

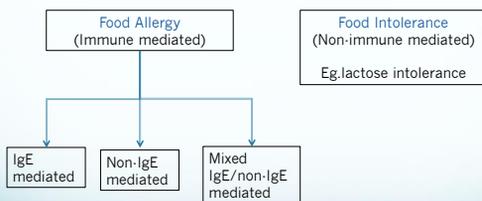
## Cow's Milk Allergy

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## Overview

- Classification of Allergy
  - IgE-mediated/Non IgE-mediated/Mixed
- Risk Factors
- Clinical Presentation
- Diagnosis
- Management
- When to refer

## Adverse Food Reactions



## Lactose Intolerance

- Lack of enzyme lactase, which helps to digest the milk sugar
- Symptoms: diarrhoea, vomiting, abdominal pain & flatus
- Does not cause rashes or anaphylaxis
- Small amounts of cow's milk usually tolerated
- Yoghurts & hard cheeses usually tolerated more than cow's milk (contain less/easier to digest lactose)
- Trial of lactose-free formula (& re-introduction)
  - Diagnosis can be confirmed by a breath hydrogen test
- Manage with a lactose-free formula/milk

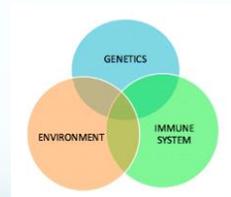
## IgE-mediated Allergy

- Symptoms usually within 1 hour of exposure
  - Urticaria
  - Angioedema
  - Vomiting/diarrhoea
  - Anaphylaxis – involves *respiratory or cardiovascular systems*
    - Difficult/noisy breathing
    - Tongue swelling
    - Swelling/tightness in throat
    - Difficulty talking and/or hoarse voice
    - Wheeze or persistent cough
    - Persistent dizziness or collapse
    - Pale and floppy (infant or young child)



## Risk Factors for IgE mediated allergy

- Strong familial association
- Environmental influences:
  - Allergen exposure
    - Skin barrier function
    - Infant feeding
  - Microbial exposure – 'Hygiene hypothesis'
  - Vitamin D hypothesis



## Microbiome

- Intestinal microbiota plays a crucial role in the development of the mucosal immune system
- Newborn's colonisation flora influenced by mode of delivery, breast or formula fed, maternal diet & use of probiotics
- Atopic children have altered intestinal microbiota
- Probiotic supplementation may promote early and more extensive colonisation with non-pathogenic bacteria. Clinical effects may be strain specific
- Currently insufficient evidence to recommend probiotic use by infants to prevent allergic disease
- Exclusion of any particular foods from maternal diet during pregnancy or breastfeeding is not recommended

## How can we reduce the risk of food allergy?

- Early introduction of allergenic foods
- Owning a dog & having siblings
- Maintain vitamin D in normal range (first year of life)
- Prevention of eczema through maintaining skin barrier function

Allen JACI In Practice 2016

## ASCIA Infant Feeding Guidelines

- Introduce solids around 6 months (but not before 4 months) when infant is ready
- Give allergenic solids including peanut butter, cooked egg, dairy & wheat products in the first year of life.
  - This includes infants at high risk of allergy
- Hydrolysed infant formula are not recommended for prevention of allergic disease
- Delayed introduction of solids may be associated with an increased risk of food allergy

## Diagnosis of IgE-mediated allergy

- SPT or serum specific IgE must be considered with the clinical history
  - Should not be ordered if the food is already tolerated
  - Allergy testing to 'food mixes' are not useful
- Size of sIgE or SPT wheal predicts the **likelihood** of an allergic reaction.
  - **It does not predict the severity of a reaction**
- Negative testing has a high predictive value
- Oral food challenge is the gold standard for diagnosis



## Management

- Strict avoidance
  - ? Cow's milk in baked goods
- ASCIA Action Plan
- Epipen training & prescription
- Education in recognition & management of reactions, carrying & storage of device
- Evaluation & treatment of concomitant allergic diseases
- Dietitian input if multiple dietary restrictions
  - Calcium supplementation

## Indications for Epipen

- Recommended if:
  - History of anaphylaxis
- May be recommended if:
  - Generalised allergic reaction PLUS risk factors
    - Geographically isolated
    - Age – adolescence or adult
    - Asthma
    - Nuts or stinging insects
- Available on PBS authority prescription: 2 epipens
- Also available without a prescription at full retail price

www.allergy.org.au

## Non-IgE mediated allergy

- Delayed eczema
- Delayed vomiting & diarrhoea
- Loose, frequent bowel actions or mucus in stools
- Irritability & unsettledness in infants
- FPIES
- Proctocolitis
- Food protein induced enteropathy

- Ingested food protein causes an immune response resulting in delayed inflammation, normally in skin or GI tract
- Symptoms usually occur 2-24 hours after ingestion
- Diagnostic tests usually negative

## Food protein-induced enteropathy

- Age < 3 years, usually in early infancy
- Symptoms:
  - Vomiting, diarrhoea
  - Poor growth, malabsorption & poor nutrition
  - Abdominal distension
  - Anaemia
- Onset: 1-3 days after exposure
- Cow's milk most frequent cause
- Endoscopy/biopsy: patchy villous atrophy with cellular infiltrates
- Management:
  - Avoidance of trigger
  - Improvement usually seen within 3-7 days of elimination, but up to 2-4 weeks
  - Most resolve by 1-2 years. Reassess and challenge around 12 months of age then 6-12 monthly after (usually home challenge)

## Food protein-induced enterocolitis syndrome (FPIES)

- Most commonly present at 4-6 months
- Most resolve by 3-4 years of age
- Clinical: Usually occurs within 2-4 hours after exposure with profuse vomiting, lethargy, pallor. Can also develop hypothermia & hypovolaemia (15%) with delayed diarrhoea
  - Post-reaction, up to 50-70% of children have an elevated neutrophil and/or platelet count.
- Major triggers: Cow's milk, soy, rice/oats.
  - Can be seen with other foods eg. Grains, poultry, vegetables
- 60% react to first exposure to food. If on subsequent exposure, often history of tolerating then break from trigger food
- Approx. 20-50% with CM FPIES may cross react to soy. Also cross-reactivity between rice & oats
- Management:
  - IV fluid resuscitation
  - Some evidence for use of ondansetron with reactions

## Food protein-induced proctocolitis

- < 3 months
- Usually present with bloody stools in an otherwise well child
- Milk and soy are common triggers. 50% breast fed
- Resolution occurs in 50% by age 6 months
  - 95% by age 9 months
- Reintroduce the offending food at 12 months of age.
- Symptoms usually resolve within days of elimination

## Diagnosis of Non-IgE CMPA

- Allergy testing not useful
- Elimination diet followed by re-challenge
  - Only means of confirming diagnosis of non-IgE mediated food allergy
- Endoscopy & biopsy
  - May confirm allergic inflammation/eosinophilic infiltrate
  - Not routinely done other than for diagnosis of EOE

## Mixed IgE & non-IgE mediated food allergy

- Symptoms caused by one or both mechanisms
- Include:
  - Eosinophilic oesophagitis
  - Eczema

## Eosinophilic oesophagitis

- Inflammation with eosinophils in the oesophagus
- 60% are atopic
- Delayed diagnosis is common
- Symptoms:
  - Food sticking
  - Choking on food
  - Regurgitation of foods
  - Prolonged time to eat/excessive chewing & drinking with food intake
- Diagnosis by endoscopy
- Some patients with EOE may have food component

## Breastfeeding & food allergy

- Anaphylaxis in exclusively breastfed infants from maternal allergen ingestion is very rare
  - Mothers should be encouraged to continue breastfeeding if their infant has anaphylaxis
- Complete maternal exclusion of food allergens is not usually required
  - Short-term maternal dietary exclusion is *sometimes* recommended on a trial basis in some allergic conditions
  - Ensure adequate nutrition of mothers during dietary exclusion
  - Assess effect of dietary exclusion. If no improvement, mother should return to normal diet
  - If resolution of symptoms in the infant occurs with maternal dietary exclusion, suspected food protein should be reintroduced into mother's diet to confirm the allergy

## CM Alternative Formulas

- 1<sup>st</sup> line: Soy Protein Formula
  - 50-80% can tolerate soy based formula
  - Only use in > 6 months
- 2<sup>nd</sup> line: Extensively hydrolysed formula
  - Allerpro/PeptiJNR/Alfare
  - Modified proteins to reduce allergenicity
  - Contains 85% amino acids & some cow's milk proteins
    - Tolerated by 90% of infants with CMPA
- 3<sup>rd</sup> line: Amino acid based formula
  - Contains 100% amino acids
  - Alfamino/Neocate/Elecare
- Go straight to 3<sup>rd</sup> line:
  - EOE
  - IgE mediated CMPA with anaphylaxis

## Introducing eHF or AAF

- Not very palatable
- Can be more difficult to introduce to older infants
- Monitor infant closely until taking adequate amounts
- Mix formula with EBM & increase concentration over few days
- Add 1% golden syrup or 2 drops vanilla essence (then gradually reduce)

## Alternative Formulas

- Similar proteins in other mammalian milks eg. Goat's milk.
- A2 milk is unsuitable for cow's milk allergic children.
- Partially hydrolysed formula (HA) also not suitable for CMPA
- Rice milk – suboptimal nutritional profile
  - Low in fat & protein.
  - New rice formula – limited evidence

**2 Formula feeding in syndromes associated with cows milk protein allergy\***

Syndrome	Onset of reaction	Maternal elimination of CMPA <sup>b</sup> breastfeeding?	Choice of formula			NHMRC level of evidence <sup>c</sup>	Consensus panel agreement <sup>d</sup>
			First <sup>e</sup>	Second (if first not tolerated)	Third (if second not tolerated)		
<b>Immediate reaction</b>							
Immediate food allergy	< 1 h	Yes	aHF (≤ 6 months) Soy (≥ 6 months)	AAF	—	II	11/11
Anaphylaxis	< 1 h	Yes	AAF followed by urgent consultation with paediatric allergist	—	—	IV	11/11
Food protein-induced enterocolitis syndrome	1–3 h	No	aHF	AAF	—	IV	10/11
<b>Delayed reaction</b>							
Atopic eczema	Hours to days	Yes <sup>f</sup>	aHF (≤ 6 months or > 6 months with FTT) Soy (≥ 6 months, no FTT)	AAF	—	IV	11/11
Gastrointestinal syndromes, GORD, allergic eosinophilic gastroenteritis, food protein-induced enteropathy, constipation, severe irritability (colic)	Hours to days	Yes <sup>f</sup>	aHF (≤ 6 months or > 6 months with FTT) Soy (≥ 6 months, no FTT)	AAF	—	I (bevere instability, II (GORD), IV (others))	11/11
Food protein-induced proctocolitis							11/11
Formulated	> 24 h	—	aHF	AAF	—	IV	
Breastfed	> 24 h	Yes <sup>f</sup>	—	—	—	—	
Eosinophilic oesophagitis in infants	Days to weeks	Yes	AAF	—	—	IV	11/11

CMPA = cow milk protein; NHMRC = National Health and Medical Research Council; aHF = extensively hydrolysed formula; AAF = amino acid formula; FTT = failure to thrive; GORD = gastro-oesophageal reflux disease; — = no further alternative choice.  
<sup>a</sup> Reactions to multiple or common foods is indicated, advice from a dietitian or implementation may be required.  
<sup>b</sup> Complementary to breastfeeding or exclusive formula feeding.  
<sup>c</sup> NHMRC levels of evidence for intervention studies: I = systematic review of level I studies, II = randomised controlled trial, III = non-randomised experimental trial, IV = case series with either poor test or pretest-test accuracy.  
<sup>d</sup> Number of panel members in agreement with decision. <sup>e</sup> May also need maternal elimination of other foods.

Kemp et al MJA 2008

## When to refer to an allergist

- IgE mediated allergy
- Severe eczema
- Non-IgE mediated allergy not responding to simple elimination
- FPIES
- Possible EOE
- Urgent:
  - Anaphylaxis
  - Failure to thrive
  - Severe vomiting or diarrhoea
  - Reactions to multiple staple foods