

Eosinophils in the stomach
Gastrointestinal Symptoms

• **Stool Irregularities**
  – Diarrhea and/or greater than three bowel movements/day
  – Some children may have enteritis, malabsorption and failure to thrive
  – May have eosinophilic colitis or allergic proctitis

Visuals courtesy of Dr. Winter
Gastrointestinal Symptoms

- Stool Irregularities: Bloody diarrhea (hematochezia)
  - Most often streaks of bloody mucus mixed with stool
  - Often painless
  - Lymphoid hyperplasia in the colon
  - Eosinophilic colitis or allergic proctitis

![Allergic Colitis](image1)

![Allergic Proctitis](image2)
Excessive Crying/Irritability

• Multiple causes exist in infants
  – GER
  – Dairy or soy protein intolerance
  – Neurological impairment
  – Colic
Most Common Infant Food Allergens: Dairy and Soy Milk Proteins

Milk allergy is an adverse response to protein:

- 80% occurs in 1st year of life\(^1\) with overall prevalence of 2 - 5%\(^2\)
- Up to 50% of infants allergic to milk protein are allergic to soy protein\(^3\)
  - AAP: Infants with cow milk protein allergy should not be given isolated soy protein-based formula routinely\(^4\)

Most Common Infant Food Allergens: Dairy and Soy Milk Proteins

Milk allergy is an adverse response to protein:

• Milk protein remains intact in lactose-free milk
  > Lactose-free will not resolve allergy as milk protein remains intact

• No relief will occur by switching to formulas using same protein source

Four Main Classes of Formula

• Milk (Casein or Whey)-based basic formulas
• Soy-based formulas
• Partially or extensively hydrolyzed protein formulas
• Amino acid-based formulas
Removing the Protein Allergen

Breast milk may contain allergens requiring dietary change for mom

- Cow or soy derived protein may need to be eliminated from mom’s diet
- Dairy and soy proteins are present in many products
- Avoid products with casein or whey

<table>
<thead>
<tr>
<th>Foods Possibly Containing Dairy or Soy Protein</th>
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<tbody>
<tr>
<td>Bakery glazes</td>
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<tr>
<td>Breath mints</td>
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<tr>
<td>Fortified cereals</td>
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<tr>
<td>Nutrition bars</td>
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<td>Salad dressings</td>
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</table>
All basic formulas (dairy + soy) are made of complete protein chains that trigger allergic reactions.

Hydrolysate formulas break the protein chain into pieces. This is better tolerated by many, but can still trigger an allergic reaction.

Amino Acid-based formulas are made with individual non-allergenic amino acids. They are very well tolerated and classified as hypoallergenic.
Removing the Protein Allergen

Most Allergenic

Complete protein chain

The Leading Basic Formulas (Dairy + Soy)

Hydrolyzed partial protein chain

The Leading Hydrolysate Formulas

Non-allergenic amino acid elements

The Leading Amino Acid-Based Formulas
Milk Protein Allergy Clinical Review
Atopic Dermatitis: Breast Fed Infants Study

Objective: Evaluate whether allergic infants should be breast fed

Results
- Some improvement achieved by strict maternal elimination diet
- Significant improvement in atopic dermatitis, relative length and nutritional parameters after breast feeding ended and amino acid-based formula used

Conclusion
- Promote breast feeding as primary prevention of allergy
- Breast-fed infants with allergy should be treated by allergen avoidance

<table>
<thead>
<tr>
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<th>During Breast-Feeding</th>
<th>After Breast-Feeding and Amino Acid-based Formula</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent of eczema (%)</td>
<td>21 (15 to 27)</td>
<td>7 (4 to 11)</td>
<td>t = 5.38 P&lt;.0001</td>
</tr>
<tr>
<td>Intensity of eczema</td>
<td>3 (2 to 4)</td>
<td>1 (0.5 to 1.5)</td>
<td>t = 7.43 P&lt;.0001</td>
</tr>
<tr>
<td>Subjective manifestations</td>
<td>5 (4 to 6)</td>
<td>2 (1 to 2.5)</td>
<td>t = 5.12 P&lt;.0001</td>
</tr>
<tr>
<td>SCORAD</td>
<td>20 (17 to 24)</td>
<td>7 (5 to 9)</td>
<td>T = 8.51 P&lt;.0001</td>
</tr>
</tbody>
</table>

(Isolauri, J Peds 1999)
Atopic Dermatitis: Cow Milk Formula Study

Objective: Validate effectiveness of Amino Acid-Based Formula

Results
- Significant improvement in atopic dermatitis following treatment with amino acid-based formula

Conclusion
- Amino acid-based formula resulted in a significant clinical improvement
- Feeding amino acid-based formula promoted significantly higher growth than hydrolysate-based formula

(Niggeman, Pediatr Allergy Immunol 2001)
GI Symptom Relief Study

Objective: Assess GI symptom improvement due to amino acid-based formulas among infants intolerant to hydrolysate formulas

Results
- Noncutaneous symptoms disappeared within 3 days and improved eczema (SCORAD 16 ±12 vs 35 ± 13)
- All infants gained weight with statistically significant increase in the body weight index

Conclusion
- Hydrolysate allergy is not uncommon in infants. Amino acid-based diet provides a safe alternative
- Diagnosis of allergy to hydrolysate formula requires first the institution of an amino acid-based diet, which allows symptoms to disappear before an oral challenge with a hydrolysate formula
- Significant weight gain is likely due to reduction of digestive symptoms and possibly from better intestinal function

(De Boissieu, J Peds 1997)
GI Symptom Relief Study

Objective: Assess intolerance to protein hydrolysate infant formulas and the resulting gastrointestinal symptoms in infants

Results

- 25 of 28 infants intolerant to hydrolysate formulas tolerated amino acid-based formulas
- Following 14-days on the amino acid-based formula, 8 of 25 infants were able to tolerate hydrolysate formulas

Conclusion

- Not all infants with apparent milk formula protein-induced colitis respond to hydrolysate formulas
- These infants have resolution of their symptoms when fed amino acid-based formula
- Approximately one-third of infants previously intolerant to hydrolysates could tolerate them following 14-days use of an amino acid-based formula

(Vanderhoof, J Peds 1997)
Excessive Crying Relief Study

Objective: Perform a preliminary analysis on the treatment of infant colic with amino acid-based infant formula

Results

– Amino acid-based formula use reduced crying and fussiness among infants with colic within five days
– Symptoms recurred upon challenge with bovine IgG

Conclusion

– Amino acid-based formula was well tolerated and likely effective in reducing excessive crying associated with colic

Promoting ‘Catch-Up’ Growth

Objective: Determine the performance of hydrolysate and amino acid-based formulas in infants with cow milk allergy

Results

– Both hydrolysate and amino acid-based formulas were clinically and biochemically tolerated
– Mean concentration of essential amino acids were lower than breast milk for hydrolysates and higher than breast milk for amino acid-based formulas
– Length was significantly higher among infants fed amino acid-based formulas when compared to infants fed hydrolysate formulas

Conclusion

– Amino acid-based formulas may be preferable for infants with multiple food allergies, especially for the maintenance of normal growth

(Isolauri J Peds 1995)
Today’s Treatment of Dairy and Soy Milk Protein Allergy

Today’s Common Diagnostic Approaches

Breast-Fed Infants

- Remove offending allergens from mom’s diet

Formula-Fed Infants

- Switch to other milk-based basic formula
- IF treatment fails and symptoms persist, use a soy-protein based formula
- IF treatment fails and symptoms persist, use a hydrolysate formula
- IF treatment fails and symptoms persist, seek Specialist
- Specialist tries amino acid-based formula and/or probes for non-allergy illness
Improving Treatment of Dairy and Soy Milk Protein Allergy

All Infants with milk protein allergy symptoms

Undertake 14-day trial with amino acid-based formula

IF symptoms persist, consider referring to Specialist for non-allergy diagnosis

Then, challenge with hydrolysate when allergy symptoms abate and infant is physically better able to respond favorably to the hydrolysate challenge
Improving Treatment of Dairy and Soy Milk Protein Allergy

All Infants with milk protein allergy symptoms

Undertake 14-day trial with amino acid-based formula

IF symptoms persist, consider referring to a Specialist

Then, challenge with hydrolysate when allergy symptoms abate

Three Key Advantages:

1. **Accelerates time to relief** for moderately/severely allergic infants

2. **More quickly rules out milk protein allergy** If infant fails amino-acid formula; infant referred to Specialist faster

3. **Up to one-third** of infants that would have failed hydrolysates will now successfully tolerate them due to challenging when infant is healthier
Summary

Dairy and Soy proteins are the leading infant food allergens
• Only amino acid-based formulas are made with non-allergenic elements

Amino acid-based formulas resolve symptoms quickly
• 3-days for relief of GI tract and GER symptoms
• 14-days for relief of atopic dermatitis symptoms

Consider diagnostic challenge with AA-based formula
• Negative response eliminates allergy
• If response, seek consultation with Specialist for non-allergic disease
• One-third of infants who initially fail hydrolysates tolerate them after treatment with amino acid-based formula
Symptom Summary

- Family History

- Common Symptoms and Prevalence:
  - Cutaneous or Atopic Dermatitis
  - Respiratory (wheezing/coughing/etc.)
  - Gastrointestinal
    - Esophageal Reflux or Regurgitation
    - Stool Irregularities (Diarrhea, Blood in Stool)
    - Failure to Thrive
  - Excessive Crying/severe irritability
Make the best choice of nutrition for your patient

2 month old infant with symptoms:
- No family history of atopic history
- Mild atopic dermatitis
- Irritability with >1 hour crying inconsolably
- 4-5 loose stools per day
- Thriving
- Physical exam normal
- Development normal
- Tried two different basic formulas with short-lived success and recently switched to Lactose-Free formula

- How would you manage this?
Case Study Comparing Approaches

- 2 month old infant presents with symptoms:
  - Four to five loose stools per day
  - Minor skin rash
  - Tried basic and lactose-free formula
  - Occasionally irritable for 1+ hour
  - Normal physical and developmental exam
  - No family history of food allergy

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<thead>
<tr>
<th>Step-Challenge Approach</th>
<th>Diagnostic Therapy Approach</th>
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<tbody>
<tr>
<td>Diagnosis; Challenge with Soy</td>
<td>Diagnosis; Use Amino Acid-based</td>
</tr>
<tr>
<td>FAIL</td>
<td>RELIEF; Challenge with Hydrolysate</td>
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<tr>
<td>Week 0</td>
<td>Week 2</td>
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<tr>
<td>Week 2</td>
<td>FAIL; Return to Amino Acid-based</td>
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<td>Week 4</td>
<td>Week 6</td>
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<td>Week 6</td>
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<td>Week 12</td>
<td>Week 14</td>
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<tr>
<td>RELIEF</td>
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Remember
Soy formula should not be given to infants under 6 months of age!
Thank you

Q&A

Dr. Idris Dahod
Central Mass Pediatric GI & Nutrition, P.C.