What's New in the Management of Food Allergy in Breastfed Children

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For healthcare professionals only

Guidelines on Food Allergy 2020-24

Focus on breastfed infants

McWilliam et al. World Allergy Organization Journal (2023) 16:100830
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WORLD ALLERGY ORGANIZATION JOURNAL

Open Access

World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) guidelines update – X – Breastfeeding a baby with cow's milk allergy

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EAACI POSITION PAPER

Allergy

WILEY

Diagnosis and management of Non-IgE gastrointestinal allergies in breastfed infants—An EAACI Position Paper

Rosan Meyer[1] | Adriana Chebar Lozinsky[2] | David M. Fleischer[3] | Mario C. Vieira[4] | George Du Toit[5] | Yvan Vandenplas[6] | Christophe Dupont[7] | Rebecca Knibb[8] | Pinar Uysal[9] | Ozlem Cavkaytar[10] | Anna Nowak-Wegrzyn[11] | Neil Shah[12] | Carina Venter[3]

All children

> J Pediatr Gastroenterol Nutr. 2024 Feb;78(2):386–413. doi: 10.1097/MPG.0000000

An ESPGHAN Position Paper on the Diagnosis, Management, and Prevention of Cow's Milk Allergy

Yvan Vandenplas [1], Ilse Broekaert [2], Magnus Domellöf [3], Flavia Indrio [4], Alexandre Lapillonne [5 6], Corina Pienar [7], Carmen Ribes-Koninckx [8], Raanan Shamir [9], Hania Szajewska [10], Nikhil Thapar [11 12 13 14], Rut Anne Thomassen [15], Elvira Verduci [16], Christina West [3]

Affiliations + expand

PMID: 38374567 DOI: 10.1097/MPG.0000000000003897

Munaro et al. World Allergy Organization Journal (2022) 15:100687
http://doi.org/10.1016/j.waojou.2022.100687

WORLD ALLERGY ORGANIZATION JOURNAL

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Managing food allergy: GA²LEN guideline 2022

DOI: 10.1111/all.16345

Allergy

GUIDELINES

EAACI guidelines on the management of IgE-mediated food allergy

EAACI guideline: Preventing the development of food allergy in infants and young children (2020 update)

Susanne Halken[1] | Antonella Muraro[2] | Debra de Silva[3] | Ekaterina Khaleva[4] | Elizabeth Angier[5] | Stefania Arasi[6] | Hasan Arshad[7,8,9] | Henry T. Bahnson[10] | Kirsten Beyer[11] | Robert Boyle[12,13] | George du Toit[14] | Motohiro Ebisawa[15] | Philippe Eigenmann[16] | Kate Grimshaw[8,17] | Arne Hoest[1] | Carla Jones[18] | Gideon Lack[19,20,21,22] | Kari Nadeau[23] | Liam O'Mahony[24] | Hania Szajewska[25] | Carina Venter[26] | Valérie Verhasselt[27] | Gary W. K. Wong[28] | Graham Roberts[4,7,9] | European Academy of Allergy and Clinical Immunology Food Allergy and Anaphylaxis Guidelines Group

Role of Pediatricians in Promoting and Supporting Breastfeeding: A Position Paper of the International Pediatric Association Strategic Advisory Group on Infant, Child, and Adolescent Nutrition

Ann Nutr Metab DOI: 10.1159/000534004 Received: June 14, 2023 Accepted: September 4, 2023 Published online: September 6, 2023

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All healthcare professionals

All pediatricians need to understand the basics of breastfeeding, including lactation physiology, recognize common breastfeeding problems, and advise mothers or refer them for appropriate support; training curricula for general pediatricians and all pediatric subspecialties should reflect this. Even in

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Common Scenario

- Newborn baby doesn't achieve good first feed
  - Mom/ baby exhausted
- 4-6 hours later baby woken and encouraged to latch
  - Latches incorrectly
  - Comfort feed for hour
  - Nipples start to crack and bleed
- Baby comes off breast screaming
  - HCP says baby is hungry and mom doesn't have enough milk
  - Baby offered formula
  - Drinks full bottle of formula and falls asleep
- Mom believes she doesn't have enough milk so continues formula
  - Occasionally tries to put baby on breast
  - Nipples remain cracked and bleeding
- Milk comes in after 4 days
  - Baby too full of formula to breastfeed
  - Breasts rock solid
  - Mother hand expresses and tries to pump
  - Nothing comes out due to engorgement
  - Baby continues to need formula top ups
- Mother develops fever and feels unwell, AB prescribed
- Breasts begin to soften but baby continues to scream between feeds
- Baby given more formula but becomes unsettled and crampy between feeds
- Formula changed and mother put on dairy free diet
- Mother becomes despondent and gives up breastfeeding

- Crying, fussiness, posseting and short night-time sleep duration common early infancy
- Behavioural cues of fussiness commonly interpreted as an indication that BM quality or quantity is inadequate to satisfy their infant
- Up to 50% healthy infants 0-3 months at least 1 episode regurgitation/d
- Mean time fussing or crying/d in first 6 weeks life around 2 h/ day, varying from 1-3 h
- Mean duration drops rapidly after 6 weeks to about 1 h by 10–12 weeks
- <5% infants have underlying disease requiring further investigation / treatment
- In absence of skilled and knowledgeable support, many parents change their feeding from BF to CMFs; from one CMF to another; or to specialised CMFs

- Self – reported inadequate milk supply (SRIM) "state in which mother perceives she has inadequate supply BM to satisfy infant's hunger / support adequate weight gain."
- ~45% of mothers report introducing CMF because of SRIM
- Research indicates that mother's self-assessment of milk supply frequently based on perceptions of infant satiety and satisfaction, signalled by infant behaviours, especially crying and fussiness
- Introducing CMFs can ↓ suckling, result in actual insufficient milk production
- Both prelacteal feeds and early introduction of CMFs negatively associate
- SRIM co ntroducing CMF and stopping

Pediatr Allergy Immunol. 2019 Dec;30(8):810-816. doi: 10.1111/pai.13108. Epub 2019 Aug 29.

Formula supplementation remains a risk for cow's milk allergy in breast-fed infants

Eimear Kelly [1], Gillian DunnGalvin [2], Brendan P Murphy [1 3], Jonathan O'B Hourihane [1]

- **Infant health**: Breastfeeding protects children from a vast range of illnesses, including infection, diabetes, asthma, heart disease and obesity, as well as cot death (Sudden Infant Death Syndrome)

- **Maternal health**: Breastfeeding also protects mothers from breast and ovarian cancers and heart disease

- **Relationship-building**: Breastfeeding supports the mother-baby relationship and the mental health of both baby and mother

- **Worldwide benefits**: The benefits are seen in both high- and low-income countries, with a study published in The Lancet in 2016 finding that increasing breastfeeding rates around the world to near universal levels could prevent 823,000 annual deaths in children younger than five years and 20,000 annual maternal deaths from breast cancer

- **Cost savings:** A NICE costing report estimates that Baby Friendly accreditation will start to save a facility money after three years, owing to a reduction in the incidence of certain childhood illnesses.

THE LANCET

https://www.thelancet.com/series/Breastfeeding-2023
https://www.thelancet.com/series/breastfeeding

Key Questions

- What is the prevalence of allergy in BF infants?
- What are the symptoms?
- How can IgE and non-IgE symptoms be distinguished?
- How can allergy be differentiated from gut-brain interaction disorders?
- What are the best practices for accurate diagnosis and management to prevent unnecessary elimination diets?

What is the prevalence of allergy in BF infants?

- Often over-diagnosed especially in non-IgE-mediated cases
  - Diagnosis challenging
  - Over- and underdiagnosed
- > 99% infants with proven CMA, BM insufficient allergens to trigger reactions Vandenplas et al, J.Pediatr Gastroenterol Nutr 2024
- Lack of high-quality evidence → ongoing controversy whether trace quantities of CMP found in BM can cause IgE or non IgE-mediated allergies in BF infants

Cow's Milk Proteins in Breast Milk

Source	BLG Concentration	HM vs CM
Human Milk (Average)	1.2–4.4 ng/ml	~1,000,000 times lower than fresh cow's milk levels
Fresh Cow's Milk	3 300,000 ng/ml (3.3 g/ml)	

McWilliam, et al. WAOJ 2023

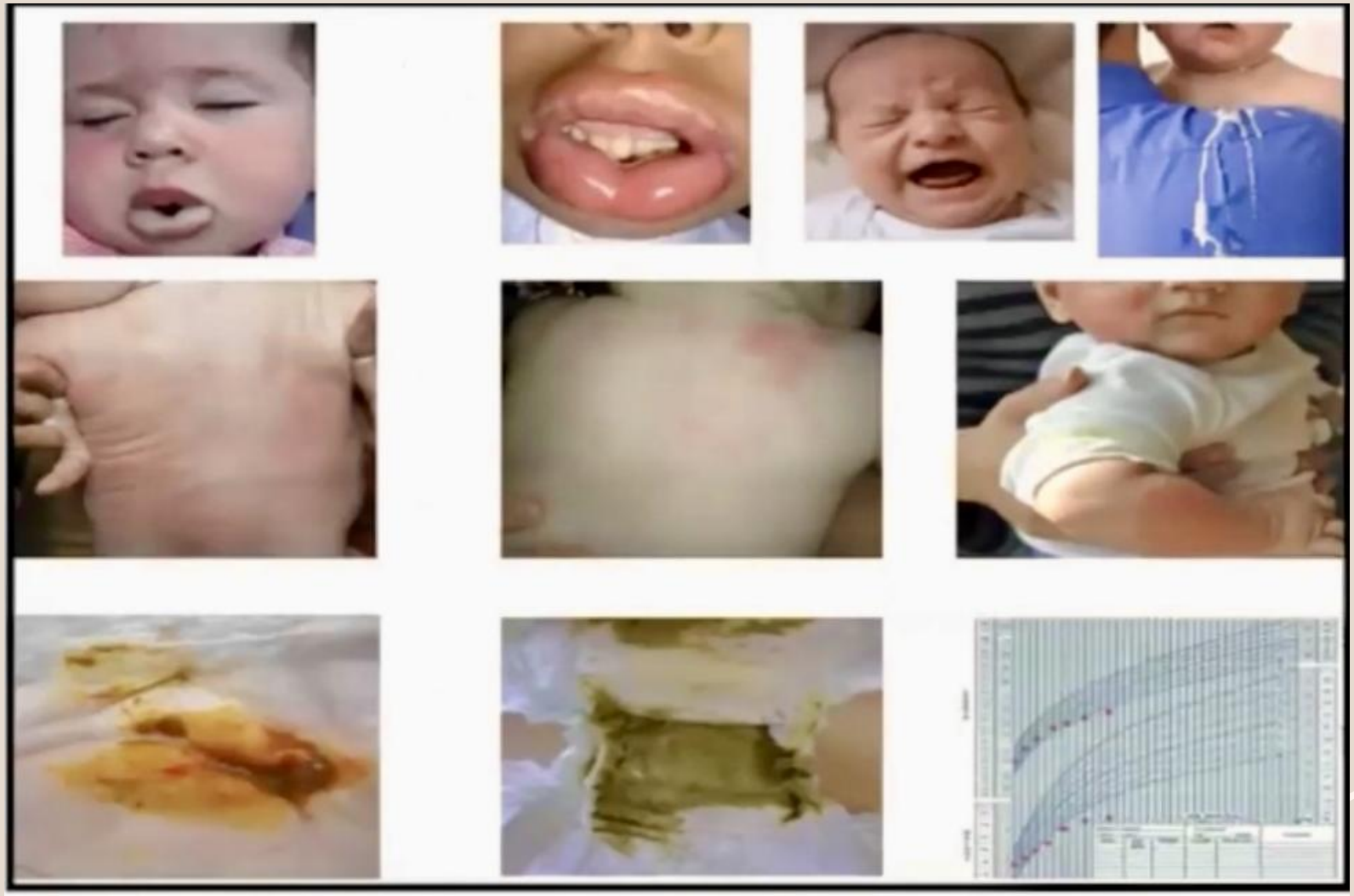
- Systematic review identified 32 studies
  - 4 studies cow's milk proteins
  - 9 egg
  - 4 peanut
  - 2 wheat
  - 3 cow's milk and egg

- Probability of an IgE-mediated allergic reaction in a food-allergic infant breastfed by a woman consuming the relevant food can be estimated as ≤ 1:1000 for cow's milk, egg, peanut, and wheat
- According to latest studies using mass spectrometry, non-human proteins most frequently found in BM come from bovine milk

Comparison of 2 reviews on CMP in Breastmilk

Aspect	JACI Pract (2022)	Foods (2022)
Focus of Review	Examines allergy risks from food proteins in breast milk.	Explores presence and impact of cow's milk antigens in breast milk.
Number of Studies	32 studies (systematic review).	27 studies (scoping review).
Key Findings	**Low levels of cow's milk proteins; very low allergy risk (<1:1000).**	Cow's milk proteins vary with maternal allergies and diet.
Type of Allergic Reactions	**IgE-mediated: Very low risk (<1:1000); β-lactoglobulin ~1 in 2893. Non-IgE: Risk is less clear but likely lower.**	Does not separate IgE and non-IgE reactions; highlights potential risks from allergen exposure.

What are the symptoms?



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How can IgE and non-IgE symptoms be distinguished?

IgE vs non-IgE symptoms in BF infants

	IgE-Mediated Allergy	Non-IgE-Mediated Allergy
Symptom Onset	• Immediate: symptoms occur **within minutes to 2 hours** after exposure.	• Delayed: symptoms develop **6 to 72 hours** or even days after exposure.
Common Symptoms	• **Skin**: Hives, swelling (angioedema). • **Respiratory**: Wheezing, nasal congestion. • **Systemic**: Anaphylaxis (rare in breastfed infants).	• **Gastrointestinal**: **FPIAP** (Blood-streaked stools), diarrhea, vomiting.colic • **FPIES**: Repetitive vomiting, lethargy, poor growth (chronic cases). • **Skin**: Persistent eczema or rash.
Systems Involved	• Multiple systems (skin, respiratory, GI)	• Primarily **gastrointestinal** or **skin**.
Resolution of Symptoms	• Symptoms resolve **quickly** (often within hours) after allergen removal.	• Symptoms improve **gradually over 2–4 weeks** with elimination diet.

Non-IgE gastrointestinal allergies

Non-IgE-mediated food allergy	Cardinal symptom	Additional symptoms	Common food allergen triggers (most common first)	Differential diagnoses
FPIES	Acute FPIES: Vomiting 1-4 h after ingestion Chronic FPIES: intermittent but progressive vomiting and diarrhoea	Acute FPIES: pallor, lethargy, hypovolaemia, hypotension, diarrhoea Chronic FPIES: faltering growth.	Cow's milk, soya, rice, oat, wheat, meat, fish	Gastro-oesophageal reflux disease, sepsis, inborn errors of metabolism, pyloric stenosis, malrotation, intussusception, gastroenteritis with vomiting.
Food protein-induced allergic proctocolitis (FPIAP)	Blood in stool	Occasional loose stools, mucous in the stools, painful flatus, anal excoriation	Cow's milk and soya	Gastrointestinal infections, fissures Infantile polyp, necrotizing enterocolitis, Meckel's diverticulum, intussusception, infantile inflammatory bowel disease (rare)
Eosinophilic Oesophagitis (EoE)	Intermitted vomiting, abdominal discomfort, feeding difficulties	Faltering growth	Cow's milk, soya, egg, wheat	Gastro-oesophageal reflux of infancy, infantile inflammatory bowel disease
Food protein-induced constipation	Straining with soft stools	Faecal impaction, bloating, abdominal pain	Cow's milk and soya	Normal straining associated with infancy, idiopathic constipation, Hirschsprung's Disease
Food protein-induced GORD	Intermitted painful vomiting/regurgitation	Faltering growth, feeding difficulties back-arching with pain	Cow's milk and soya	Gastro-oesophageal reflux of infancy, acute gastroenteritis, food poisoning.
Food protein-induced enteropathy (FPE)	Failure to thrive, diarrhoea	Mucus and bloating, abdominal pain, faltering growth, hypoalbunaemia	Cow's milk, soya, egg and wheat	Sepsis, congenital disaccharide malabsorption, metabolic disorders, chronic kidney disease, neglect, secondary lactose intolerance, chronic FPIES, autoimmune enteropathies, epithelial dysplasia syndromes, cystic fibrosis, immunodeficiencies and/or chronic infection, coeliac disease.

Food protein-induced allergic proctocolitis (FPIAP)

Cow's milk is the most common trigger

New
Nov 2024

> J Pediatr Gastroenterol Nutr. 2024 Nov 25. doi: 10.1002/jpn3.12410. Online ahead of print.

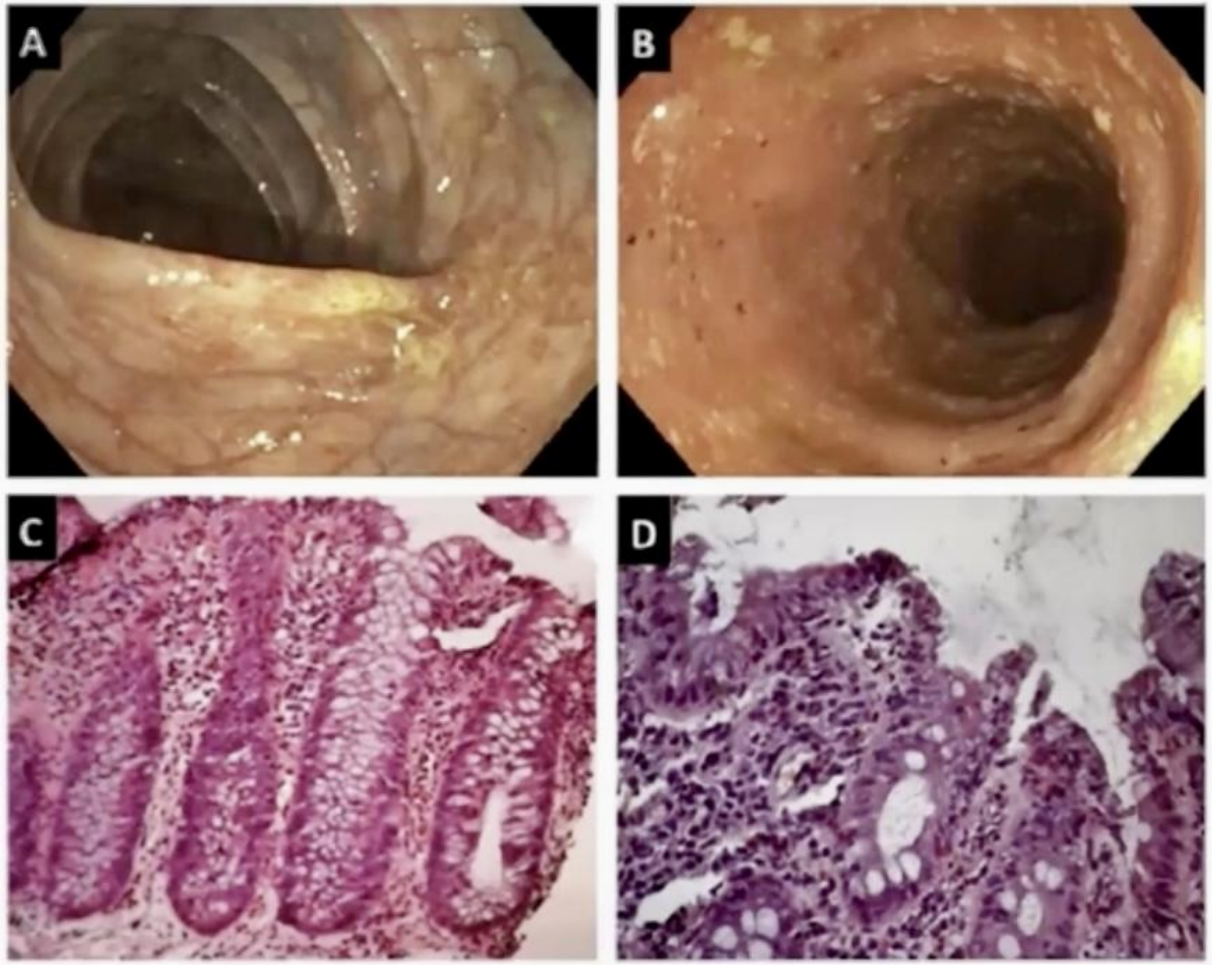
Prospective association between food protein-induced allergic proctocolitis in infancy and constipation after age 3

Michael Marget [1 2], Corey Baker [3], Isabel O'Connell [1 2], Wayne G Shreffler [1 2 4], Qian Yuan [1 4 5], Victoria M Martin [1 4 5]

Affiliations + expand

PMID: 39584247 DOI: 10.1002/jpn3.12410

- **Endoscopy with biopsies**
  - **Is rarely performed to confirm histologic diagnosis.**
  - **Might be useful to exclude other causes of bleeding in case of worsening.**



Nardo et al. J Pediatr 2018;195:128-33

Food Protein Induced Enterocolitis Syndrome (FPIES)

- Extremely uncommon in BF infants
  - usually occurs after introduction of formula / solids
  - rare cases, BF baby can develop FPIES symptoms if mother consumes foods baby allergic to
  - these reactions are generally less severe than when baby directly ingests trigger food
- **Acute FPIES**:
  - vomiting (often projectile) 1-4 hours after ingestion
  - pallor, lethargy, hypovolaemia, hypotension, diarrhoea
- **Chronic FPIES**:
  - intermittent but progressive vomiting and diarrhoea
  - faltering growth

- Common triggers: CM, soya, rice, oats, wheat, meat, fish
- Diagnosis can be challenging
  - symptoms don't always appear immediately after ingestion
  - no specific test
  - diagnosis relies on medical history, symptoms, and food challenges
- Management involves avoiding the trigger foods by mother
- In severe cases, IV fluids and medications
- Sometimes, a temporary switch to an amino acid-based / hydrolised rice formula / strict elimination diet for the mother may be needed
- Many outgrow 3 yoa
    - this can vary depending on severity of reactions and trigger foods.

Eosinophilic Esophagitis (EoE)

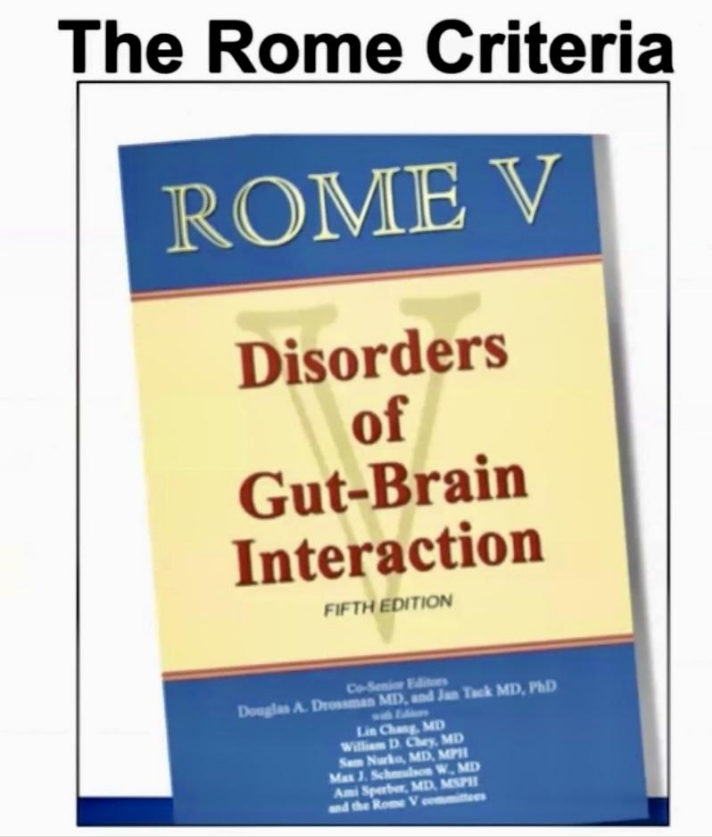
- Chronic antigen-mediated inflammatory disease that affects esophagus
  - Symptoms: intermittent vomiting, abdominal discomfort, feeding difficulties
  - faltering growth
- Cow's milk, soya, egg, wheat
- Early-life risk factors, including
  - maternal fever
  - preterm labour
  - cesarean delivery
  - formula feeding
  - antibiotic or PPI use in infancy
- having a pet in the home was protective
- dietary management
  - eliminating specific foods from the mother's diet (if BF) or
  - infant's diet (if not BF), may be necessary

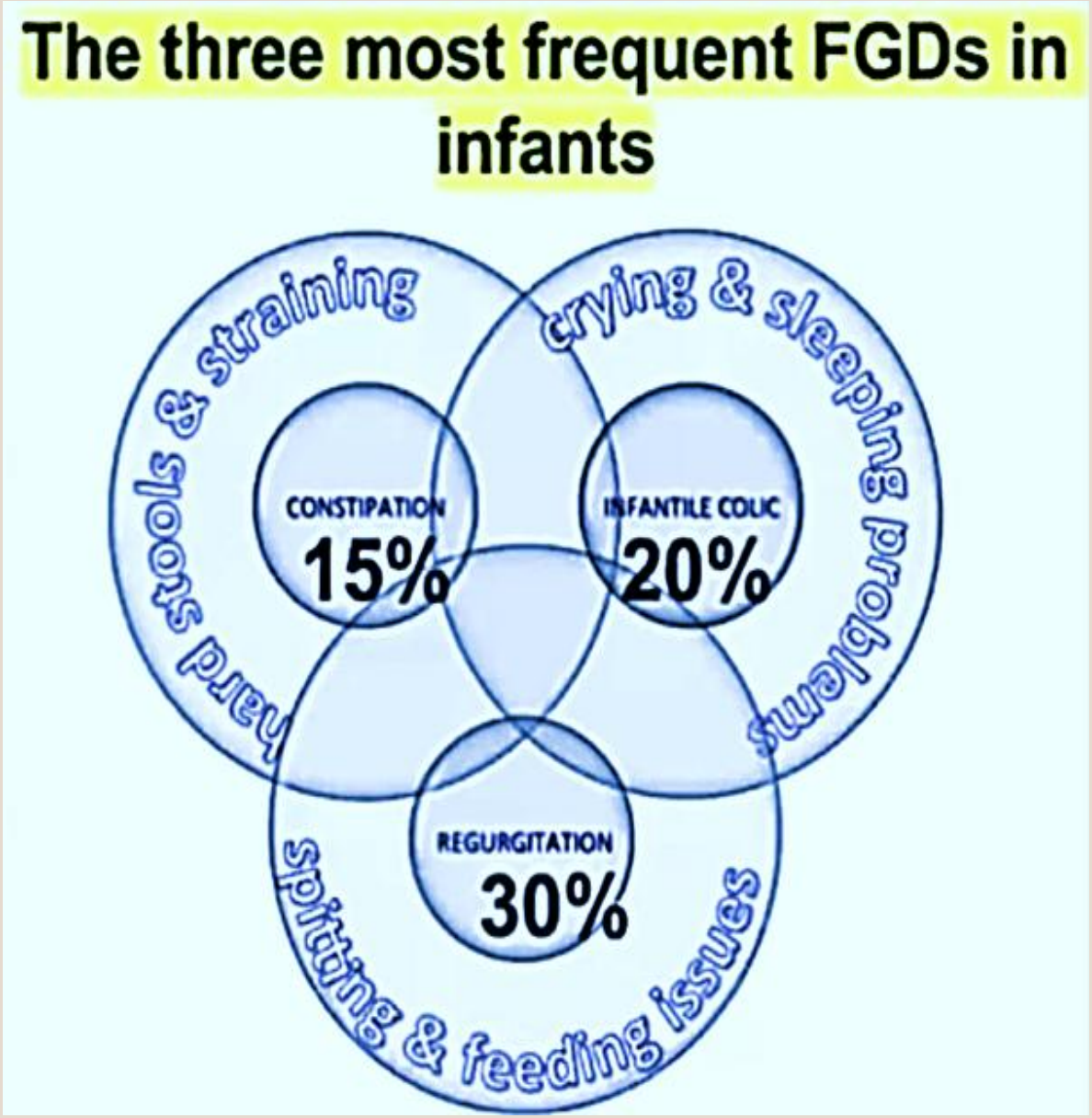
How can allergy be differentiated from gut-brain interaction disorders?

Disorders of gut-brain interaction (DGBIs)

- Previously known as functional GI disorders (FGID's)
- Group of conditions characterized by chronic GI symptoms in absence of structural/ inflammatory abnormalities
- Common in pediatric population
- Although usually considered "benign"
  - parents are worried
  - child may be in distress
  - can have major impact on QoL
  - practitioners often pressured to order tests to avoid missing serious diseases
- Gut-brain axis
  - mediates signaling between enteric nervous system of GIT and CNS
  - disruptions in this communication can lead to DGBI
- Gut immaturity, dysbiosis, genetic predisposition

- Diagnostic tests, such as endoscopy or imaging, often normal
  - no structural or inflammatory cause for symptoms
- One of main challenges for diagnosis is lack of biomarker
  - diagnosis based on specific symptom-based criteria
  - known as the Rome Criteria
    - been well defined and validated in paediatric population
- Making a symptom-based diagnosis can be challenging
- Infant may undergo many unnecessary procedures




The three most frequent FGDs in infants
hard stools & straining
crying & sleeping problems
spitting & feeding issues
CONSTIPATION
15%
INFANTILE COLIC
20%
REGURGITATION
30%

- **Infant regurgitation:**
  - Regurgitation 2 or > times/ day for 3 or > weeks
  - No retching, hematemesis, aspiration, apnoea, FTT, feeding or swallowing difficulties or abnormal posturing
  - In otherwise healthy infants 3 weeks – 12 months of age

- **Infant colic**
  - Recurrent prolonged periods of crying, fussing or irritability that cannot be resolved by caregivers
  - ≥ 3 hours per day, ≥ 3 days/ week
  - No obvious cause
  - No signs of FTT, fever or illness

- Constipation:

  - 1 month of at least 2 of the following:
    - 2 or fewer defecations per week
    - history of excessive stool retention
    - history of painful or hard bowel movements
    - history of large-diameter stools
    - presence of a large fecal mass in the rectum

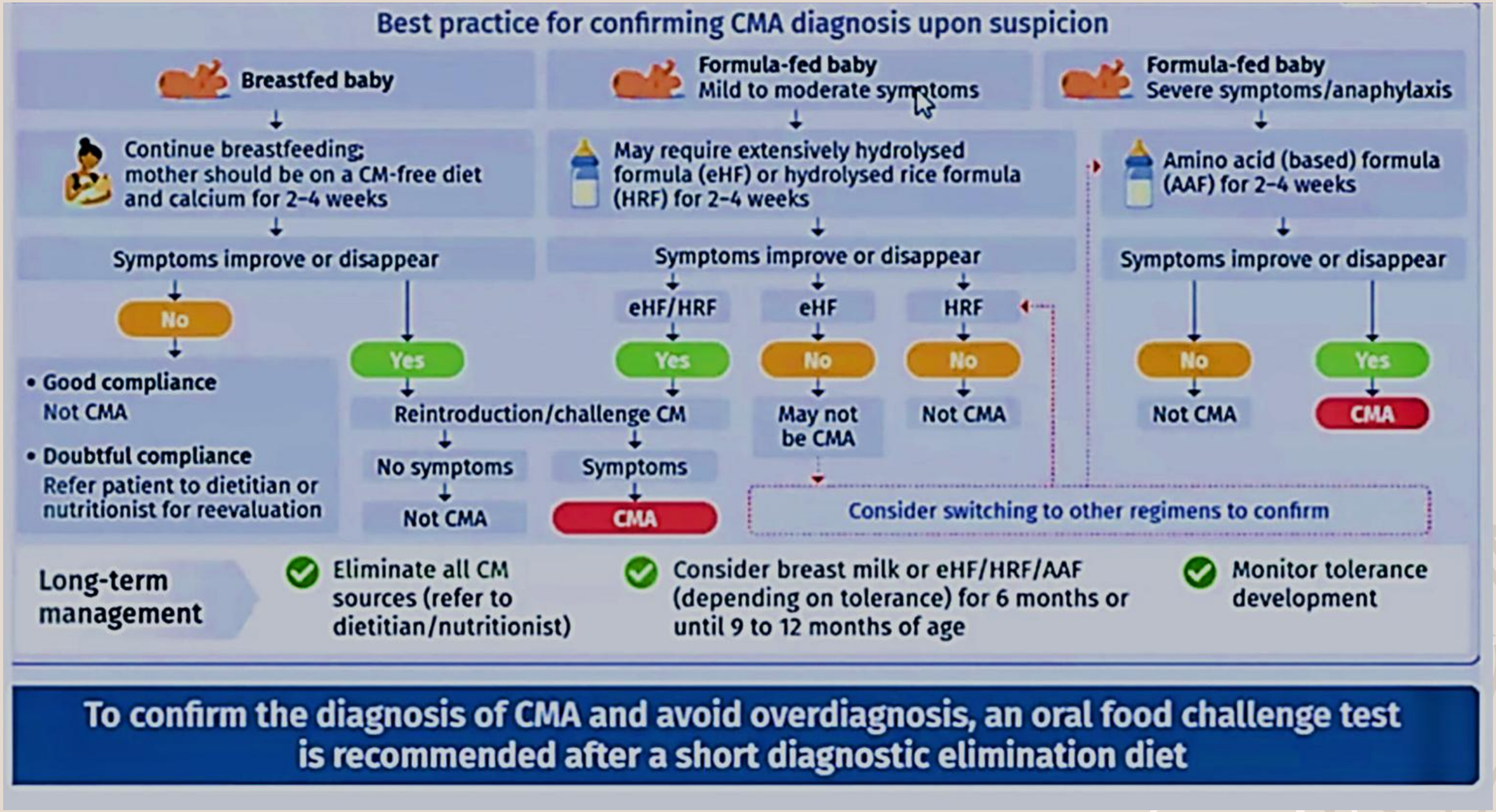
What are the best practices for accurate diagnosis and management to prevent unnecessary elimination diets?

Diagnosis in BF infants

- Diagnosis of food allergy and differentiation from DGBI difficult
- Testing challenging esp in neonates and young infants
- Requires clinical judgement
- All guidelines agree
  - In rare cases where food allergy is suspected in exclusively BF infant, cornerstone of diagnosis is maternal elimination for 2 – 4 weeks, with improvement or resolution of the infant's symptoms
  - This is followed by reintroduction of the suspected allergen, which confirms diagnosis if symptoms worsen

IgE- mediated allergies

- Skin Prick Tests
- Allergen specific IgE (RAST tests) to individual or group allergens
- IgE allergen components (RAST or ISAC or ALEX microarray chip)
- Basophil activation tests (CAST tests)



Management of Breastfed Infants

GA²LEN 2022	• Most breastfeeding mothers ***do not*** need to avoid the offending food if their infant has a food allergy. • *Rare* exceptions may require maternal dietary elimination.
WAO 2023	• **IgE-Mediated CMA.** Maternal CM avoidance is ***not*** recommended unless the infant has symptoms during exclusive breastfeeding. • **Non-IgE-Mediated CMA.** Maternal CM avoidance is advised only if history and examination strongly indicate CMA.
ESPGHAN 2024	• FPIAP in breastfed infants is usually benign and easily recognized. Treatment may ***not*** be necessary in mild cases.
EAACI 2024	• Mothers of breast-fed infants may need to exclude mammalian milks (or another culprit allergen) from their own diet (although this is **rarely needed**),

Reintroducing Food Allergens in Breastfed Children with Non–IgE-Mediated Food Allergies

Reintroduction of Cow's Milk	• Confirm resolution of non–IgE-mediated allergies (excluding FPIES) by reintroducing cow's milk **6 (12) months post-diagnosis** or allergens in the maternal diet over one week.
IgE Testing	• Exclude IgE-mediated allergy before home-based reintroduction for other non-IgE-mediated conditions.
Reintroduction of Other Allergens	• No consensus exists for reintroducing allergens

Key Take Away Points to Remember in Breastfed Infants with Food Allergy

For healthcare professionals only

- FA in exclusively breastfed infants rare
- BF should be encouraged and supported
- Maternal dietary elimination is rarely needed
  - Should be considered carefully
  - Balancing benefits for infant and potential impacts on mother
  - Avoid unnecessary elimination diets
- Differentiation from DGBI requires clinical judgement
  - No reliable tests
- No recommendation for or against using BF to prevent food allergy in infants and young children

THANK YOU

Questions??