Balancing the Practical and Clinical Management of Food Protein-Induced Enterocolitis Syndrome (FPIES)

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About our Speakers

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Disclosures

- Compensation provided by Nutricia
- Fallon Schultz:
  - I-FPIES
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- ***None pose any conflict of interest for this presentation***

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Learning Objectives

- **Utilize case-based learning to:**
  - Identify signs and symptoms of FPIES
  - Recognize the social impact of FPIES
  - Understand the International Consensus Guidelines for the Diagnosis and Management of FPIES
  - Learn how to manage FPIES

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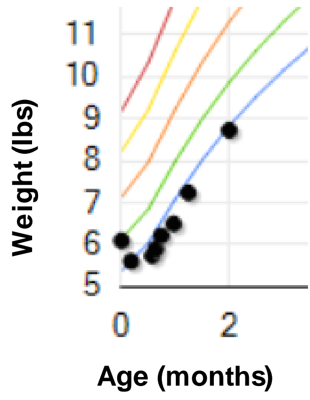
Hailey

Hailey: The First Few Weeks



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Hailey: The First Few Weeks

Our Colicky Baby

First Acute FPIES Reaction

Our Colicky Baby

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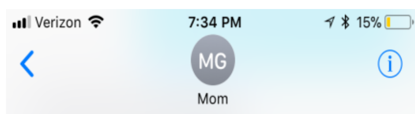
Our Colicky Baby



And....pls get ranitidine rx refilled or I may call in sick tomorrow!!!

fingers crossed that restarting it makes her feel better!

She repeatedly "wakes up" during nap screaming, but not awake. Takes pacifier and sleeps a little more but then does the same thing over and over again.

same at night

Your babe is being so cranky!!! Nothing makes her happy for more than a couple Minutes! 😳😠

Tue, Jun 27, 10:37 AM

Fell asleep (just now) in the swing watching her mobile and talking. She screamed and screamed earlier - wouldn't

I can't figure your babe out! I know you don't get what's going on with her either. But geez - nap, scream, still asleep, take pacifier, sleep, scream......

Pick her up and hold her and same thing. Trying a 🍼 now.

Our Colicky Baby

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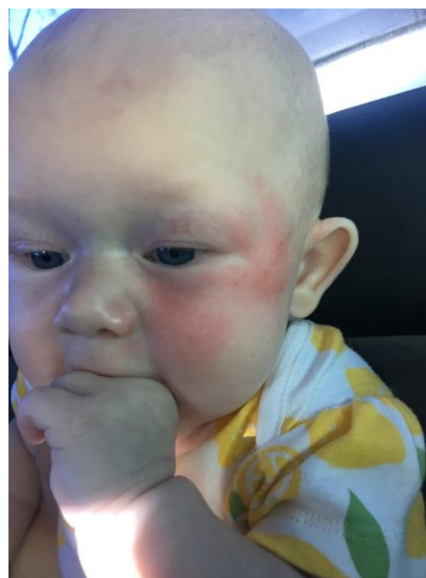
Our Colicky Baby



Our Colicky Baby

She didn't do well last night?

No she was awful

Ugh. Sorry, sweetie. It has to be so frustrating and so exhausting

Andy took her down to the pool at 6am so I slept from 6-9

Like just to get her out of the room so all 3 of us weren't awake

I just feel overwhelmed by it

Is she still doing the SCREAMING?

I know re: overwhelmed by it. It's so frustrating.

What can I do, if anything, to

She's still doing the screaming the last 2 days seemed better until last night. And I breastfed her yesterday so who knows. There are just too many variables

You can just check in and be supportive bc I think you are the only person besides andy who really knows how hard this has been

I feel like everyone else probably thinks we are up playing how awful it's been and think it's just a normal baby phase

It feels lonely

Well I can vouch for how difficult and frustrating it's been and that it's not just a normal baby phase

Oh Jenna. 😭😭😭

I'm sorry that it feels lonely, but I get that no one really understands how hard it is unless they've been around her non-stop for a while. And even then, if you're not the person taking care of her, trying to calm her and soothe her and get her to sleep and keep her from scratching her face, taking her in the car while she screams in the car seat, etc, I don't think someone gets how wearing it is

And I have not dealt with the nights and lack of sleep, and that makes it a lot harder.

Prior to 2nd Acute FPIES Reaction

2nd Acute FPIES Reaction

July 7th, 2017: 4-8pm

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2nd Acute FPIES Reaction

2nd Acute FPIES Reaction: Recovering

July 7th: 9pm

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2nd FPIES Reaction: Back to Baseline

July 8th: The next morning

Searching for a Diagnosis

- "I have a 4.5 month old & my supply is running low & had to tap into the freezer stash when I went back to work full-time. In anticipation of needing standard formula, she also needed supplementation from 2-6 weeks old & did fine with it then, we have given it to her twice in the last 3 weeks. Both times, 2 hours later, she has thrown it all up, then retching up yellow stomach acid, lethargic & grunting for about 6 hours before we could try rehydrating. Today we used a brand new can & same exact thing. I'm worried for when the freezer supply runs out & I'm at work."

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FPIES Diagnosis

- “That seems like an unusual reaction to formula. Especially if she tolerated the same formula before. I never like to hear babies described as lethargic.”
- “Sounds like possible FPIES like reaction. She probably needs in depth evaluation.”
- “Sounds like FPIES. Baby needs further evaluation.”
- “Same thought as above. Sounds like it could be FPIES.”

Skin Testing

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Introduction of Amino Acid-Based Formula

Your baby has acted like a totally normal baby today exclamation

I don't think coincidence anymore. She was doing better on it a couple days, gave her breastmilk and she did awful, gave her formula again and she did better

Like the only days I haven't cried in 10 days were like Friday Saturday and Monday. Which coincide w all formula

Awwww Jenna! 😭😭

Introduction of Amino Acid-Based Formula

Last time we came here she screamed the whole time and I cried the whole time

That looks way more enjoyable

I feel like a new person

I'm glad babe

I love you tons

I was not doing well there for a while

I was starting to think I was depressed

We were exhausted and stressed out

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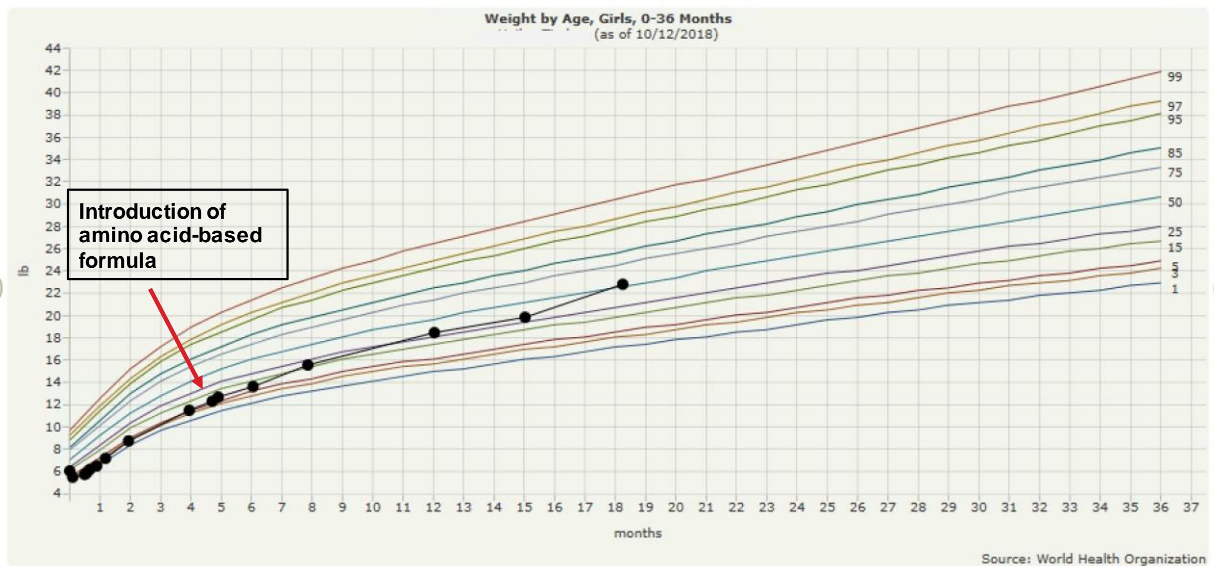
Hailey's Growth Charts



Introduction of Solid Foods

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A New Normal

A New Normal

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Balancing the Practical and Clinical Management of FPIES

Fallon Schultz, MSW, LCSW, CAM

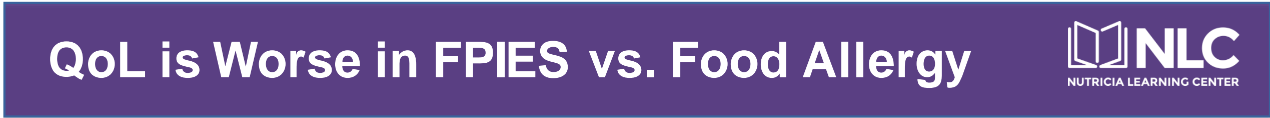
International Consensus Guidelines for the Diagnosis and Management of Food Protein-Induced Enterocolitis Syndrome

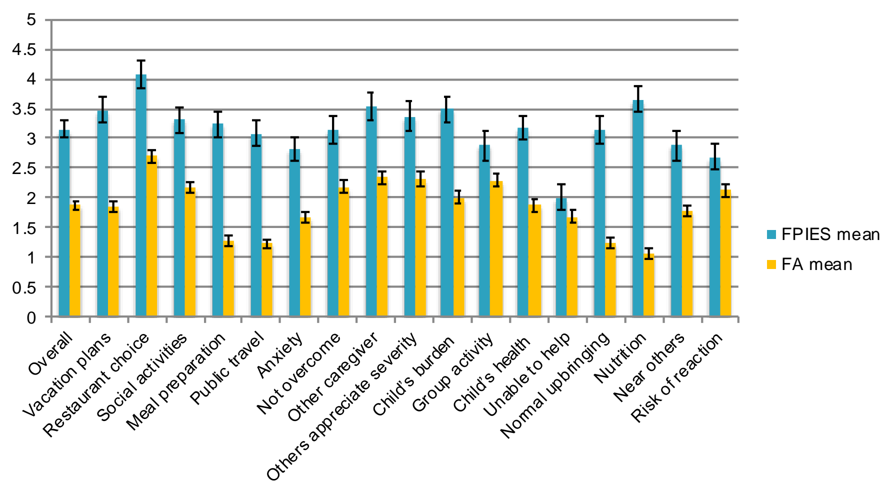
Available at:

www.fpies.org

Nowak-Wegrzyn A et al. International Consensus Guidelines for the Diagnosis and Management of Food Protein Induced Enterocolitis Syndrome. J Allergy Clin Immunol. 2017;139:1111-26.

- Lack of diagnostic biomarkers due to poorly understood pathophysiology
- Comorbidities are common
- Patients and caregivers greatly suffer; Quality of Life (QoL) is very poor
- Fear and provider mistrust

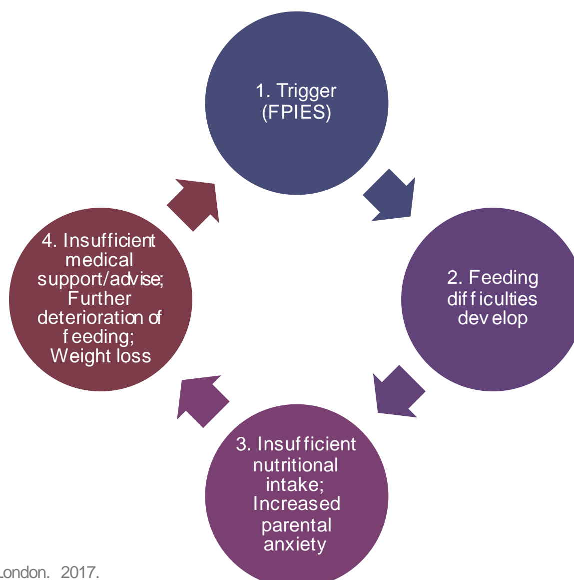




- **Total and domain specific QoL is better in the food allergy population**

Greenhawt et al. J Allergy Clin Immunol. 2016; 37:1251-3. e5.

Disjointed Relationship with Food



Adapted from Meyer R. Imperial College London. 2017.

Management Plan Applicability

- Non-compliance with management recommendations occurs often due to impractically of implementation
  - Often clinically focused and absent of practical management - predictor of outcomes
- Plans need to reflect the patients short- and long-term goals with diet, lifestyle and caregiver ability taken into consideration
  - ✓ Referral to allied health providers
  - ✓ Inclusive of educational and supportive component
  - ✓ Provide credible and effective resources for day-to-day management
  - ✓ Recognize traditional food allergy resources do not apply to FPIES

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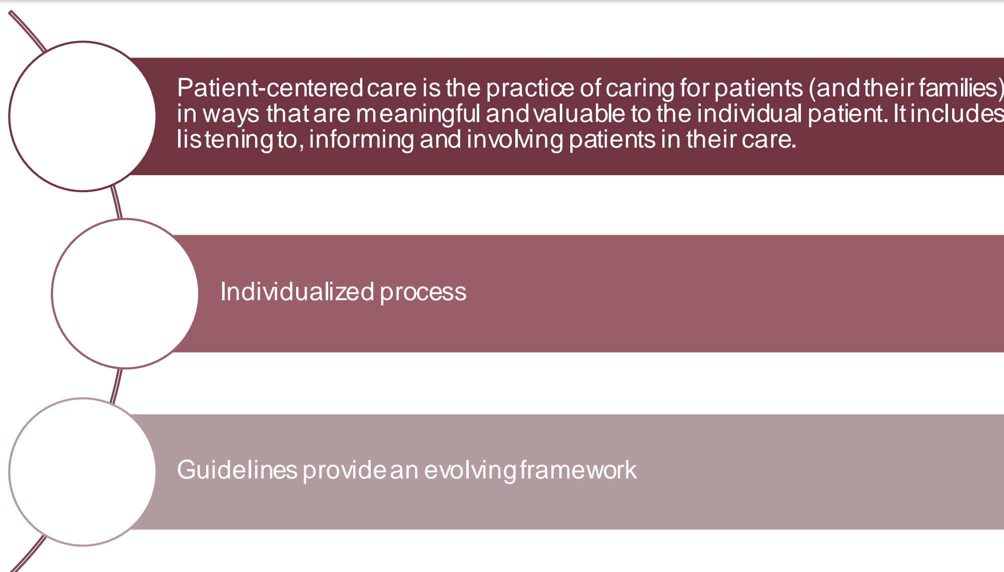
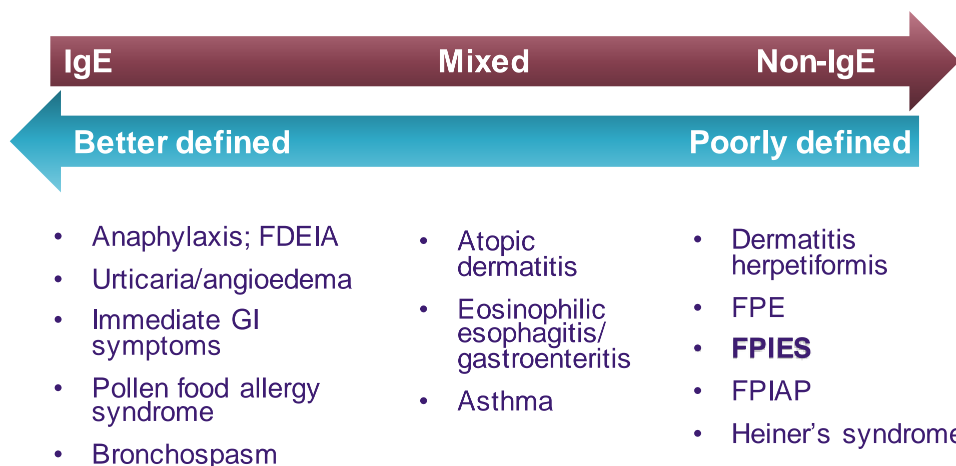
Patient-Centered Care



Diagnostic Criteria and Interpretation

Food Allergy: Immune System-Mediated Adverse Food Reaction

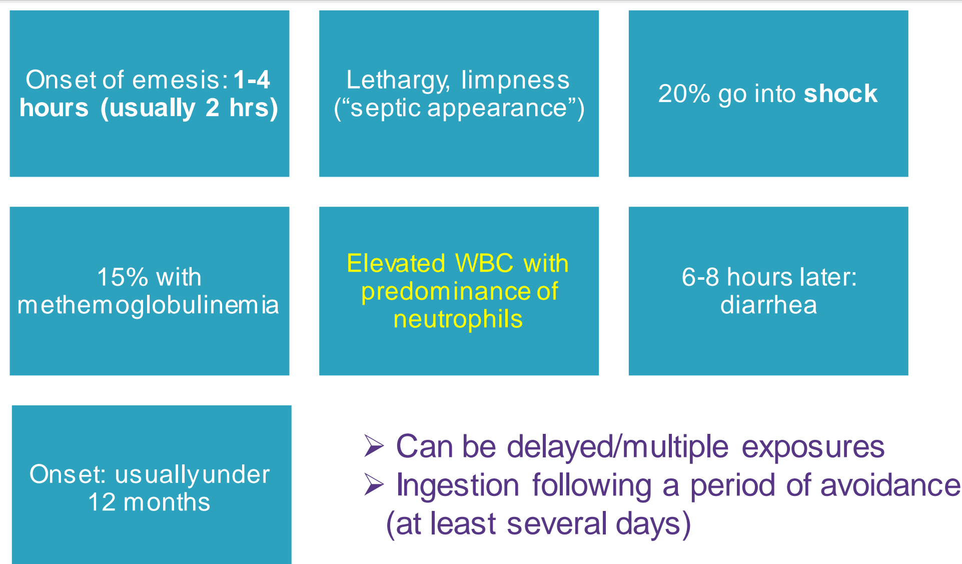


- Anaphylaxis; FDEIA
- Urticaria/angioedema
- Immediate GI symptoms
- Pollen food allergy syndrome
- Bronchospasm

- Atopic dermatitis
- Eosinophilic esophagitis/ gastroenteritis
- Asthma

- Dermatitis herpetiformis
- FPE
- **FPIES**
- FPIAP
- Heiner's syndrome

Acute FPIES



- Can be delayed/multiple exposures
- Ingestion following a period of avoidance (at least several days)

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Diagnostic Criteria for Patients Presenting with Possible Acute FPIES

Major Criterion

- Vomiting in the 1-4 hour period after ingestion of the suspect food and the absence of classic IgE-mediated allergic skin or respiratory symptoms

< 3 Minor Criteria

1. A second (or more) episode of repetitive vomiting after eating the same suspect food
2. Repetitive vomiting episode 1-4 hours after eating a different food
3. Extreme lethargy with any suspected reaction
4. Marked pallor with any suspected reaction
5. Need for emergency room visit with any suspected reaction
6. Need for intravenous fluid support with any suspected reaction
7. Diarrhea in 24 hours (usually 5-10 hours)

Important Points: Acute FPIES

If only a single episode has occurred, a gold-standard diagnostic oral food challenge (OFC) should be strongly considered to confirm the diagnosis, especially since viral gastroenteritis is so common in this age group.

Acute FPIES reactions will typically completely resolve over a matter of hours, compared to the usual several day time course of gastroenteritis.

The patient should be asymptomatic and growing normally when the offending food is eliminated from the diet.

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Chronic FPIES

Watery diarrhea

Mucous, blood in stools

Intermittent emesis

Low albumin and total protein

Elevated WBC with predominance of neutrophils

Failure to thrive

Young infants fed continuously with milk or soy formulas

Onset: First 1-3 months of life

Diagnostic Criteria for Patients Presenting with Possible Chronic FPIES

Severe Presentation

- When the offending food is ingested in on a regular basis [e.g., infant formula].
- Intermittent but progressive vomiting and diarrhea (occasionally with blood) develop, sometimes with dehydration and metabolic acidosis.

Milder Presentation

- Lower doses of the problem food (e.g. solid foods or food allergens in breast milk) lead to intermittent vomiting, and/or diarrhea, usually with poor weight gain/ failure to thrive, but without dehydration or metabolic acidosis.

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Important Points: Chronic FPIES

- The most important criterion for chronic FPIES diagnosis is resolution of the symptoms within days following elimination of the offending food(s) and acute recurrence of symptoms when the food is reintroduced, onset of vomiting in 1-4 hours, diarrhea in 24 hours (usually 5-10 hours).
- Without confirmatory challenge, the diagnosis of chronic FPIES remains presumptive.

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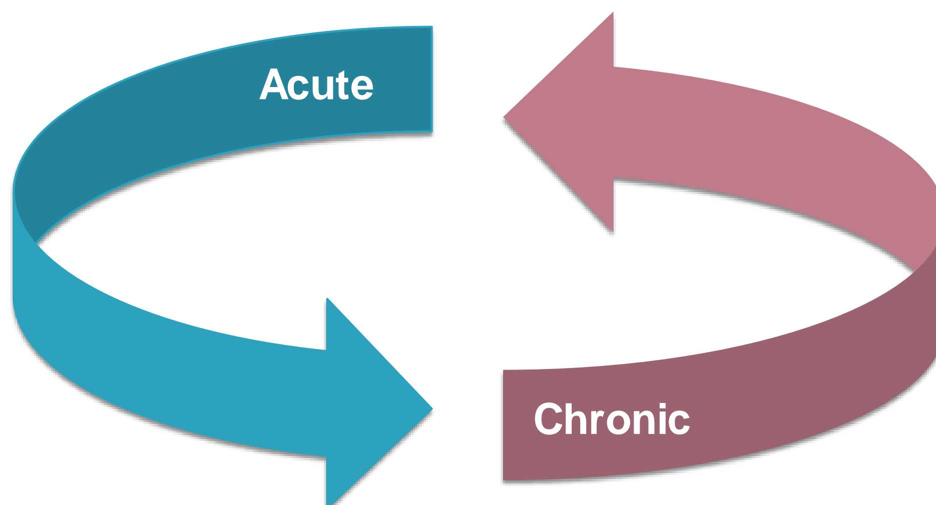
FPIES Phenotype Depends on the Dose and Frequency of Food Allergen Ingestion



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FPIES Management

Ongoing Management ACUTE and CHRONIC: Avoidance

Summary Statement 20: Eliminate any trigger food(s) as the primary management of FPIES

1. Avoidance is the hallmark of management
2. Removal of trigger foods leads to symptom resolution
3. Trigger removal is only half the battle
   - Need to provide diet/nutrition support
   - Practical management support (food labeling, social inclusion, etc.)
4. Multiple food FPIES complicates avoidance

***Summary Statement 22: Reintroduce the foods triggering FPIES under physician supervision

Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

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Acute Management

FLUIDS	ANTI-EMETICS
Summary statement 17: **Treat acute FPIES as a medical emergency**, and be prepared to provide aggressive fluid resuscitation as nearly 15% of patients may develop hypovolemic shock	Summary statement 19: Consider ondansetron as adjunct management of emesis
Stabilize hemodynamics with aggressive fluid management	Ondansetron is 5-HT3 antagonist developed for chemo-induced emesis
10-20ml/kg normal saline boluses	2 case series have noted this can be helpful (5 pt US series-all resolving within 30 mins, 5 pt Italian series, all responded within 15 min)
If milder reaction, consider oral hydration or breastfeeding	No need for additional fluids in either series, but no non-responders noted
Sequelae from hypovolemia may include acidosis, methemoglobinemia and possibly cardiac collapse in small infants	Further studies needed, but worth consideration
Can consider 1 mg/kg solumedrol to decrease GI inflammation - Controversial, not supported by any study	***Intravenous or intramuscular administration recommended**

Management of Acute FPIES at the Medical Facility

TABLE VI: Management efforts are dependent on severity; mild, moderate, severe

- Mild: oral rehydration, ondansetron may be considered, monitor for 4-6 hours post-onset
- Moderate - ADD: IM/IV ondansetron, consider peripheral line for saline bolus, transfer to ED or ICU, monitor vitals, must tolerate clear fluids before discharge
- Severe - ADD: peripheral line to rapidly administer normal saline boluses, administer IV ondansetron, consider IV methylprednisolone, correct acid base and electrolyte abnormalities, correct methemoglobinemia if present, monitor vitals, discharge 4-6 hours post-onset, transfer to ED or intensive care unit for further management in case of persistent or severe hypotension, shock, extreme lethargy, respiratory distress

Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

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Management of Acute FPIES Episode at Home - Guide for Caretakers

- Child with history of severe FPIES reaction:
  - Call emergency medical (911) or go to the emergency department if the triggering food was definitely ingested, even in the absence of symptoms or with any symptoms regardless of severity
- Child with no history of severe FPIES reaction:
  - Mild symptoms (1-2 episodes of vomiting, no or mild lethargy)
    - Attempt oral rehydration at home (e.g., breastfeeding or clear liquids)
  - Moderate-Severe symptoms (> 3 episodes of emesis and moderate-severe lethargy)
    - Call 911 or go to emergency department

****PROVIDE ALL PATIENTS AND CARETAKERS WITH FPIES EMERGENCY LETTER: www.fpies.org****

Nutritional Management

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Reported Food Triggers

- Vary by region
- Most common triggers seem to be first foods of introduction per country
- Resolution of symptoms vary by region with a more protracted course identified in the US
- ANY food can be a trigger

1. Jarvinen KM et al. J Allergy Clin Immunol. 2013;1:317-22. 2. Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

Co-FPIES/Multiple FPIES

- Soy and milk FPIES
  - May be higher likelihood if onset in 1st month of life
  - Country specific
    - US reported rates of 23, 29, and 50% in 3 studies
    - Israel, Australia, Italy series: no co-FPIES to soy
  - Recommend hypoallergenic formula or breastfeeding
    - Goat/sheep milk not appropriate
    - Up to 20% may not tolerate eHFc and need elemental formula
    - Inconclusive data regarding safety of baked milk
  - Strongly consider an OFC to introduce the potential co-trigger
- Multiple FPIES
  - Summary statement 23: Recognize that infants with CM or soy-FPIES may be at increased risk of having FPIES to other foods.
    - No discrete risk or odds known
    - Most common co-trigger is rice or oat
    - Do not delay introduction past 6 months of life, use similar OFC approach
  - CHOP cohort (largest case series on multiple foods)
    - 70% reactive to 1-2 foods, 30% reactive ≥ 3 foods, 41.6% to multiple grains
  - If is concern, may elect to introduce fruit/vegetable first, then meats and cereals

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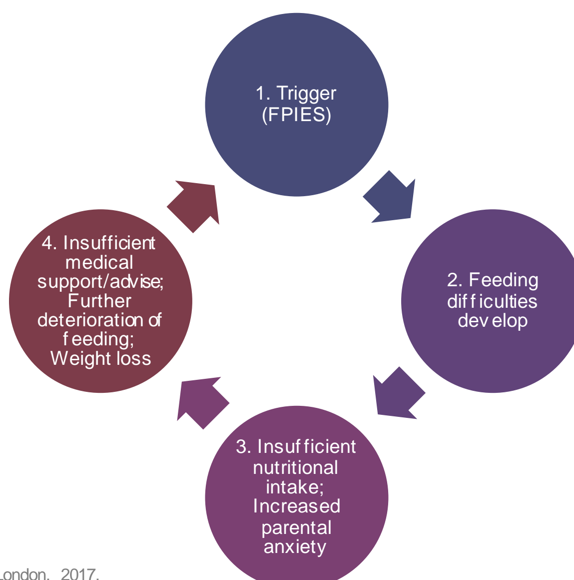
Breastfeeding and FPIES

- Summary statement 21: Do not recommend routine maternal dietary elimination of offending triggers while breastfeeding **if the infant is thriving and remains asymptomatic.**
  - Exclusive breastfeeding seen as protective
  - Isolated case reports of breast milk transmission
  - Parents report chronic symptoms in breastfed babies
  - Only recommend to remove trigger if is FTT or the symptoms persist

1. Jarvinen KM et al. J Allergy Clin Immunol. 2013;1:317-22. 2. Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

Disjointed Relationship with Food



Adapted from Meyer R. Imperial College London. 2017.

Food Introduction

Ages & stages	Lower-risk foods	Moderate-risk foods	Higher-risk foods
4-6 mo (as per AAP, CoN)	Vegetables		
• If developmentally appropriate and safe and nutritious foods are available: Smooth, thin purees and progress to thicker purees,	Broccoli, cauliflower	Squash, carrot	Sweet potato, green pea
6 mo (as per WHO)	Fruits		
• Complementary feeding should begin no later than 6 mo of age	Blueberries, strawberries	Apple, pear	Banana
8 mo of age or when developmentally appropriate: offer soft-cooked and bite-and-dissolve textures	Lamb, fortified quinoa	Beef, fortified grits and corn cereal	Fortified infant rice and oat cereal
12 mo of age or when developmentally appropriate	Tree nuts and seed butters (thinned with water or infant puree)	Peanut, other legumes (other than green peas)	Milk, soy

Adapted from Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

Dietary Guidance

- **Summary Statement 24:** Provide guidance during the introduction of complementary foods to ensure nutritional adequacy during this time and beyond.

- **Summary Statement 28:** Recommend foods that enhance developmental skills in infants in the complementary feeding period to prevent aversive feeding behaviors and delay in the development of food acceptance and feeding skills. [Strength of recommendation: Weak; Evidence strength: IV; Evidence grade: D]

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Nutritional Considerations

Immediate goals

- Provide guidance during the introduction of complementary foods to ensure nutritional adequacy during this time and beyond
- Monitor growth (weight and height/length) regularly in children with FPIES.
- Use hypoallergenic formula in formula-fed infants or infants that can no longer breast-feed who are diagnosed with FPIES due to CM.

Long-term goals

- Do not routinely recommend avoidance of products with precautionary allergen labeling in patients with FPIES
- Recommend foods that enhance developmental skills in infants in the complementary feeding period to prevent aversive feeding behaviors and the delay in the development of food acceptance and feeding skills.

Special Considerations

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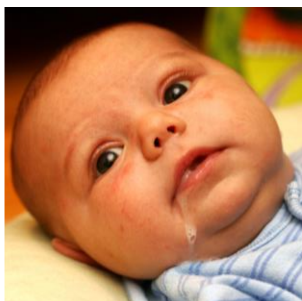
Atypical FPIES

- **Summary Statement 4:** Consider specific-IgE testing of children with FPIES to their trigger food, as a co-morbid IgE-mediated sensitization to triggers such as CM may infer greater chance of persistent disease
  - Special population of patients, (typically older) with mean resolution of 13.8 years
  - Food-sIgE in FPIES is an epiphenomenon and does not play a role in FPIES pathophysiology
  - Evidence from a case series that 7/17 atypical FPIES to milk had prolonged course
    - May shift to an IgE mediated reaction pattern
    - Overall, 4-20% may develop sIgE to the trigger, 20-40% to other foods
  - Population exists but needs more robust study

Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

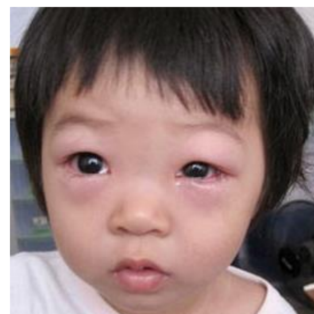
Atypical FPIES

FPIES & IgE-mediated allergy can occur in the same child



Cow milk-FPIES
1 in 4 develop
+CM-IgE

1 in 3 progress to immediate IgE-mediated CMA



Overall 1 in 3 have IgE-FA to another food

Caubet JC, et al. JACI. May 2014.

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Parental Education

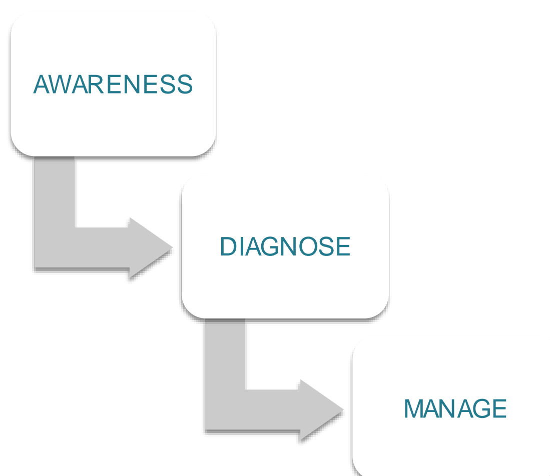
- **Summary statement 18:** Manage acute-FPIES individually according to severity, and review treatment strategies with the caregivers of each patient.
  - Review signs and symptoms of a reaction
  - Create an emergency action plan and review with caregiver to emphasize the need for prompt hydration
  - Educate about triggers and avoidance
  - Refer for dietary support and caregiver support groups (e.g., I-FPIES)

Nowak-Wegrzyn A et al. J Allergy Clin Immunol. 2017;139:1111-26.

Highlights

Two phenotypes

- Avoidance of trigger foods is key
- Utilize OFC to confirm diagnosis and resolution
- Provide clear treatment plan and ER letter
- Provide or refer for nutritional support, recognize poor QoL



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