

Continuing Professional
Development

CPD

60 Second Summary

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IgE-mediated food allergy is immediate, can occur with tiny amounts of the allergen present, and causes a reaction within 2 hours of contact (but usually within minutes). Allergic reactions can be mild, moderate, or severe. A type of enterocolitis (Food Protein-Induced Enterocolitis Syndrome, FPIES, from non-IgE allergies) can result in hypovolaemia and require emergency management.

The most important diagnostic tool for food allergy is a detailed clinical history. If an allergy is suspected, the parent should be encouraged to provide a detailed account of what was observed.

NICE guidelines suggest that based on the results of the allergy-focused clinical history, if IgE-mediated allergy is suspected, an IgE test can be offered, but only when performed and interpreted by healthcare professionals with the appropriate training to do so.

Immune tolerance occurs when the immune system adapts and becomes unresponsive in the presence of allergens. In non-allergic people this happens naturally. However, in allergy, IgE antibodies are rapidly developed on exposure.

Cow's Milk Protein Allergy presents in infancy and is relatively common. The BSACI estimates a prevalence of between 2% and 4.9% during the first 12 months in the UK.

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1. REFLECT - Before reading this module, consider the following: Will this clinical area be relevant to my practice?

2. IDENTIFY - If the answer is no, I may still be interested in the area but the article may not contribute towards my continuing professional development (CPD). If the answer is yes, I should identify any knowledge gaps in the clinical area.

3. PLAN - If I have identified a

knowledge gap - will this article satisfy those needs - or will more reading be required?

4. EVALUATE - Did this article meet my learning needs - and how has my practise changed as a result? Have I identified further learning needs?

5. WHAT NEXT - At this time you may like to record your learning for future use or assessment. Follow the

4 previous steps, log and record your findings.

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Food Allergy in Infants

Introduction

Food allergies cause an adverse immune response to food allergens. This can be classified into IgE-mediated (immediate), non-IgE-mediated (delayed) and mixed IgE and non-IgE allergy.¹ Food allergies are distinct from the non-specific term "intolerance". Food intolerances are adverse reactions to food, with various non immune-mediated mechanisms that can be related to e.g. enzyme deficiencies, pharmacological agents and naturally occurring substances. Symptoms of food allergy present after ingestion of the allergen, and do not occur when it is not ingested. When the allergen is excluded, symptoms improve, but when reintroduced symptoms reoccur.²

The prevalence of food allergy in Europe and North America has increased over the past few decades. It is estimated that up to 6-8% of children 3 years and under are affected. IgE-mediated food allergy is common, occurring in 5-6% of young children in Ireland, and 1-2% of older children and adults in the UK. The well known and common trigger allergens are the cause of over 90% of cases.³ The correct diagnosis of food allergy, followed by appropriate advice, is important; because it reduces both the rate of adverse reactions caused and the unnecessary dietary exclusion of foods.

Food Allergy Symptoms: IgE vs Non-IgE

IgE-mediated food allergy is immediate, can occur with tiny amounts of the allergen present, and causes a reaction within 2 hours of contact (but usually within minutes). Peanut allergies are always IgE mediated, and often severe. Egg and cow's milk reactions can be either IgE or non-IgE mediated. Cow's milk is the most common non-IgE mediated reaction.

IgE mediated allergiesymptoms^{1,2:}

- Skin: urticaria, pruritus, erythema, angioedema (most commonly lips, face and eyes)
- Gastrointestinal: pain, vomiting, diarrhoea, nausea, angioedema of the tongue and palate
- Respiratory tract: blocked or runny nose, sneezing, cough, wheeze, shortness of breath
- Red or itchy eyes
- Cardiovascular: drowsiness, dizziness, pallor, collapse

Non IgE mediated allergy symptoms can occur more than two hours after ingestion, often at 24-48 hours. They are primarily gastrointestinal:

- Feeding difficulties
- Back arching
- Gastro-oesophageal reflux disease

- Abdominal pain
- Food refusal/aversion
- Vomiting
- Constipation or diarrhoea
- Blood or mucus in stools
- Failure to thrive or gain weight

Additional skin symptoms (pruritus, erythema, atopic eczema) may be present. Many of these symptoms are non-specific and could describe e.g. colic. However, the more gastrointestinal symptoms present and the more they worsen with ongoing allergen exposure, the more likely a non-IgE mediated allergy is.

We still do not know exactly what causes colic, although it occurs more frequently in premature babies and in homes where someone smokes cigarettes. Symptoms of colic include^{4,5:}

- Restlessness, difficulty settling the infant
- Drawing the legs up to the stomach
- Arching of the back
- Clenching fists
- Going red in the face
- Seeming to settle, but then having another spell of crying
- The baby's stomach rumbles or there is a lot of wind

Allergic reactions can be mild, moderate, or severe. A type of enterocolitis (Food Protein-Induced Enterocolitis Syndrome, FPIES, from non-IgE allergies) can result in hypovolaemia and require emergency management. Many non-IgE allergic reactions are thought to be T-cell-mediated although they are still poorly defined both clinically and scientifically. Some allergic reactions involve a mixture of both IgE and non-IgE responses and are classified as mixed IgE and non-IgE allergic reactions.^{1,2}

Diagnosis of Food Allergy

Food allergy is primarily made based on clinical history, in particular symptoms that

- Occur in response to ingesting a particular allergen(s)
- Occur with each ingestion of that allergen
- Occur in a particular time frame
- Do not occur in the absence of ingestion or other contact with the allergen

The most common allergens for infants less than 3 years old are eggs, cow’s milk, and peanut. In children 3 years of age and older the most common allergies are to peanut, tree nuts (all nuts

including almond and cashew; but not coconuts, pine nuts or nutmeg which are not nuts despite their name), kiwi, fish and pulses. Soya and wheat are rarely allergenic, but often show low positive blood tests on food allergy screens which are unhelpful. A facial skin irritation is often caused by citrus fruits, tomatoes and berries, especially those with eczema; however, this is not an allergic reaction.

When certain symptoms in children do not respond to usual treatment, e.g. atopic eczema, gastro-oesophageal reflux disease, or chronic gastrointestinal symptoms, including chronic constipation, the possibility of food allergy should be considered.^{1,2}

Allergy-focused Assessment

The most important diagnostic tool for food allergy is a detailed clinical history. If an allergy is suspected, the parent should be encouraged to provide a detailed account of what was observed, including:

- Symptoms and signs
- All food ingested during the 2 hours before the onset of the suspected reaction; or if non IgE mediated is suspected, in the prior 24-72 hours
- How long after food ingestion

the reaction occurred, the frequency and duration of reaction

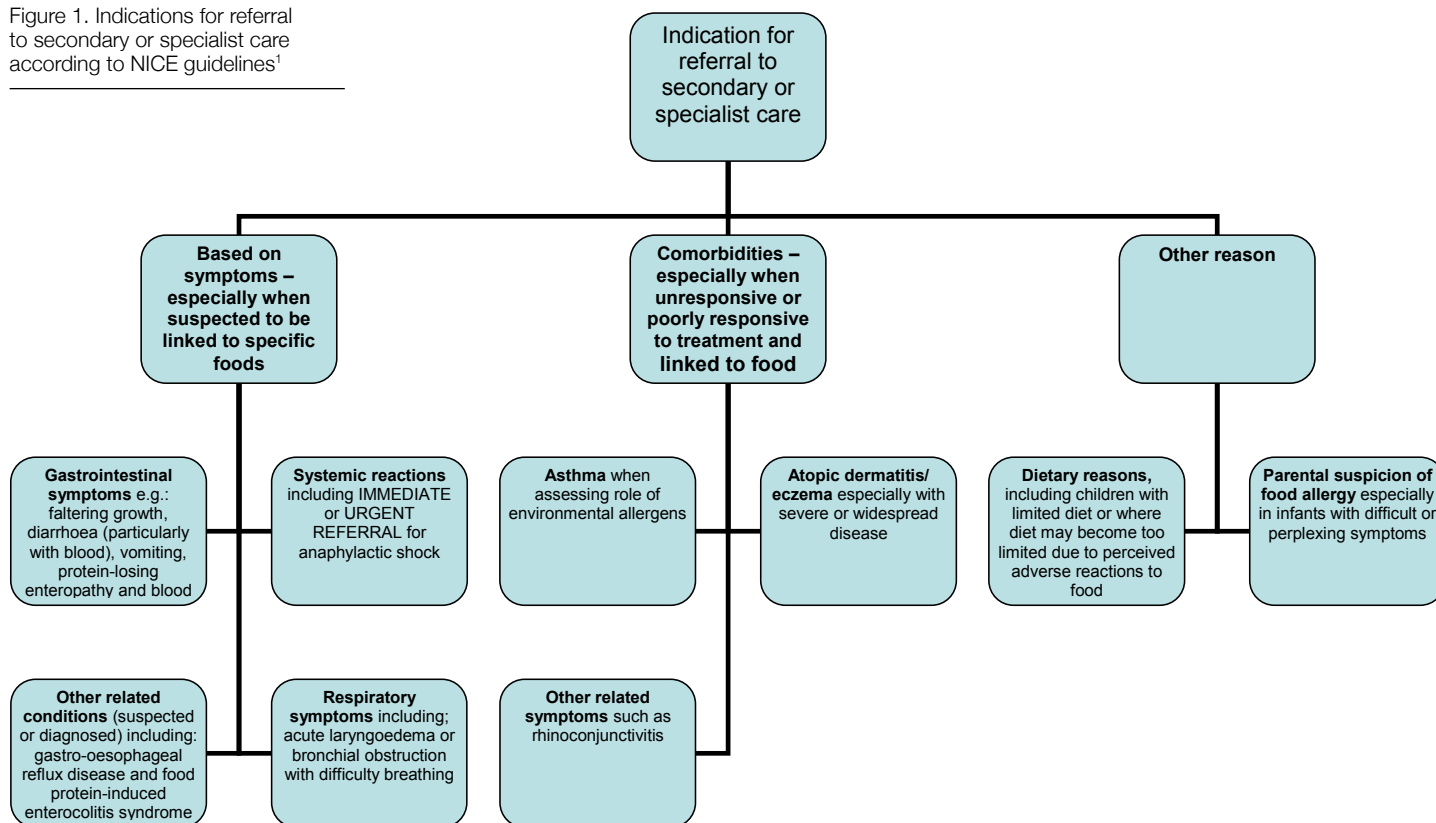
- Setting, e.g. location, possible nut exposure or animal contact
- Any additional factors e.g. exercise, illness, medication (which may exacerbate an allergy)
- Which primary allergens (milk, egg, peanut, tree nuts) have been ingested or eaten regularly by the infant
- Food aversions
- Other allergies or atopy, e.g. allergic rhinitis, asthma, eczema. Infants with severe or early onset (<3 months) eczema are at highest risk of food allergies. Poorly controlled asthma may worsen allergic reactions
- Family history of allergies and atopic conditions
- What the suspected allergen is
- Any cultural/religious factors affecting the foods eaten in the family

The use of Serology Specific IgE testing, which measures the level of IgE antibodies in response to individual allergens, is generally not required and is of limited value

in primary care. A positive result is an indication of sensitisation, rather than specifically an allergy. The term “sensitised to” means that the individual has a positive allergy test to the allergen (either a skin prick test or specific IgE), but may not have a true allergy, i.e. in the absence of a past history of allergic reactions. Guidance from the Irish College of General Practitioners advises that this test, along with skin prick testing, should be reserved for specialist centres and used in conjunction with clinical history. In suspected IgE mediated allergy, testing may help to confirm or exclude the diagnosis, but is often unnecessary. Laboratory testing has no role in confirming suspected non-IgE mediated allergy diagnosis.

NICE guidelines suggest that based on the results of the allergy-focused clinical history, if IgE-mediated allergy is suspected, an IgE test can be offered, but only when performed and interpreted by healthcare professionals with the appropriate training to do so. These results should be interpreted in the context of information from the allergy-focused clinical history. Alternative diagnostic tests such as kinesiology and hair analysis are not recommended.

Figure 1. Indications for referral to secondary or specialist care according to NICE guidelines¹



If a food elimination diet is advised as part of diagnosis, the following information should be provided:

- What foods/drinks to avoid
- How to interpret food labels
- Alternative sources of nutrition to ensure adequate intake
- Safety and limitations of an elimination diet
- Proposed duration of elimination diet
- where/when/how a food challenge or reintroduction may be done
- The safety and limitations of a food challenge

If an elimination diet does not help with the allergy symptoms, the infant should be referred to specialist care.^{1,2}

Good communication between healthcare professionals and young children with a suspected food allergy and their family is important. Advice provided should be supported by evidence-based written information and specifically tailored to the needs of the child and family.

Allergen Tolerance and Avoidance

Immune tolerance occurs when the immune system adapts and becomes unresponsive in the presence of allergens.² In non-allergic people this happens naturally. However, in allergy, IgE antibodies are rapidly developed on exposure. Tolerance can develop in children with IgE-mediated food allergy, and in the case of cow's milk protein allergy (CMPA) and egg allergy, it develops in over 85% of children. The development of tolerance to other food allergens e.g. peanut, tree nut, seed, fish, and shellfish is not common (10-20%). These allergies persist, and avoiding the allergens is necessary, along with carrying adrenaline autoinjectors (AAIs) in case of emergency. The mechanism of tolerance development in non-IgE mediated food allergy, e.g. CMPA, is poorly understood.

Allergy Prevention

The earlier the introduction of food allergens into the diet (once the infant is on solids) the better, because of the natural tendency of the infant immune system to develop tolerance through regular

oral exposure. All infants are at risk of developing allergy, even in the absence of other risk factors. Allergens to introduce include egg, peanut, tree nut, dairy, fish and seafood. These should be introduced one at a time so the source of any potential reaction is clear. The longer the delay in introducing egg and peanut in particular, the higher the chance of allergy. There is strong evidence that introducing egg and peanut early in a child's diet can prevent allergy to these developing. Infants with moderate or severe eczema and those with IgE mediated CMPA are at high risk of developing IgE food allergy, and early introduction of these two foods may be particularly beneficial for these groups. The presence of egg allergy indicates an increased risk of peanut allergy, and having both severe eczema and IgE food allergies means there is a very high risk.

The presence of one IgE-mediated allergy is a flag for a significantly higher risk of other IgE-mediated allergies. It is possible that peanut allergy will have developed in this high-risk group (presence of one IgE-mediated allergy) even by the time solids are introduced; however, infants are more likely to benefit from allergy prevention via early introduction, with special emphasis on peanut and egg. Guidance from the British Society for Allergy and Clinical Immunology (BSACI) recommends introduction of peanuts from at least 4 months of age to avoid missing the window of prevention (HSE guidance recommends the introduction of solids from 4-6 months of age). Delaying the introduction of egg and peanut much later than 6 months is strongly discouraged. If the allergens introduced are well tolerated, they should then be given regularly in their diet to prevent allergy occurrence.

Although an infant may have developed an allergy by the time the allergen food is offered, no life-threatening reactions have been reported to allergens introduced early, in line with this guidance. A severe reaction is theoretically possible; however, the risk of waiting is potentially greater. Anaphylaxis type reactions typically happen when peanuts are introduced later.

Introducing Potential Allergens

Egg: only cooked egg should be introduced to infants, giving the

baby at first a small amount to taste. In infants with eczema, their eczema should be adequately controlled with emollients and steroids to reduce the risk that eczema symptoms are misinterpreted as an allergic reaction to egg. If there is a mild-moderate reaction to egg, the Irish Food Allergy Network egg ladder⁶ should be used to test for and promote tolerance under the supervision of a dietitian, nurse or doctor.

Peanut: whole/coarse nut peanuts are a choking hazard and should never be given to young children or infants. Smooth natural peanut butter can be used, in small amounts, e.g. thinned with milk/water, added to fruit/cereal/yogurt. As advised above, infants with eczema should ideally have their symptoms under control.

About 20% of infants under 2 years of age with moderate to severe eczema have some kind of food allergy. Although eczema is not specifically caused by food allergy, there is a strong association. The cause of eczema is a skin barrier defect that leads to water loss, altered pH and reduced antimicrobial defence. The majority of urticaria in children is either idiopathic or viral: in these cases, the clinical history should help rule out any association of the rash with food intake.

Cow's Milk Protein Allergy

CMPA presents in infancy and is relatively common. The BSACI estimates a prevalence of between 2% and 4.9% during the first 12 months in the UK (5). A small number of breastfeeding infants (0.5%) react to cow's milk protein found in breastmilk. There are IgE and non IgE mediated forms of CMPA. IgE-mediated requires specialist help for ongoing management, whereas non IgE-mediated CMPA is generally managed in the community. Children allergic to cow's milk protein will also be allergic to the milk from most other 4 legged animals e.g. goat sheep, buffalo. Most children outgrow this allergy by adulthood, but in cases where the allergy is IgE-mediated, there is a higher sensitivity, or there are multiple food allergies/asthma or allergic rhinitis, it is more likely to persist. Cow's milk allergy in adults is frequently severe, although rare with an estimated prevalence of 0.4% to 0.6%. It usually arises in adulthood, but can persist from childhood.

Symptoms of IgE-mediated CMPA typically involve urticaria/erythema round the face and neck, with severe symptoms like anaphylaxis possible. Currently this type of CMPA requires specialist management, with reintroduction of milk in the community setting not recommended. There is no need for breastfeeding mothers of these infants to remove dairy from their diet.

Symptoms of non-IgE mediated CMPA occur more than two hours after ingestion, often at 24-48 hours, but up to 72 hours. Symptoms include:

- Vomiting with back arching and screaming
- Feed refusal
- Dysphagia and food impaction
- Diarrhoea
- Constipation or straining with defecation, but producing soft stools
- Blood and or mucus in stools
- Failure to thrive or poor weight gain
- Pallor and tiredness
- Colic
- Non-specific skin symptoms such as erythema and eczema flares (although milk should not be removed from the diet on the basis of skin symptoms alone)
- FPIES

Non-IgE mediated CMPA usually presents within the first few weeks in formula fed infants, and also soon after birth in exclusively breastfed infants whose mothers ingest dairy products. No tests should be done if this type of CMPA is suspected because there are no definitive in vitro tests for these types of allergies. Diagnosis is based on exclusion of dairy from the diet and the type of symptoms observed upon reintroduction. In non-IgE mediated food allergy, a small dose of the allergen may be tolerated, but incremental doses are not.

Management of Non-IgE Mediated CMPA

A period of complete milk exclusion for usually about 4 to 6 weeks, followed by reintroduction, is recommended. In formula fed infants, regular cow's milk formula should be replaced with extensively hydrolysed formula (EHF; not partially hydrolysed



formula which is unsuitable), which contains cow's milk protein that has been broken down into short segments. More severe cases, i.e. those with symptoms such as anaphylaxis, faltering growth, multisystem involvement, multiple food allergies and eosinophilic oesophagitis, may require an amino acid formula.^{1,2,7} Soya formula may not be well tolerated in infants with mostly abdominal symptoms, so is not recommended in non-IgE mediated CMPA (although this can be used in IgE-mediated CMPA). Approximately 10-14% of infants and children with IgE-mediated cow's milk allergy are also allergic to soya, however, up to 60% of those with gastrointestinal symptoms can develop non-IgE mediated soya allergy. Soya formula should not be used under the age of 6 months also due to high concentrations of phytoestrogens.⁷

In breastfed infants, a trial period of complete dairy exclusion from the mother's diet for 4-6 weeks is required. Ideally, a dietitian should have input into the milk exclusion period to ensure that infants and breastfeeding mothers are receiving enough vitamin D and calcium.

Every 6-12 months from the age of 10-12 months, infants and children should be reassessed for suitability of reintroduction of cow's milk. The IFAN Cow's Milk Ladder⁸ can be used to assist with reintroduction. For non-IgE mediated milk allergies, this is usually carried out at home under medical advice. Reintroduction should be trialled in hospital if⁹:

- Previous reactions have affected breathing or circulation
- There is coexisting asthma that requires a preventative inhaler
- There are multiple food allergies or reactions attributed to trace amounts of allergen

Usually infants are better able to tolerate baked forms of milk which are less allergenic than whole milk, which is the most allergenic form. The IFAN Cow's Milk Ladder starts with small amounts of baked milk. Upon reintroduction, if vomiting, loose stools or distress is evident in the infant, it is advised to wait at least 2-3 months before attempting again. If some forms of cow's milk are being tolerated, these can be continued. If severe enterocolitis or FPIES occurs in non IgE mediated

CMPA, specialist input is required for milk reintroduction.

Egg Allergy

This is present in about 3% of Irish children (9). Well-cooked egg (e.g. sponge, muffin, cake pancake) is less allergenic than raw or lightly cooked, and the reaction is usually dose dependent. The majority of children outgrow this allergy and usually do not require adrenaline autoinjectors for anaphylaxis. In these mild to moderate reactions, usually the IFAN Egg Ladder can be used to reintroduce egg in the primary care setting, but referral to a specialist is also recommended because egg allergy is also a marker for other food allergies. Uncooked egg is hidden in many foods, and may be present on e.g. egg cartons used in arts and crafts. The MMR vaccine does not contain egg, so there is no need to avoid this.¹⁰

Anaphylaxis

This is a severe and rapidly progressing allergic reaction affecting multiple systems in the body. Symptoms are

- Airway involvement (tongue swelling, wheeze, shortness of breath, cough, hoarseness)

- Circulatory (pallor, clamminess, feeling faint, hypotension, tachycardia, bradycardia)
- Loss of consciousness
- Cutaneous (widespread flushing, urticaria, angioedema of the face and lips)

When this occurs, the allergen should be removed if still present, adrenaline should be administered (the recommended site of administration is the outer thigh) and an ambulance should be called.

Adrenaline autoinjectors (AAIs) should be prescribed for any child with a prior severe immediate allergic reaction or anaphylaxis to any food allergen, and those with food allergy and moderate to severe asthma (high risk of anaphylaxis). Ideally a child should carry 2 devices at all times, as a second adrenaline injection may sometimes be required, or the first may fail. Although additional factors such as the distance from the nearest medical facilities may influence prescribing decisions, AAIs should not be prescribed for "just in case" situations because there is the risk of causing unnecessary anxiety and monetary cost to the family. All infants and children who have food allergies should have a non-sedating antihistamine available in liquid form at all times (when age appropriate).

For children 15-30kg, the AAI dose is 150mcg of adrenaline. For those >30kg it is 300mcg, and for >50kg it is 500mcg. Infants under 15kg should only be prescribed AAIs with specialist advice. When AAIs are prescribed and dispensed, clear instructions of how and when to use them should be provided. Following diagnosis of a serious food allergy, if there is a risk of anaphylaxis, those at risk should be encouraged to wear or carry some form of medic alert identification.¹¹

IFAN provide a printable sample emergency plan¹² for managing allergic reactions which can be adapted to suit the individual child's needs depending on the setting, e.g. home, at school. It includes a description of the symptoms of mild reactions and treatment (e.g. antihistamine), a description of a severe life threatening reaction (Airway obstructed, Breathing difficulty, Circulation impaired, Disability, Exposure) and the suggested response.

References available on request