Friday General Session

Pediatric Food Allergies and Food Intolerance

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Educational Objectives
By the end of this educational activity, participants should be better able to:
1. Identify various presentations and mechanisms of food adverse events.
2. Develop rational approach to diagnosis of food related disorders.
3. Implement proper treatment and recommendations for these disorders.
4. Discuss current guidelines for acute allergic reactions including anaphylaxis.

Speaker Disclosure
Dr. Anmuth has disclosed that he has no actual or potential conflict of interest in relation to this topic.
Food Allergy Mystery: A Tale of Three Babies
David M. Anmuth MD
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Houston, TX

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Learning Objectives
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Case 1
- 2 month old breast fed infant develops visible blood and mucus in the stool
- No irritability or discomfort
- Normal appetite
- No physical findings on exam
- Infectious work-up is negative for bacteria and parasites

ARS Question – Case 1
What is the diagnosis?
1. IgE mediated food allergy/anaphylaxis
2. Food protein–induced enterocolitis (FPIES)
3. Allergic Proctocolitis
4. Lactose intolerance

Allergic Proctocolitis
- Initial Presentation: Blood tinged stools, pain on defecation, diarrhea/loose stools, failure to thrive
- Endoscopic Findings: Focal rectal erythema or erosions, lymphoid nodular hyperplasia
- Most Common Culprits:
  - Cow’s Milk (65%)
  - Egg (19%)
  - Corn (6%)
  - Soy (3%)
  - Combined (5%)
  - Unidentified (12%)

**Differential Diagnosis of Rectal Bleeding in Infancy**

- Mild/Moderate
  - Anal fissure
  - Perianal dermatitis
  - GI infection
  - Coagulation disorder
  - Vitamin K deficiency
  - Allergic proctocolitis

- Severe
  - Necrotizing enterocolitis
  - Sepsis
  - Hirschprung's
  - Intussusception
  - Volvulus
  - FPIES

**Management of Allergic Proctocolitis**

- Elimination in maternal diet or hypoallergenic formula (casein hydrosylate)
- Introduce solids at 4–6 months of age
- Consider allergy skin prick or blood test at age 12 months especially with known eczema
- Home introduction of foods after 12 months if testing negative

**Outcome of Case 1**

- Mother avoids milk and soy in her diet with disappearance of gross blood and mucous within three days
- Allergy testing is negative at 12 months
- Introduction of milk and soy into diet at 12 months tolerated without issue

**Case 2**

- 6 month old female exclusively breast fed
- Brief cow’s milk formula exposure at 4 months of age
- Intake of cow’s milk formula at 6 months as supplement
- 90 minutes later with repetitive, projectile emesis and lethargy

**ARS Question – Case 2**

What is the diagnosis?

1. IgE mediated food allergy/anaphylaxis
2. Food protein–induced enterocolitis (FPIES)
3. Viral gastroenteritis
4. Lactose intolerance

**Case 2**

- Brought to emergency department and undergoes sepsis evaluation
- Given IV fluids and antibiotics
- Improved after three day hospitalization with diagnosis of viral gastroenteritis
- Given cow’s milk again once better with same reaction
Food Protein-Induced Enterocolitis (FPIES)

- **Acute**
  - Ingestion following a period of avoidance
  - Onset: 2–4 hours
  - Lethargy, limpness
  - Septic appearance
  - Shock
  - Methemoglobinemia
  - Onset usually under 12 months

- **Chronic**
  - Young infants fed continuously with milk or soy formula
  - Watery diarrhea
  - Mucous and/or blood in stools
  - Intermittent emesis
  - Low albumin and/or total protein
  - Failure to thrive
  - Onset in the first 1–3 months of life

Common Foods in Pediatric FPIES

- Cow’s Milk
- Soybean
- Rice
- Oat
- Fish
- Poultry
- Egg
- Peanut
- Wheat

Acute FPIES and Misdiagnosis

- Lack of “classic” allergic skin and/or respiratory symptoms
- Multiple episodes for baby cereals (rice and oatmeal) that are usually well tolerated
- Shock and sepsis like picture causing infectious workup
- May even prompt laparotomy (ileus like picture) with evaluation for intussusception and volvulus

FPIES Differential Diagnosis

- **Mild/Moderate**
  - GI infection
  - Coagulation disorder
  - Metabolic disorders
  - Vitamin K deficiency
  - Allergic proctocolitis

- **Severe**
  - Anaphylaxis
  - Necrotizing enterocolitis
  - Sepsis
  - Hirschprung’s
  - Intussusception
  - Volvulus
  - Ileus

Diagnosis of FPIES

- History of typical symptoms
- Oral food challenge
- Skin prick tests and specific IgE usually negative but up to 25% may become positive over time (atypical FPIES)
- IgE positivity may be associated with protracted course
- Biopsy in chronic FPIES: Eosinophilic inflammation in the colon, villous blunting

Treatment of Acute FPIES

- Fluid bolus: Normal saline 10–20 mL/kg
- Methylprednisolone Sodium Succinate 1 mg/kg/dose (single dose)
- Potential role of ondansetron
- Epinephrine generally not helpful
- Extreme cases: Vasopressors and life support
**Management of Milk/Soy FPIES**
- Food avoidance
- Breast feeding or hypoallergenic formula
- Solid food introduction at 4-6 months
- Consider starting with fruits/vegetables (approximately 20% react to solid food)
- Allergy test every 12 months: 25% may convert to positive allergy test
- 35% will develop immediate allergic symptoms
- Re-challenge every 12-18 months (supervised office challenges)
- A letter for the patient in case of accidents to show in the Emergency Department

**Management of Solid Food FPIES**
- Avoid grains, legumes, and poultry during first year of life
- Approximately 50% reactive to more than one food and 40% reactive to another grain
- Tolerance to one food from a food group suggests that other foods will be also tolerated (i.e. soy for legumes, rice/oat for grains, and chicken for poultry)

**Outcome of Case 2**
- Child was diagnosed as cow’s milk FPIES based on history alone
- IgE mediated testing for milk was negative
- No other clinical reactions to foods were seen
- Age 3 tolerated an in hospital challenge with emergency treatment available upon need

**Case 3**
- 12 month old breast fed infant girl
- Known eczema that is well controlled
- Mother attempting to wean to cow’s milk
- On first ingestion, develops diffuse urticaria and vomits within 15 minutes

**Case 3**
- Mother phones on call physician who recommends diphenhydramine and to bring baby to the emergency department
- Upon arrival the baby is well appearing and hives have resolved

**ARS Question – Case 3**
**What is the diagnosis?**
1. IgE mediated food allergy/anaphylaxis
2. Lactose intolerance
3. Eosinophilic esophagitis
4. Viral gastroenteritis
Food allergy: An adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food

Food allergens: Specific components of food recognized by allergen-specific cells and eliciting specific immune reactions resulting in characteristic symptoms

Food induced anaphylaxis: A serious allergic reaction that is rapid in onset and can cause death

The prevalence of food allergy is uncertain because studies vary in approaches/methods

Food allergy is estimated to affect more than 1% to 2% and less than 10% of the population

About 1 in 13 children have food allergies

People can be allergic to almost any food

But 90% of food allergic reactions are caused by eight foods

- Cow’s Milk
- Peanuts
- Eggs
- Tree nuts
- Wheat
- Fish
- Soybean
- Shellfish

Anaphylaxis: Mechanism

Immediate Reaction

Late Phase Reaction
Summary Statement 1: Evaluate the patient for possible food allergy with the understanding that a relatively small number of allergens cause a high proportion of food allergy (cow’s milk, hen’s egg, soy, wheat, peanut, tree nuts, fish, and shellfish).

Summary Statement 2: Advise patients who are allergic to certain specific foods about the risk of ingestion of similar cross-reacting foods:
- Other tree nuts in patients with tree nut allergy (i.e. walnut and pecan or pistachio and cashew)
- Crustacea in patients with crustacean seafood allergy
- Vertebrate fish in patients with fish allergy
- Other mammalian milks in patients with cow’s milk allergy

Summary Statement 4:
- Advise patients with seafood allergy that they are not at increased risk of a reaction to radiocontrast media.
- There is NO DOCUMENTED RELATIONSHIP between non-IgE mediated anaphylactic reactions to radiocontrast media and allergy to fish, crustacean shellfish, or iodine.

Summary Statement 10: Determine whether the reported history of food allergy, which often proves inaccurate, and laboratory data are sufficient to diagnose food allergy or whether an oral food challenge (OFC) is necessary.

Summary Statement 23: The clinician should use specific IgE tests (SPTs, serum tests, or both) as diagnostic tools; however, testing should be focused on foods suspected of provoking the reaction, and test results alone should not be considered diagnostic of food allergy.
Because of the low PPV of self-reported symptoms and lack of pathognomonic signs on physical examination, the accurate diagnosis of IgE-mediated food allergy should be aided by laboratory allergy testing, including skin prick and/or serum IgE testing.

Testing for the presence of food allergen IgE in the form of skin or in vitro laboratory testing is highly sensitive (low rate of false-negative results=90%) but only moderately specific (higher rate of false-positive results=50%) and must always be selected and interpreted in the context of the patient’s specific clinical history.

Summary Statement 24: Component-resolved diagnostic testing to food allergens can be considered, as in the case of peanut sensitivity, but it is not routinely recommended even with peanut sensitivity because the clinical utility of component testing has not been fully elucidated.

Summary Statement 34: Unproved tests, including allergen specific IgG measurement, cytotoxicity assays, applied kinesiology, provocation neutralization, and hair analysis, should not be used for the evaluation of food allergy.

Management of Food Allergy

- Summary Statement 44:
  - Review recognition and treatment of IgE-mediated food related allergic reactions with each patient and caregivers, as appropriate
  - Emphasis should be placed on prompt awareness of anaphylaxis and swift intervention


Summary Statement 47: Ensure that self injectable epinephrine is readily available to the patient and instruct the patient, caregiver, or both on the importance of its use and self-administration, as relevant.

Intramuscular epinephrine is the first-line treatment in all cases of anaphylaxis.

All other drugs have a delayed onset of action.

Repeat epinephrine dosing should be used when symptoms progress or response is suboptimal.

Natural History of Food Allergy

- Summary Statement 11: Consider the natural course of allergies to specific foods when deciding on the frequency of food allergy follow-up evaluations, recognizing that allergies to certain foods (milk, egg, wheat, and soy) generally resolve more quickly in childhood than others (peanut, tree nuts, fish, and shellfish).

- Summary Statement 48:
  - Evaluate children with food allergies at regular intervals (1-2 years), according to the patient’s age and the food allergen, to determine whether he or she is still allergic.
  - If food allergy is unlikely to change over time, as in adults, periodic re-evaluation (2-5 years) is recommended, depending on the food allergy.

Prevention of Food Allergy

- Summary Statement 12: Encourage exclusive breast feeding for the first 4 to 6 months of life.

- Summary Statement 13: For infants with a family history of atopy, consider a partially or extensively hydrolyzed infant formula for possible prevention of atopic dermatitis and infant cow’s milk allergy if exclusive breast feeding is not possible.
Prevention of Food Allergy

- **Summary Statement 14:** Do not recommend maternal allergen avoidance or avoidance of specific complementary foods at weaning because these approaches have not proved effective for primary prevention of atopic disease.
- **Summary Statement 15:** Do not routinely recommend supplementation of the maternal or infant diet with probiotics or prebiotics as a means to prevent food allergy because there is insufficient evidence to support a beneficial effect.

Treatment of Food Allergy

- **Summary Statement 61:** Although immunotherapeutic approaches, such as oral immunotherapy (OIT), in clinical trials show promise in treating food allergy, they are not ready for implementation in clinical practice at the present time because of inadequate evidence for therapeutic benefit over risks of therapy.
- **Summary Statement 62:** Develop a written action plan for treatment of allergic reactions to food for adults and children.
- **Summary Statement 64:** Teach patients that ingestion, rather than casual exposure through the skin or close proximity to an allergen, is almost the only route for triggering severe allergic/anaphylactic reactions.

Education and Plan of Action

- **Summary Statement 62:** Develop a written action plan for treatment of allergic reactions to food for adults and children.
- **Summary Statement 64:** Teach patients that ingestion, rather than casual exposure through the skin or close proximity to an allergen, is almost the only route for triggering severe allergic/anaphylactic reactions.

Food For Thought: LEAP (Learning Early About Peanut Allergy)

- The prevalence of peanut allergy has doubled over the past 10 years in the US and other countries that advocate avoidance of peanuts during pregnancy, lactation, and infancy.
- The LEAP study was based on a hypothesis that regular eating of peanut-containing products, when started during infancy, will elicit a protective immune response instead of an allergic immune reaction.

Study Design

- Over 600 children between 4 and 11 months of age at high risk for peanut allergy were randomized to either consume or avoid peanut until age 5 in order to compare the incidence of peanut allergy between the two groups.
- Children in the peanut consumption arm of the trial ate a peanut containing snack food at least 3 times each week, while children in the peanut avoidance arm did not ingest peanut containing foods.

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Results and Conclusions

- Of the children who avoided peanut, 17% developed peanut allergy by the age of 5 years.
- Only 3% of the children who were randomized to eating the peanut snack developed allergy by age 5.
- Therefore, in high-risk infants, sustained consumption of peanut beginning in the first 11 months of life was highly effective in preventing the development of peanut allergy.

Summary

- Food adverse reactions can be complex and multifactorial
- Proper recognition and diagnosis is essential to accurate treatment recommendations
- Current knowledge is great but there is still so much more to learn
- Recommendations are always changing and hopefully new treatments are on the horizon
The following medications were discussed in this presentation. The table below lists the generic and trade name(s) of these medications.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
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<tbody>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Adrenaclick, Adrenalin, Auvi-Q, EpiPen, Twinject</td>
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<tr>
<td>Methylprednisolone</td>
<td>Solu-Medrol</td>
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<tr>
<td>Ondansetron</td>
<td>Zofran</td>
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