

# Diagnosis and Management of Pediatric Food Protein-Induced Enterocolitis Syndrome (FPIES)

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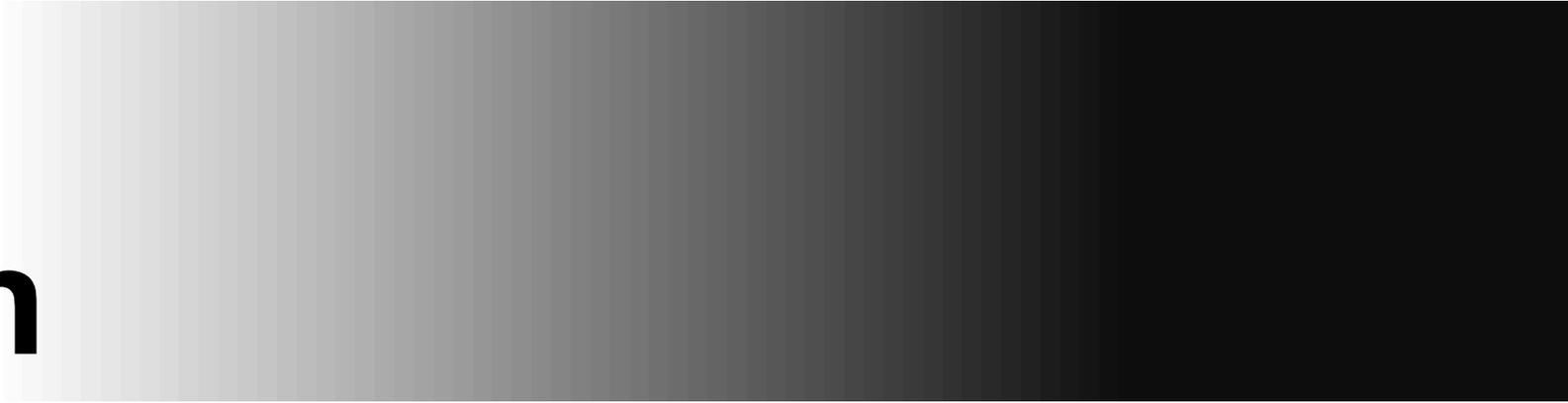
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# Objectives

- Review the diagnostic criteria for FPIES
- Review classic and atypical FPIES
- Identify the common FPIES food triggers
- Understand the management of FPIES
- Potential treatment avenues for FPIES

# **Case Presentation**



# Healthy Infant with Severe Delayed Vomiting

- Infant (7mo) with 3 separate episodes of **severe delayed vomiting**.
- **Sweet potato** and **carrots** were introduced at 5-months old & tolerated at least 5 times.
- At 6 mo & 6.5mo, she ate ½ jar of sweet potato puree & **1.5hrs later developed:**
  - **Repetitive vomiting (>10 episodes)**
  - **Lethargy**
  - **Pallor**
  - **Floppiness**
  - **Diarrhea (started 6h later)**
- Mom assumed a “viral GI bug” & gave ondansetron
- One week later, carrot puree caused similar symptoms



# Reactions After Sweet Potato & Carrots



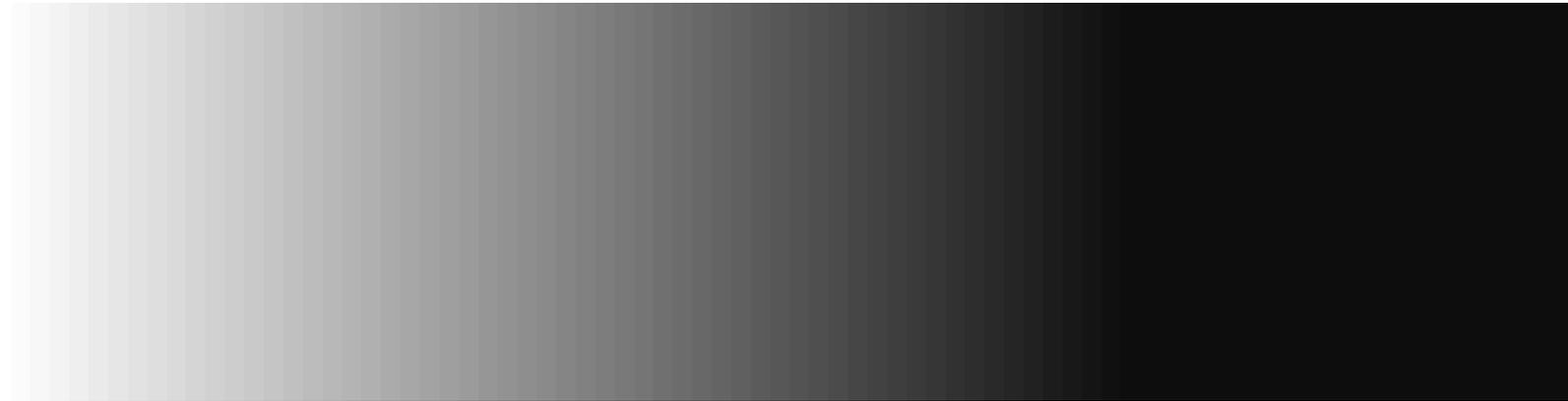
**24 hours later...**



# Differential Diagnoses To Rule Out

Differential Diagnoses
<b>Infectious Gastroenteritis</b>
<b>Food Poisoning</b>
<b>Sepsis</b>
Gastroesophageal reflux disease
Obstructive GI (i.e. pyloric stenosis, intussusception)
Eosinophilic gastroenteropathies (e.g. EoE)
Intolerance of short-chain fermentable carbohydrates
Lactose intolerance
Fructose intolerance
Inborn errors of metabolism
Neurologic disorders
Inborn errors of immunity

**What is  
FPIES?**



# FPIES: Clinical Diagnosis



**FPIES is a constellation of symptoms**



**No biomarker to confirm diagnosis**

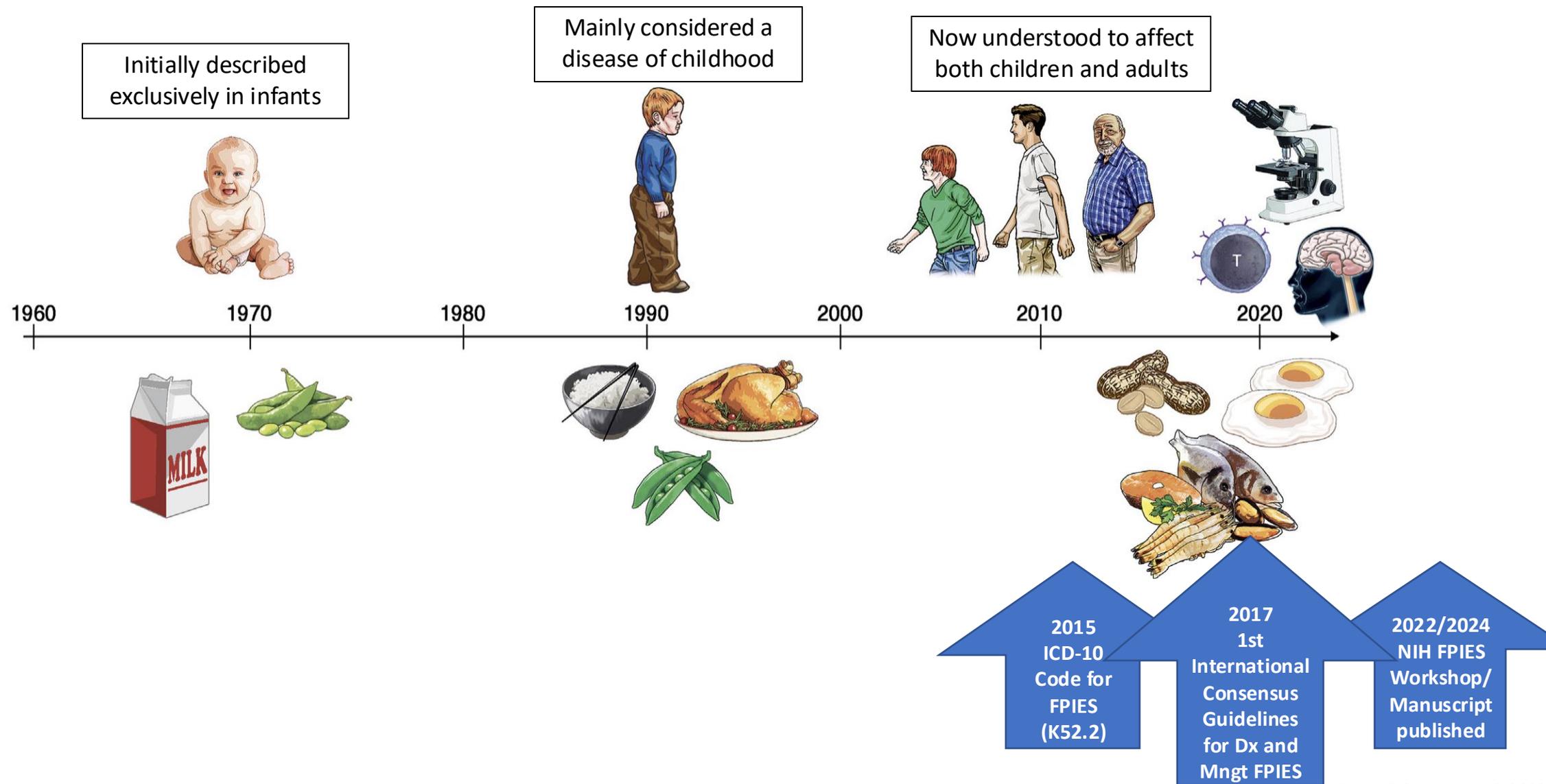


**Limited insights in pathophysiology**



**Diagnosis is delayed**

# FPIES Timeline



# Acute FPIES Diagnostic Criteria

**1** MAJOR CRITERION

+

**3+** MINOR CRITERION

**VOMITING 1-4 HRS  
+  
ABSENCE OF SKIN  
& RESPIRATORY  
SYMPTOMS**

>1 episode to the same food

Repetitive vomiting 1-4h after  
eating another food

Lethargy

Pallor/Gray

Emergency room visit

Hypotension; IV fluid support

Diarrhea in 24h

# Chronic FPIES Diagnostic Criteria

## • Mild Presentation

- Lower doses of the trigger food (*e.g. food allergens in breastmilk*)
- **Findings:**
  - Intermittent vomiting
  - +/- Diarrhea
  - Failure to thrive
  - +/- Low albumin, Low total protein

## • Severe Presentation

- Offending food ingested on a daily basis (*e.g. infant formula*)
- **Findings:**
  - Intermittent but progressive vomiting
  - Diarrhea (+/-blood)
  - Failure to thrive
  - Low albumin, Low total protein
  - Leukocytosis & neutrophilia
  - Possible metabolic acidosis

**CRITERION:** 1) Resolution of symptoms **WITHIN DAYS** of removing the offending food trigger(s);  
2) **Reintroduction** of the food trigger(s) will lead to **ACUTE** FPIES symptoms (vomiting 1-4h, etc).

# ADULT: Acute FPIES Diagnostic Criteria

**1** MAJOR CRITERION

+

**3+ points**

MINOR CRITERION

2+ episodes of  
ABDOMINAL PAIN  
-or-  
VOMITING  
1-6h post food  
ingestion

>1 episode to the same food (3)

Lethargy (1)

Pallor (1)

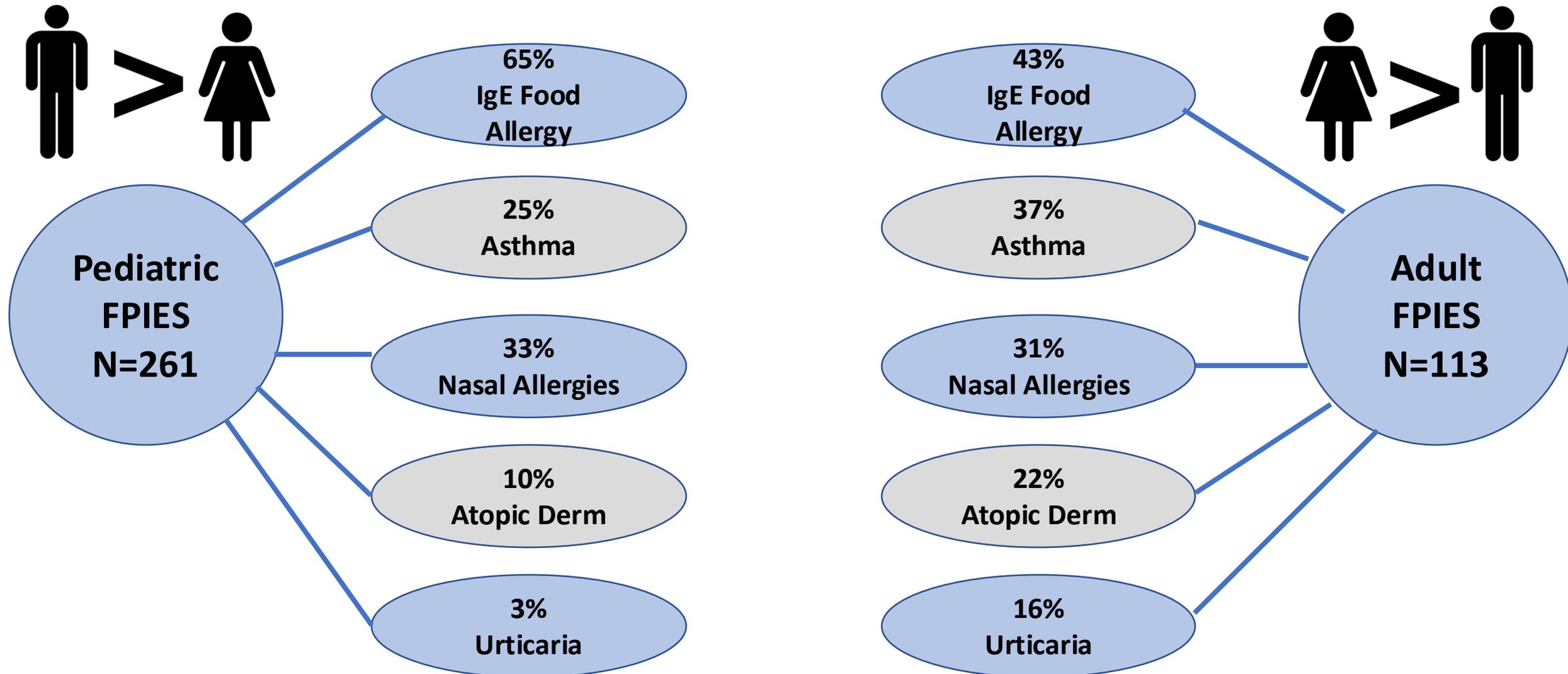
Diarrhea within 24h (1)

Hypotension (2)

Hypothermia (1)

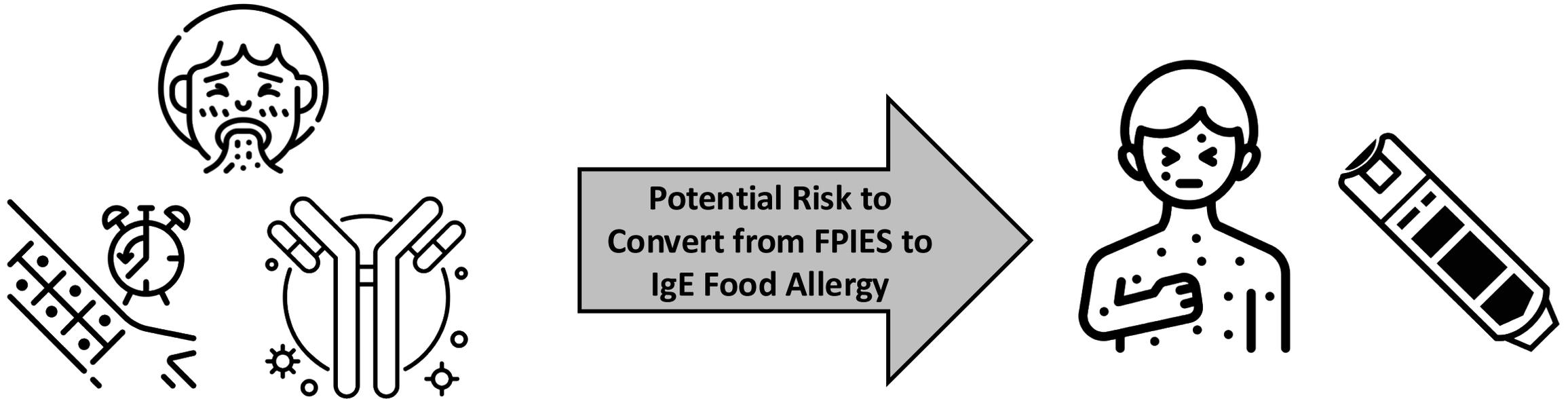
Nausea (1)

# High Rates of Allergic Co-Morbidities in U.S. FPIES Patients



# **Atypical FPIES:** ***A Rare Phenotype***

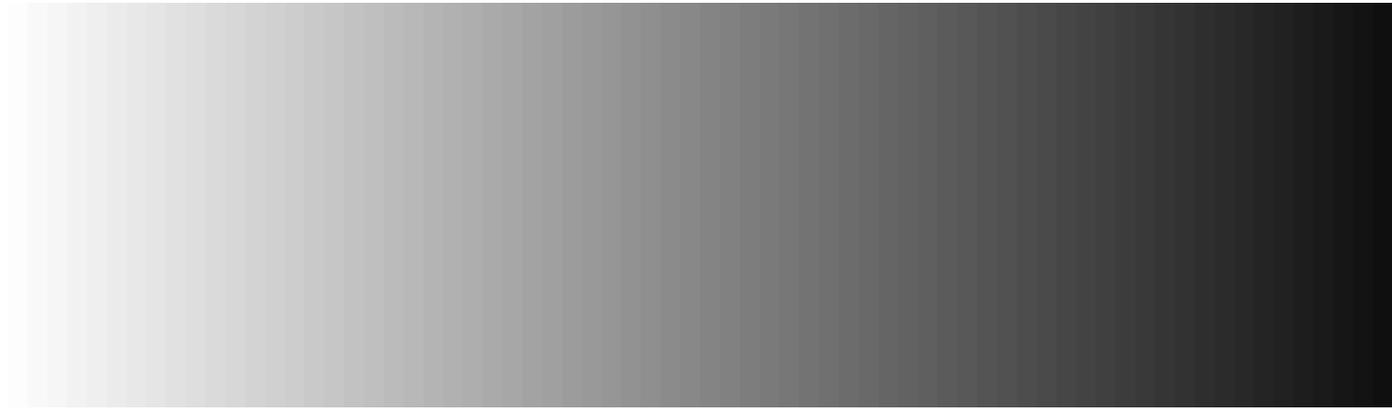
# FPIES Phenotypes – Atypical FPIES



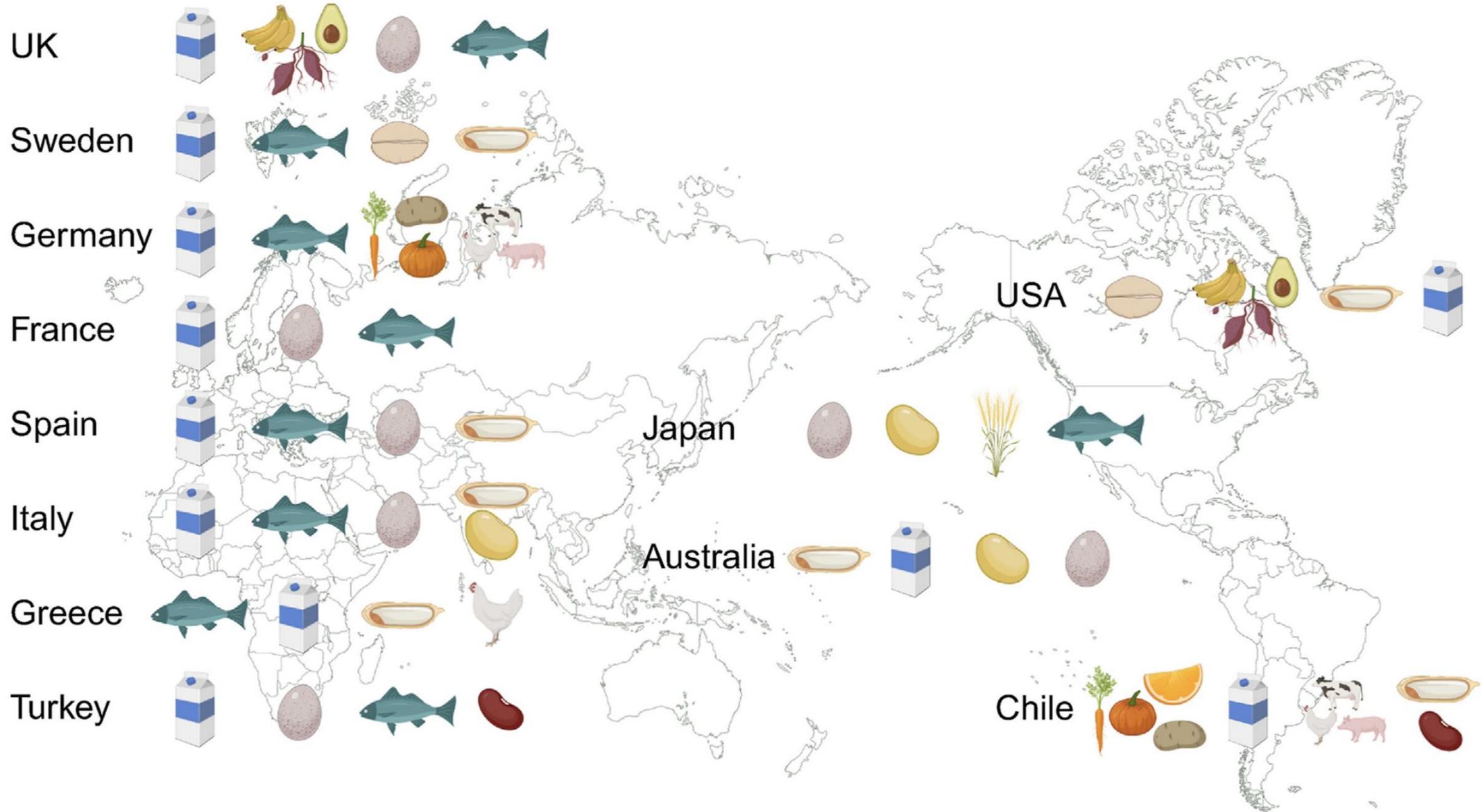
- **CLASSICAL FPIES** - No IgE to FPIES food trigger
- **ATYPICAL FPIES** - Detectable IgE (skin or blood test) to FPIES trigger
  - Prolonged course of FPIES
  - Potential risk of conversion to IgE food allergy
    - **Cow's Milk (CM) FPIES (*Caubet et al 2014*)**
      - 1 in 3 CM FPIES → CM IgE allergy

**FPIES:**

**Food Triggers**



# FPIES Food Triggers – Across The Globe

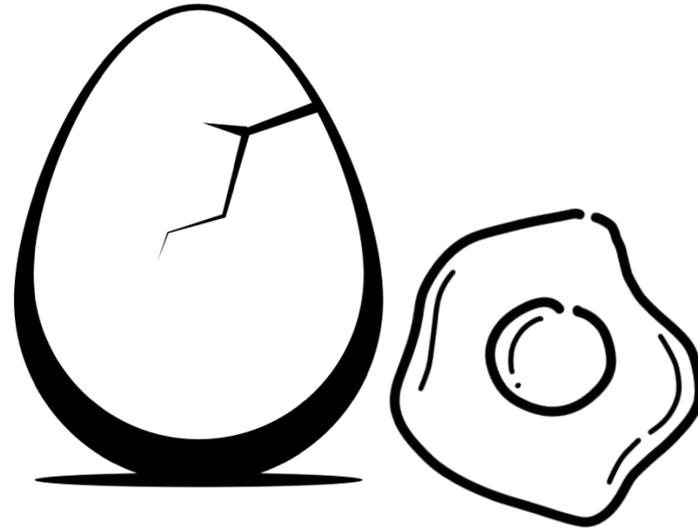


# Emerging FPIES Food Triggers

**PEANUT**

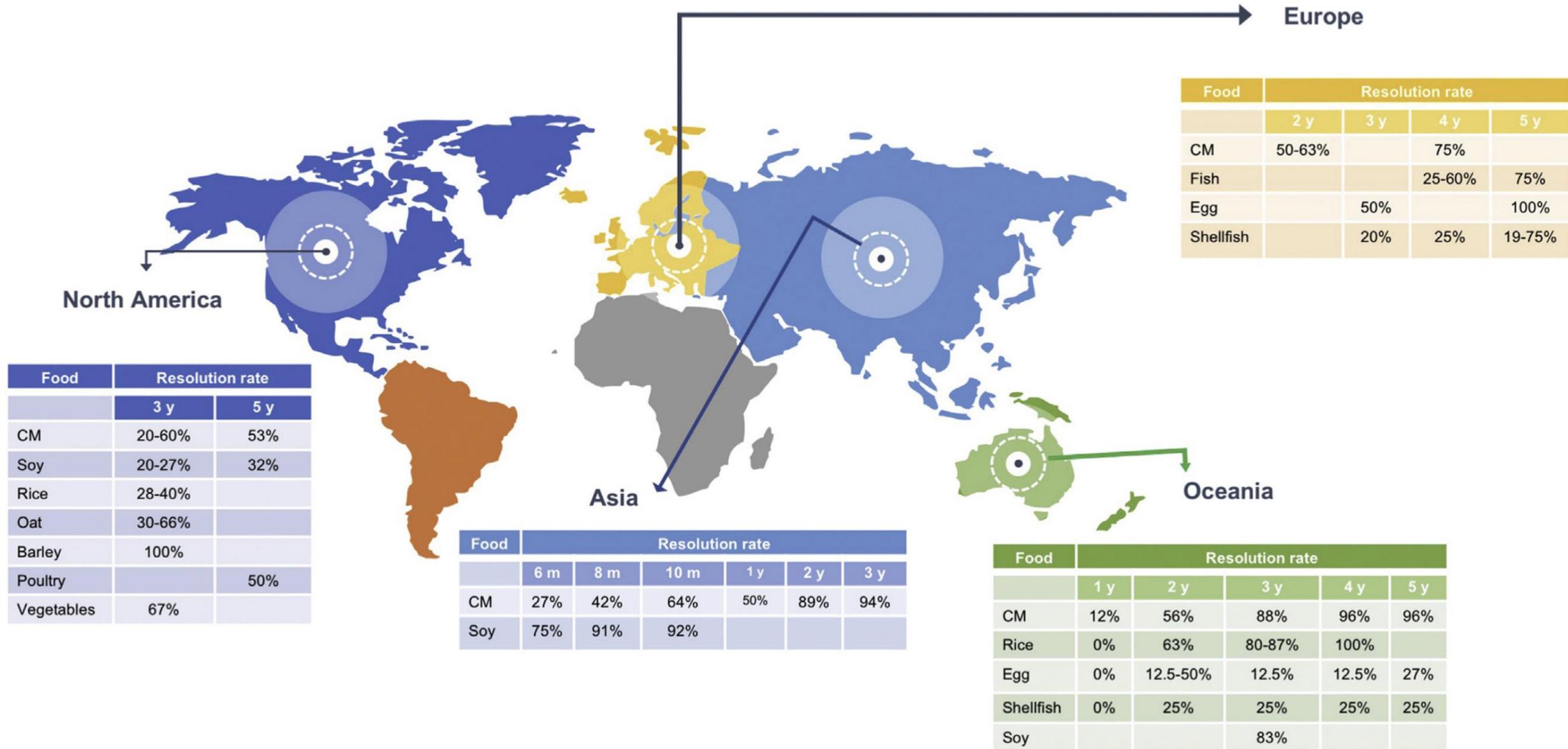


**EGG**

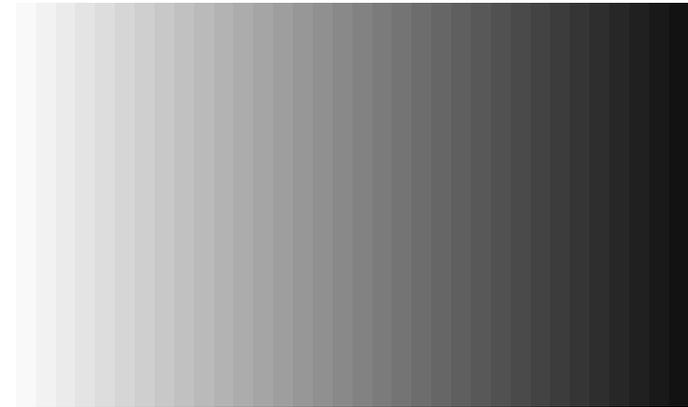


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# FPIES Resolution Rates Vary Globally



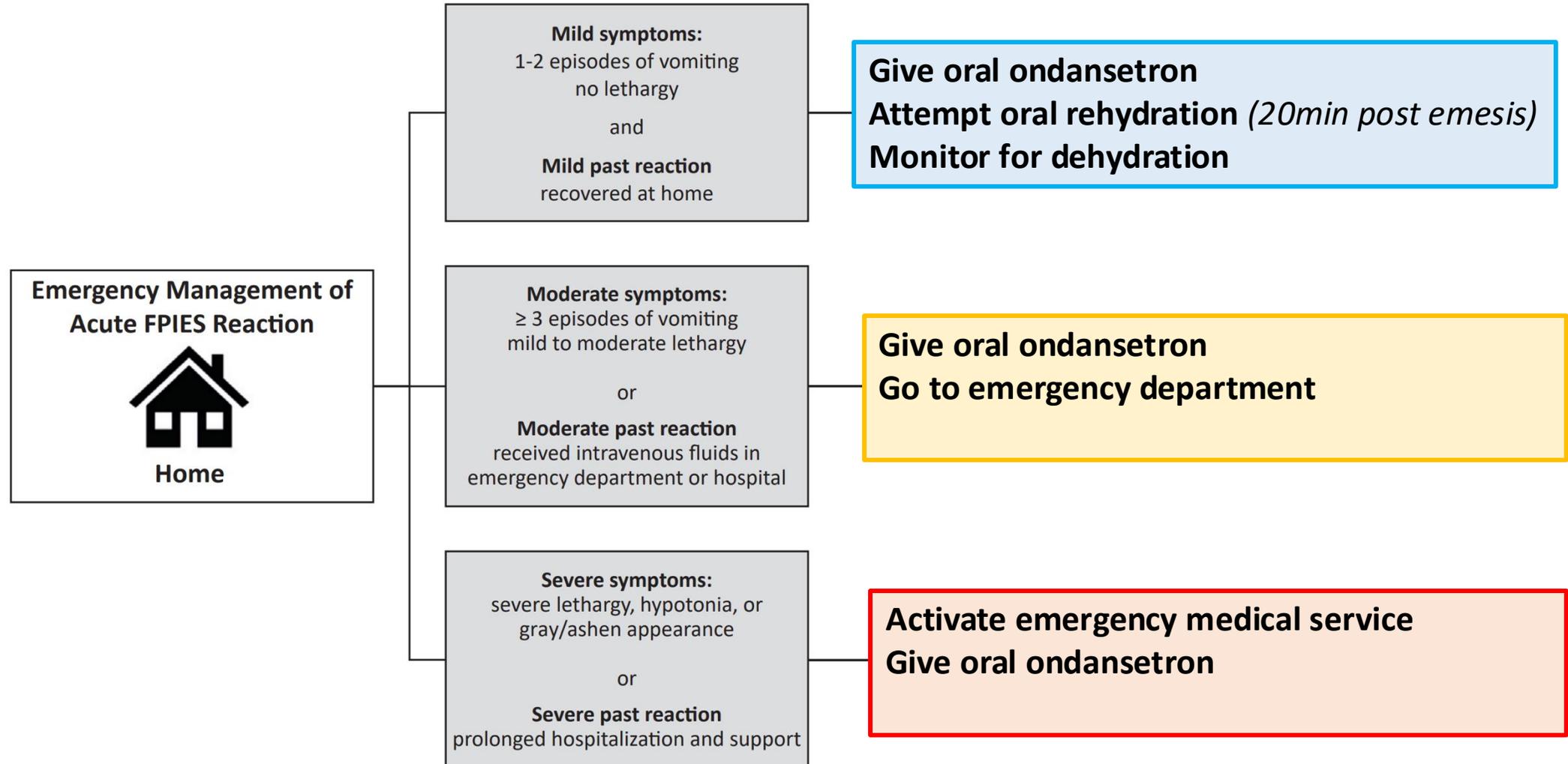
# **FPIES: Management**



# Weaning Following an FPIES Diagnosis

FOOD GROUP	LOWER RISK	MODERATE RISK	HIGHER RISK
<b>Milk and Dairy; Alternatives</b>	<ul style="list-style-type: none"> <li>Breast Milk, Hypoallergenic Formula</li> </ul>		<ul style="list-style-type: none"> <li><b>Cow's Milk and other mammalian milks</b></li> <li><b>Soy, pea, oat, rice milks</b></li> </ul>
<b>Meat, Fish, Poultry</b>	<ul style="list-style-type: none"> <li>Lamb, beef, pork, bison</li> </ul>		<ul style="list-style-type: none"> <li><b>Fish</b></li> <li><b>Poultry</b></li> </ul>
<b>Other Protein Foods</b>	<ul style="list-style-type: none"> <li>Tree nuts, seeds</li> </ul>	<ul style="list-style-type: none"> <li><i>Peanuts</i></li> </ul>	<ul style="list-style-type: none"> <li><b>Soy</b></li> <li><b>Egg</b></li> </ul>
<b>Grains</b>	<ul style="list-style-type: none"> <li>Quinoa, millet, amaranth</li> </ul>	<ul style="list-style-type: none"> <li>Wheat</li> <li>Corn</li> </ul>	<ul style="list-style-type: none"> <li><b>Rice</b></li> <li><b>Oat</b></li> </ul>
<b>Vegetables</b>	<ul style="list-style-type: none"> <li>Broccoli, cauliflower, parsnip, turnip, beet, spinach, zucchini, tomato</li> </ul>		<ul style="list-style-type: none"> <li><b>Green pea</b></li> <li><b>Sweet potato</b></li> </ul>
<b>Fruit</b>	<ul style="list-style-type: none"> <li>Blueberries, plum, raspberries, grape, strawberry, watermelon</li> </ul>		<ul style="list-style-type: none"> <li><b>Avocado</b></li> <li><b>Banana</b></li> </ul>

# Management of FPIES Reactions



## FPIES (Food Protein-Induced Enterocolitis Syndrome) ACTION PLAN

<b>Name:</b> _____	<b>Date of Birth:</b> _____	<b>Weight:</b> _____	lbs/kg (circle one)
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**FPIES triggers/foods:** \_\_\_\_\_

**IgE-mediated food allergy:** if checked, this individual also has food allergies where there is at risk for anaphylaxis. Please follow their Allergy & Anaphylaxis Emergency Plan if appropriate.

<b>What to Look For: FPIES Symptoms</b> Typically delayed (1-4 hours) after ingestion			
			
<b>GUT</b> Vomiting Abdominal pain Nausea Diarrhea	<b>SKIN</b> Pale Blue/Grey Cool Clammy	<b>HEART</b> Dizzy Fainting/Passing out Fast or slow heartbeat Weak pulse	<b>OTHER</b> Sleepiness/Unresponsive Weakness Limp/Floppy (infants)



<b>What to Do</b>
<ol style="list-style-type: none"> <li>1. Give prescribed ondansetron (Zofran®) if vomiting occurs</li> <li>2. Notify parent/guardian or emergency contact</li> <li>3. Monitor symptoms                             <ul style="list-style-type: none"> <li>• If sleepy or lethargic, place individual on their side to prevent choking on vomit.</li> <li>• If there has been no vomiting for 20-30 minutes, give clear liquids/ice-chips/breastmilk as tolerated.</li> </ul> </li> <li>4. <b>Call 911</b> if:                             <ul style="list-style-type: none"> <li>• the vomiting does not stop</li> <li>• the individual is very sleepy, unresponsive, faints, passes out, or is floppy (infants/young children)</li> <li>• the skin appears pale, blue, or grey</li> <li>• the individual appears <u>dehydrated</u> (e.g., dry lips/tongue, not making saliva or tears, not urinating/peeing)</li> </ul> </li> </ol>

<b>MEDICATION: Ondansetron hydrochloride (Zofran®)</b>
<input type="checkbox"/> Orally disintegrating tablet (placed in mouth): ____ 2 mg (half of 4 mg tab) ____ 4 mg ____ 8 mg <input type="checkbox"/> Liquid dose _____ <i>Maximum single dose of either tablet or liquid: 16 mg</i> <i>May repeat the dose once if the individual vomits within 10 minutes of the initial dose.</i>

HEALTH CARE PROVIDER Name	Signature	Phone number	Date
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NURSE/PERSONNEL Name	Signature	Phone number	Date
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PARENT/GUARDIAN Name	Signature	Phone number	Date
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*I, the parent/guardian, authorize the childcare or school to follow this plan and to contact the Health Care Provider if needed, I release the school district and any other childcare or school personnel who follow this plan from civil liability*



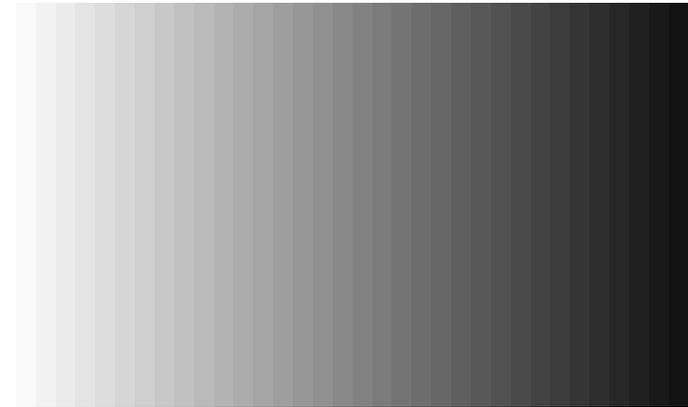
**DO NOT HESITATE TO ADMINISTER MEDICATION OR CALL 911  
EVEN IF PARENTS/GUARDIANS CANNOT BE REACHED**



# FPIES Action Plan

**FPIES:**

**Treatment Avenues**



# CANADIAN EGG LADDER



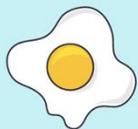
for hen's egg allergy

## INSTRUCTIONS

- Start at Step 1 and work your way up to Step 4
- Give the food daily. May be taken with a meal
- Start with a grain or pea sized amount, and over several days or weeks gradually increase to an age appropriate amount
- Once at an age appropriate amount, spend a minimum of 1-3 months in each category, before advancing on to the next category
- If after advancing to the next category there are allergic symptoms, then go back to the lower category for a month before re-trying the higher category

Step  
4.

(OPTIONAL)



Sunny Side Up, Soft Boiled,  
or Lightly Scrambled Egg



Raw Egg

(e.g. ice cream, meringue, buttercream,  
cookie dough, mayonnaise)

Step  
3.



Hard Boiled or  
Steamed Egg



Well-Cooked  
Scrambled Egg



French Toast

Step  
2.



Pancake or  
Crêpe



Waffle



Fresh Egg  
Noodles/  
Pasta



Egg as a  
Binder  
(e.g. hamburger  
patty, dumplings)

Step  
1.

Baked Goods with Egg Ingredients



muffin or cupcake



well-baked cookie



Dried Egg  
Noodles/  
Pasta

# Using the Canadian egg ladder in children with FPIES: a case series (Ye et al 2023)

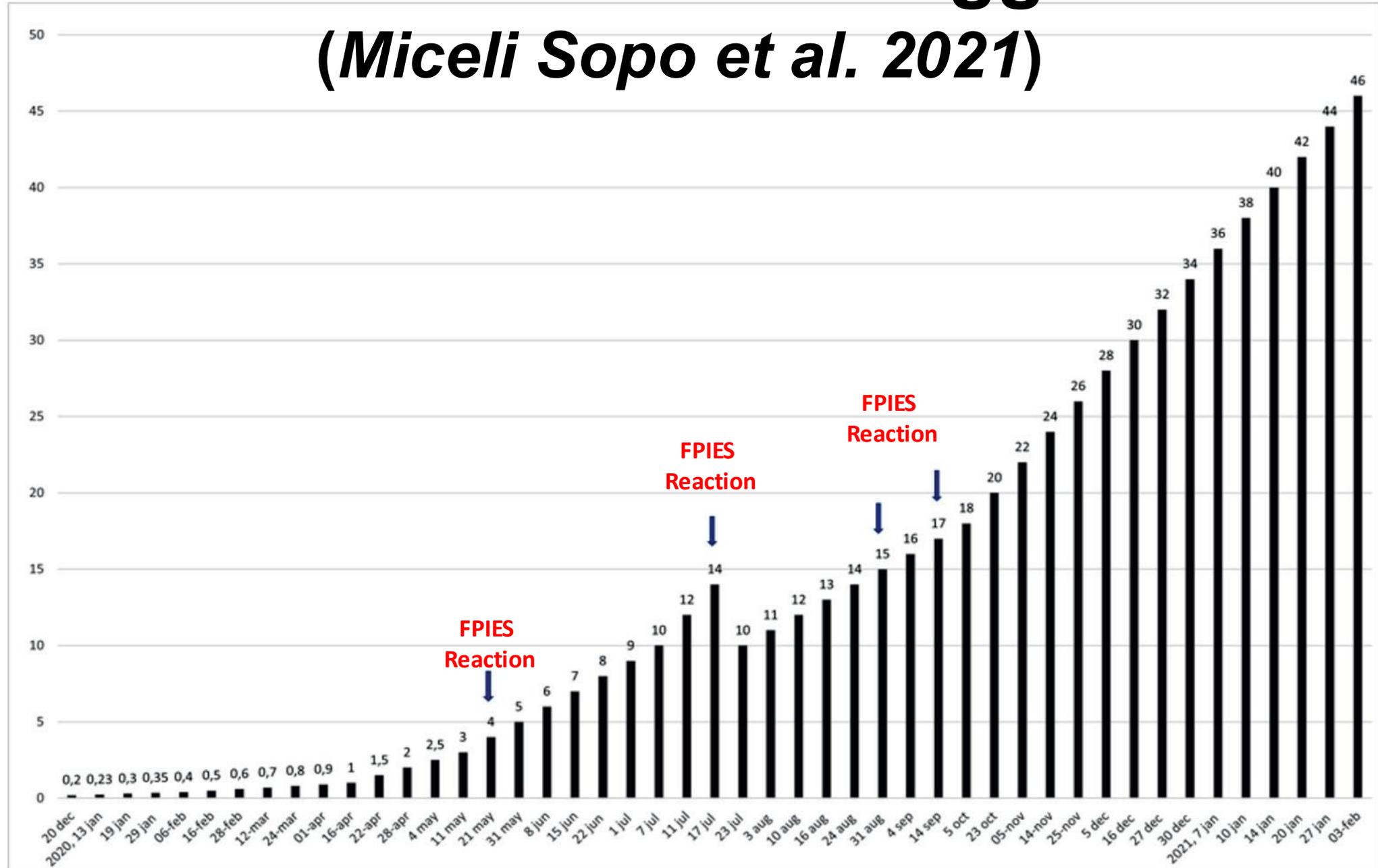
- **Pea-sized** amount, increased gradually over several days or weeks to age-appropriate dose
- Spent a **minimum of 1-3 months** in that “STEP” category before advancing to the next step



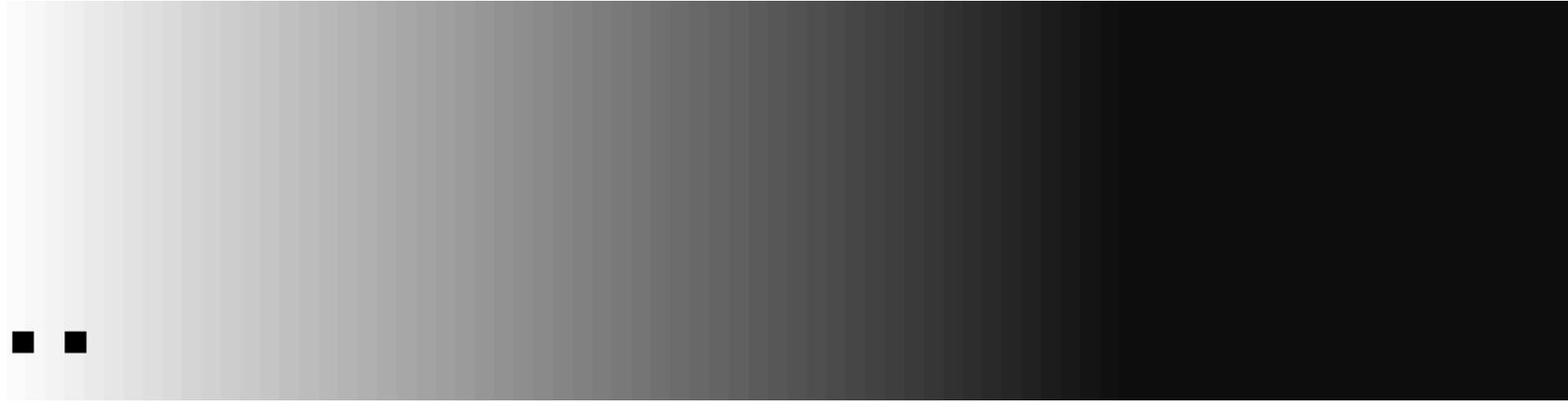
# Oral desensitization in egg FPIES

*(Miceli Sopo et al. 2021)*

Amount of raw egg intake(ml)



**Back to our  
FPIES case...**



# Our patient

- Clinical history consistent with a diagnosis of **SEVERE FPIES** to:
  - **Sweet potato**
  - **Carrots**
- Oral ondansetron prescribed
- FPIES action plan provided
- Oral food challenge (in Allergy office) → 12-18 months after last reaction

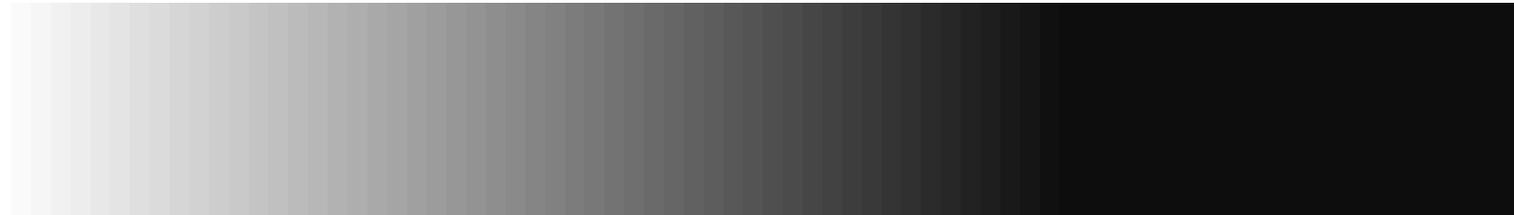


# Oral Food Challenges

- **Carrots** – Tolerated in A/I clinic
- **Sweet potato** – Tolerated in A/I clinic



# Summary



# Key Messages



- FPIES reactions are a **MEDICAL EMERGENCY** and should be promptly treated
  - **Vomiting** → administer ondansetron
  - **Dehydration/Hypotension** → administer fluids
- FPIES can occur in both pediatric and adult patients
  - **Pediatrics:** (MAJOR) Vomiting + 3 MINOR
  - **Adults:** (MAJOR) Severe abdominal pain -OR- Vomiting + 3 MINOR
- There is **limited insight** on the pathophysiology of FPIES

# Key Messages



- Depending on the food trigger, **assess for FPIES resolution** at least **12 months** after the last FPIES reaction
- Consider **skin testing** to assess for **atypical FPIES**
- FPIES patients should receive:
  - **FPIES Action Plan**
  - **Oral ondansetron (0.15mg/kg/dose)**
- Studies are needed to assess safety and efficacy of FPIES desensitization

**THANK YOU!**  
**Questions?**



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