Quality and Safety in Practice Committee

Food Allergy in Children Quick Reference Guide

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QUALITY AND SAFETY IN PRACTICE COMMITTEE

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Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

In this document you will see that evidence and recommendations are graded according to levels of evidence (Level 1 – 5) and grades of recommendations (Grades A-C) respectively. This grading system is an adaptation of the revised Oxford Centre 2011 Levels of Evidence.

Levels of Evidence

Level 1: Evidence obtained from systematic review of randomised trials
Level 2: Evidence obtained from at least one randomised trial
Level 3: Evidence obtained from at least one non-randomised controlled cohort/follow-up study
Level 4: Evidence obtained from at least one case-series, case-control or historically controlled study
Level 5: Evidence obtained from mechanism-based reasoning

*Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small;

Level may be graded up if there is a large or very large effect size. Where possible, systematic review evidence is presented.

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Summary

Food allergy is an adverse reaction to food that is immune-mediated. It occurs in up to 6% of children in Ireland. Intolerance is a non-specific term and does not refer to an immune mediated process e.g. lactose intolerance is not a food allergy and is not related to cow's milk protein allergy. This document deals only with food allergy.

Types of Food Allergy

Table 1: Types of Food Allergy

	IgE Mediated (Immediate)	Non IgE Mediated (Delayed)
Symptoms	Urticaria, sudden reddening, angioedema, acute rhinitis, abdominal pain and vomiting (but with cutaneous symptoms) and in severe cases respiratory or circulatory compromise	Predominantly gastrointestinal and can be significant
Risk	Can be life threatening	Not life threatening

Diagnosis of Food Allergy

Clinical History elicits an association between the intake of the suspected allergenic food and the reaction in question if allergy is the cause

- Symptoms do not occur in the absence of ingestion or other contact with the allergen
- Symptoms improve on exclusion of the allergen and return on its reintroduction

Immune Tolerance

- Is a process where the immune system adapts to develop an unresponsive state when exposed to allergens
- Happens naturally in non-allergic individuals
- Can develop in children with IgE mediated food allergy

Tolerance to milk and egg develops in over 85% of children:

- Age of achieving tolerance is variable
- Regular exposure to baked milk and egg where appropriate can help achieve tolerance.

Developing tolerance to other foods e.g. peanut, tree nut, and seed, fish and shellfish allergy is uncommon (only 10-20%).

Persistence

Means that once the allergy is established, it persists for life. These patients carry a lifetime risk.

Strict allergen avoidance and emergency preparedness, including carrying adrenaline autoinjectors, is usually indicated. See Peanut Allergy and Adrenaline Autoinjectors.

Sensitisation

The term "allergic to" means that the individual has had an allergic reaction to that allergen.

The term "sensitised to" means that the individual has a positive allergy test (Skin Prick Test or Specific IgE) to the allergen but may or may not have an allergy to it (only about 50% correlation with allergy in the absence of a supporting clinical history).

Allergy Testing

Is mostly relevant to specialist allergy centres, where both Specific IgE serology and Skin Prick Testing are performed. Occasionally in primary care, Specific IgE testing can be helpful, but in limited circumstances and only ever for IgE mediated allergy. This test is specific but not sensitive, with a high rate of false positives.

Other tests that may be offered in some centres or online such as specific IgG testing, applied kinesiology or hair testing have no role in diagnosis of food allergy and should not be performed.

Eczema

- Is NOT caused by food allergy (it is a skin barrier defect).
- Is a significant risk factor for the development of IgE mediated food allergy and important when identifying high risk groups in relation to allergy prevention.
- In primary care, foods should not be removed from the diet with the aim of improving eczema.
- The focus in managing eczema is skin care with adequate topical steroids, liberal emollient use etc.
- Eczema that does not respond to usual treatment, or that is associated with multiple food allergies, requires specialist input (dermatologist/ allergist). See Eczema and Food Allergy.

Adrenaline autoinjectors (AAI)

- GPs, if comfortable, can initiate AAIs in primary care while awaiting specialist input or after discussion with specialist.
- The indication for the AAI must be clear- either a history of anaphylaxis or the patient is considered at risk of anaphylaxis.
- AAIs should not be prescribed "just in case".
- The affected child must have 2 in-date devices with them at all times
- Safety plan
- Adrenaline autoinjectors and trainer devices

Cow's Milk Protein Allergy (CMPA)

- Presents in infancy
- Can present as both IgE and Non IgE forms

IgE mediated CMPA

- Is associated with other immediate food allergies
- Early prevention strategies required (see Allergy Prevention)
- Refer to a specialist for ongoing management

Non IgE mediated CMPA

- Can generally be managed in the community
- Refer in non-responding cases, or where the infant fails to thrive

Children with Food Allergy in Society

It is important that society recognises the right of children with food allergy to be included in school, extracurricular and social activities. As primary care physicians, our role may include advocating for these entitlements of our individual patients.

Quality of Life

Food allergy has a negative impact on quality of life. Refuting or confirming all food allergy diagnoses is imperative. Our focus must be on reintroducing foods where safe and appropriate and avoiding unnecessary or blanket exclusions.

Allergy Prevention

Evidence strongly demonstrates that early introduction of egg and peanut in a child's diet can prevent allergy to these two foods developing in high risk groups. GPs and other healthcare professionals should now provide advice about early allergen introduction for the purpose of allergy prevention.

Children who benefit most from early introduction include:

- Infants with moderate to severe eczema (are at high risk of developing IgE food allergy)
- The presence of one IgE mediated allergy (acts as a flag for significantly increased risk of other immediate-type food allergies)
- IgE mediated CMPA allergy flags an increased risk of egg and peanut allergy (cow's milk is often the first common allergen ingested)
- Egg allergy flags an increased risk of peanut allergy. The presence of both severe eczema AND one or more IgE food allergies in an infant makes them very high risk

Introduction

Background

Food allergy in children is common occurring in 4-6% of children in Ireland [1]. Infants and children with food allergy often present in primary care. Food allergy has a significant negative impact on quality of life for patients and their families.

Allergy is a medical discipline in which recommended practice has changed greatly in the past decade based on emergence of new robust evidence. Updated guidance is needed specifically for general practitioners. This guidance document intends to provide GPs with guidance on managing food allergy in children in primary care.

Aims of the Document

This guidance should enable GPs to:

- Advise parents regarding early allergen introduction in the weaning diet.
- Evaluate children presenting with possible food allergy.
- Make a diagnosis of food allergy or rule it out.
- Determine which patients require specialist referral to a paediatrician or allergist.
- Provide advice and manage those patients while waiting for specialist input.
- Effectively manage cases which do not require a specialist.

Throughout this guidance, where "specialist" is referred to, this can indicate an allergist in tertiary care or a paediatrician with an interest in allergy, depending on local referral pathways.

Section 1: Food Allergy Overview

1.1 What is Food Allergy?

Food allergy is a type of adverse reaction to food that is immune-mediated. Food allergy can be immediate (IgE mediated allergy) or delayed (Non IgE mediated allergy)[2]. In contrast, food intolerances are adverse reactions to food with varying mechanisms, which are not immune-mediated. Allergy and intolerance should not be confused. This guidance document deals only with food allergy in infants and children.

1.2 Diagnosis of Food Allergy

Diagnosis of food allergy is primarily made on the basis of a good clinical history. History taking should pay particular attention to symptoms which: [3]

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

A list of the most common food allergies in Ireland is given in Table 1.

For suspected IgE mediated allergy, testing can sometimes help to confirm the diagnosis or, with even higher accuracy, rule it out (see *Investigations in Allergy* below). However, testing is often not necessary, as the diagnosis may be made clinically, and tests can be difficult to interpret or misleading [4] [5].

For suspected Non IgE mediated allergy, laboratory or other testing should NEVER be done, as there is no reliable test for this type of allergy. Diagnosis can usually be made by improvement of symptoms on the exclusion of the allergen, and return of symptoms on its reintroduction, which is a key part of the diagnostic process in the absence of relevant testing.

Table 2: Most common food allergies in Ireland

<3 years of age [1]	**>3 years of age**
• Eggs • Cow's Milk • Peanuts	• Peanuts • Tree nuts* • Kiwi • Fish • Pulses
Soya and wheat are rarely allergenic and often show low positive blood tests on food allergy screens, which are **nearly** always unhelpful and should not be performed. The laboratory in Our Lady's Children's Hospital, Crumlin, Dublin has discontinued these screens. Tomatoes, citrus fruits and berry fruits often cause a facial skin irritation when eaten by infants, especially those with eczema. This is not an allergic reaction, and these are not common allergenic foods. *Tree nuts refer to all nuts including almond and cashew (not botanically nuts) except peanuts (which are legumes). Nutmeg, coconuts and pine nuts (really a seed) are **not** nuts despite their names. Allergy to these foods exist but are extremely rare; therefore, there is no requirement for children with peanut and/or tree nut allergies to avoid them.	

1.3 Allergy-focused Assessment

A carefully taken clinical history is **the** most important diagnostic tool in food allergy (Level 5).

Food allergy cannot be diagnosed without a history of exposure and reaction. Below are the key aspects of a history where food allergy is suspected:

1. Encourage the parent to provide a detailed account of what they observed (ask if they took photos)

   Essential details include:

   - Symptoms and signs observed.
   - All foods ingested in the 2 hours prior to the perceived reaction (if Non IgE mediated allergy is suspected, ask about foods in the previous 24-72 hours).
   - How soon after eating the suspected allergen did the reaction occur?
   - Details regarding the environment: party; restaurant; garden; possible nut exposure; animal contact; cooking activities.
   - Other factors: exercise, concurrent illness, medication (these may exacerbate an allergic reaction).

2. Take a full feeding history – breast/formula/solids. Establish which of the primary food allergens (milk, egg, peanut, and tree nuts) have ever been ingested or are being eaten regularly by the infant or child. Note if there is refusal of, or aversion to, any particular foods.

3. Ask about other allergies and atopy: allergic rhinitis, asthma, eczema. If eczema: ask about severity and age of onset (onset <3 months of age is significant). Infants with severe or early onset eczema are at the highest risk for food allergies. Assess current control of these conditions if present (poorly controlled asthma may also exacerbate an allergic reaction)[6 7].

4. Ask about family history of allergies and atopic conditions.

Differentials to Consider during History Taking

While taking a history of symptoms, there are many differentials for allergy to consider, especially when Non IgE mediated allergy is suspected because the timing of onset is less clear. In any infant with irritability, vomiting, etc., particularly if they appear unwell, consider sepsis and other medical causes. With any other GI symptoms such as blood in the stools, consider other intestinal or surgical conditions.

Idiopathic urticaria and viral-induced urticaria cause the majority of episodes of urticaria in children [8]. An allergy-focused history should easily identify the absence of association with food intake in these cases. Urticaria present for the first time early in the morning is very unlikely to be due to food eaten the previous day.

Distinguishing between IgE Mediated and Non-IgE Mediated Allergy

IgE Mediated Allergy

- Immediate type allergy
- Can occur in response to very small amounts of allergen
- Reaction by definition must be within 2 hours of ingestion or contact[9] but is usually within minutes

Allergens in IgE Mediated Allergy

The most common allergen in IgE mediated reactions in children is egg [1] (reaction is often mild, usually IgE mediated), followed by peanut (reaction is often severe, always IgE mediated) and cow's milk (reaction can be mild or severe and IgE or Non IgE mediated) [10] [11].

Symptoms in IgE Mediated Allergy[12]

1. **Skin**: urticaria, pruritus, erythema and angioedema
2. **Gastrointestinal**: abdominal pain, vomiting (repeated or profuse), diarrhoea
3. **Respiratory tract and eyes**: red or itchy eyes, blocked or runny nose, sneezing, cough, wheeze, shortness of breath.
4. **Cardiovascular system**: drowsiness, dizziness, pallor, collapse.

Severity of Reaction in IgE Mediated Allergy [12]

Ranges widely in severity from mild reactions with skin symptoms only to anaphylaxis.

- Skin reactions and facial or lip angioedema are considered mild-moderate symptoms
- Any involvement of the airway (tongue swelling, wheeze, shortness of breath or even sudden onset cough or hoarseness)

  OR
- Any circulatory compromise, vomiting; lethargy or feeling faint are all considered severe symptoms which equate to anaphylaxis (see management of anaphylaxis).

Non-IgE Mediated Allergy [13]

- Delayed type allergy
- Reaction can be dose dependent so small amounts can be tolerated, with incremental increases eliciting a reaction
- Reaction is delayed for hours or even days after ingestion (24-72 hours)

Allergens in Non-IgE Mediated Allergy

The most common allergen in Non IgE mediated allergy is cow's milk (cow's milk allergy can also be IgE mediated).

See section on *cow's milk protein allergy* [14].

Symptoms in Non-IgE Mediated Allergy

Primarily gastrointestinal and include the following:

- Feeding difficulties or refusal of food
- Back arching
- Vomiting
- Constipation or loose stools
- Blood or mucus in the stools
- Failure to thrive or poor weight gain

Clearly many of these symptoms in isolation are common in infancy and alone do not indicate allergy. However, the greater the number of gastrointestinal symptoms and the more they progress with ongoing exposure to the allergen (typically cow's milk) the more likely it is a Non-IgE mediated allergy. See section cow's milk protein allergy.

Severity of Reactions in Non-IgE Mediated Allergy

Reactions range in severity from mild, such as constipation or mild upper GI upset, to severe reactions such as the under-recognised Food Protein-Induced Enterocolitis Syndrome (FPIES). FPIES is a form of enterocolitis which, although different from anaphylaxis, can still result in shock due to profound hypovolaemia. FPIES requires emergency management and cannot be diagnosed or managed in primary care.

1.4 Examination

Measure and plot centiles for height and weight. Perform a general exam focusing on general appearance, any pallor, signs of eczema, allergic rhinitis and asthma.

1.5 Investigations

Specific IgE Testing [4 5]

Specific IgE testing of blood (serology) has replaced "RAST testing", a now obsolete term. Specific IgE testing can be ordered and interpreted in primary care, depending on local laboratory facilities.

When to Use

Serology for Specific IgE testing is generally not necessary and is of limited value for allergy assessment in primary care because a diagnosis is primarily clinical. However, if choosing specific IgE testing, do so judiciously selecting one suspected allergen implicated in presentation or at most 3 [5](level 4) . Suspected common co-allergens to the one in question may also be tested (e.g. egg in cow's milk allergic children if immediate type reaction; peanut in egg allergic children) but only those NOT already being tolerated in the diet. Broad panels should NEVER be requested.

Specific IgE levels are not affected by antihistamine use whereas skin prick testing affects Specific IgE levels.

When Not to Use

Do NOT use specific IgE in the following situations:

- To assess any allergen that the child is already ingesting regularly and uneventfully in their diet; by definition they are tolerating that allergen.
- To assess any allergen suspected of causing Non IgE mediated allergy in infants (this is the incorrect mechanism).
- To assess toddlers or children experiencing abdominal symptoms: pain, bloating, constipation, diarrhoea, mucus noses and chests or frequent otitis media.
- To assess idiopathic urticaria, coeliac disease or other non-immune mediated food intolerances.
- To test siblings of children with food allergy who are apparently well and have not had symptoms of allergy.

Interpreting Specific IgE Test Results

Specific IgE has a high negative predictive value (>95%) therefore a negative result can usually rule out an allergy. However, this only provides short term reassurance because allergies can subsequently develop especially in cases where that allergen is avoided.

Specific IgE is less sensitive with a relatively low positive predictive value (only 50% in the absence of a supportive clinical history) and therefore should be performed only when an association with an allergen has already been made on history taking.

Clearly, false positives are common. One factor is the presence of eczema, which can cause raised total IgE (not generally measured in primary care) of >10,000 KU/L and low level positive specific IgE to food allergens, levels typically 1 – 3 KU/L.

Specific IgE levels that are likely to reflect genuine allergy, regardless of eczema or consumption of the allergen to date, are as follows:

- Cow's milk > 6 KU/L
- Egg > 6 KU/L
- Peanut or tree nuts >15 KU/L

It is important to remember that specific IgE levels do not predict a child's ability to tolerate baked cow's milk or egg; these levels reflect likely allergenic reaction to whole cow's milk and almost raw egg. However, children with positive histories and specific IgE levels lower than those listed above are still likely to have an allergy to the tested food allergen [5] (Level 4). This is uncovered in the history which takes precedence over the test. The strength of a positive test for specific IgE is not an indicator of severity in future reactions. History and previous reaction, although unreliable, tend to be better indicators.

Allergy vs Sensitisation

Specific IgE testing is often incorrectly referred to as "allergy testing". However, a positive specific IgE is merely an indication of sensitisation. Many people are sensitised to foods which they tolerate and are therefore not allergic to those foods. Allergy means having positive specific IgE **AND** symptoms on known exposure.

If on history, a child seems to have had an immediate type reaction to a particular allergen, and the specific IgE test is positive, the test confirms the diagnosis of allergy.

If a child has a positive specific IgE test result to an allergen that they are regularly ingesting without adverse reaction, this test merely indicates sensitisation and the test should not have been done in the first instance. If specific IgE to an allergen that is being regularly tolerated is performed in error, patients should **NOT** be advised to avoid this allergen.

If a child has a positive specific IgE to a food they have not yet ingested (which may be tested for as a likely co-allergen), it is not clear whether the test indicates sensitisation or a likelihood of allergy. If the risk of the allergy is considered high, specialist advice is warranted to determine whether there is a need to avoid the allergen pending further evaluation.

Table 3: Summary of advantages and disadvantages of specific IgE testing

Advantages	**Disadvantages**
Highly specific: negative predictive value >95%, so a negative test usually out rules allergy.	Less sensitive: positive predictive value approximately 50% in absence of a supporting clinical history. High rate of false positives, indicating sensitisation rather than allergy. Therefore, doing an allergy test without a pre-test clinical hypothesis makes the test impossible to interpret.
At present, this test is accessible in many parts of Ireland via local laboratories.	It is a costly test. On this basis, it should only be done in particular circumstances. There is no role for broad panels of allergens: only the suspected allergen (and occasionally 1-2 likely co-allergens) should be tested.
There is no risk involved when actually performing this test i.e. taking a serum sample (in contrast with skin prick testing which carries some risk and should only be carried out in specialised centres).	Interpreting results may pose challenges in primary care: it is often preferable to take a detailed history and refer for testing to be done under specialist care.
It can occasionally be useful in suspected IgE mediated allergy where the diagnosis is uncertain. If the diagnosis is clear from the history, testing is often not needed. Equally if the diagnosis can be ruled out on history, testing should not be done.	The test never trumps clinical history: the history is always key.

Total IgE Levels

Total IgE levels do not provide any additional useful information in primary care. The test should be reserved for specialist centres.

Skin Prick Testing

This is a reliable test in evaluating IgE mediated food allergy. It should be reserved for specialist centres because it requires training, experience to interpret and may carry some risks. GPs with a special interest in allergy may wish to receive training in the skill in order to provide it in primary care.

Other Testing

There are other types of allergy test advertised as being carried out in the community which are not used or endorsed by allergists or professional medical societies. These include specific IgG testing, applied kinesiology or hair testing. These tests are NOT recommended in the diagnosis of food allergy [5](level 3).

1.6 Management

Development of Tolerance versus Avoidance[5]

Tolerance is an immunological phenomenon where allergens can be inhaled or ingested without triggering an IgE mediated adverse response. In non-allergic individuals, the infant immune system actively develops a state of unresponsiveness to each allergen to which they are exposed. In contrast, allergic individuals rapidly develop IgE antibodies to the allergen. Resolution of IgE mediated allergy to certain allergens can occur in allergic infants. For example, tolerance can develop gradually to allergens including egg and cow's milk.

Where appropriate and safe, giving graded exposure to an allergen is one way to use the allergen itself as a treatment for certain types of IgE mediated food allergy, thus promoting tolerance. Most children will grow out of allergies to cow's milk and egg i.e. they develop tolerance to the allergen, in which case the allergens can be reintroduced in the diet [15]. Most children will NOT grow out of allergies to peanut, tree nut, fish and shellfish and, because these allergies persist, the allergens must be avoided [15]. The concept of tolerance in Non IgE mediated food allergy e.g. cow's milk protein allergy (CMPA) is poorly understood.

Promoting Tolerance

To improve quality of life, the current focus of managing food allergy is on avoiding unnecessary exclusions and re-introducing foods into the diet where appropriate. In some instances, modified versions of the food implicated in the allergic reactions can be reintroduced. This is because, in some types of food allergy, it is possible to promote development of tolerance of the allergen by regularly ingesting that allergen, usually slowly increasing at specified intervals in graded concentration as tolerated (e.g. using the IFAN Egg ladder in egg allergy)[16]. In a sense, this is a form of immunotherapy, using the allergen itself as a treatment for the allergy. It is also possible to prevent some types of allergy developing in infants at risk by early and regular ingestion of the allergen (see Allergy Prevention).

Avoidance[5]

In some cases of food allergy, where the risk of future reactions is considered high or a previous reaction was severe, the focus is on careful avoidance of the allergen[12].

The following cases fall into this category:

- All peanut and other nut allergies
- Any food allergy (egg, cow's milk, etc.,) which caused a severe reaction or anaphylaxis.
- Where other factors deem the child to be high risk.

In such cases, reintroduction or food challenges should not be attempted outside of the specialist setting. In these higher risk cases, in addition to avoidance, an emergency management plan is key. Infants and children who have experienced anaphylaxis or are considered at risk of anaphylaxis, should be prescribed adrenaline autoinjectors (AAIs) as part of their emergency management plan, ideally by a specialist. Prescription of AAIs can be initiated in primary care, whilst assessment in specialist clinics is awaited. However if there is any uncertainty regarding the indication, or if the GP is uncomfortable prescribing an AAI, the case may need to be discussed with a specialist.

Section 2: Allergy Prevention

Food allergy prevention can be achieved by manipulation of the natural tendency of the infant immune system to develop tolerance through regular oral exposure to some food allergens (peanut, egg and others) [17] [18] . By proactively introducing these food allergens earlier in the diet, allergy prevention can be achieved. Default medical advice should be to "eat, just in case" rather than "avoid, just in case".

Conversely, if food allergens are avoided, there is a higher risk that the infant or child will develop an allergy during the avoidance period and will react when the allergen is introduced in the diet [19], leading to a potentially preventable condition, which may be permanent, being established. The longer the avoidance period, the higher the risk of allergy developing. Food allergy has a significant negative impact on quality of life for children and their families [20]. Even in *egg allergy*, which most children will outgrow by developing tolerance to egg, the period during which the allergy persists is typically a difficult one for the child and their family and can be associated with significant morbidity.

Two landmark studies, Learning Early about Peanut Allergy (LEAP) [17] and Enquiring About Tolerance (EAT)[18] study demonstrated that a significant proportion of common food allergies including peanut could be prevented by earlier, safe introduction of those food allergens to high risk groups, as long as precautions were taken regarding the form in which the allergen was given.

2.1 Allergen Introduction

Allergy prevention has important implications in terms of advice that GPs and other healthcare professionals give parents when discussing introducing solids to the diet.

For allergen introduction, infants are considered in two groups:

1. The general infant population
2. Infants at high risk of developing food allergy: infants with severe or early onset (by three months of age) eczema and / or existing egg allergy.

Introducing Allergens in the General Infant Population [21 22 17 19 18]

All infants must be considered at risk of developing food allergy, even if no specific risk factors are present. There is a window of opportunity for introducing an allergen in time to prevent allergy developing. GPs can advise parents and carers of children in the general population not to delay introducing common allergens in the diet, once they have started on solids. Allergens to introduce include egg, peanut, tree nut, dairy, fish and seafood. With egg and peanut, the longer the delay in introduction, the higher the chance of the allergy developing, leading to a potentially severe reaction on subsequent introduction or accidental encounter.

Allergens can be started at any time in infancy after solids have been introduced and should not be delayed beyond 12 months, especially in the case of egg and peanut [23]. Each allergen should be introduced one at a time, so that, if there is a reaction, the source is clear.

Debate is ongoing as to the appropriate age for early introduction of allergens to the diet. From an allergy prevention perspective, British Society for Allergy and Clinical Immunology (BSACI) guidance is to introduce peanut from four months of age to avoid missing the window of prevention [24].

Introducing Allergens in Infants at High Risk

Infants with severe or early onset eczema (by three months of age) are at significantly increased risk of allergy to egg and peanut [25 7]. This group represents a small proportion of infants with eczema. Infants who have a sibling with food allergy are not at a significantly increased risk and, unless they have severe eczema, should receive the same advice as the general population.

The presence of one IgE mediated allergy is a flag for significantly increased risk of other immediate-type food allergies in that individual.

- IgE mediated cow's milk allergy flags an increased risk of egg [26] and peanut allergy [27].
- Egg allergy flags an increased risk of peanut allergy [25].
- Regarding peanut allergy specifically, the infant having known egg allergy indicates a high risk, and the presence of both severe eczema and egg allergy indicates a very high risk of that infant developing peanut allergy [25].

In high risk groups, there is a high chance that peanut allergy will develop at a young age, and it is possible it has already developed by the time solids are introduced. However, this group is also most likely to benefit from allergy prevention by the earliest introduction and special emphasis on early introduction of peanut and egg should be made for these high-risk infants. On reviewing infants for vaccinations, fever etc., GPs may opportunistically identify infants at greater risk of food allergy and provide allergy prevention advice when they present to the surgery.

Again, BSACI guidance is to introduce peanut from four months of age to avoid missing the window of prevention [24]. Although not all infants are ready to wean at the same time, delay in introducing egg and peanut much later than six months in this high-risk group must be strongly discouraged. Once infants tolerate the allergens, they should be given regularly in their diet (several times a week and indefinitely) because this is the only way to effectively prevent allergy [22]. If ingestion is sporadic it may be ineffective and may even be counterproductive.

It is possible that even with early introduction in high risk groups, allergy may have already developed by the time the food is given (the same applies to a lesser extent to the general population). However, parents can be reassured that to date there have been no life-threatening reactions reported to allergens introduced early in line with this new guidance, once given in safe forms. In theory, a severe reaction is a possibility. However, the risk of waiting is greater because of a higher chance of developing an allergy with avoidance and the reaction being more severe or leading to anaphylaxis when later introduced (or accidentally encountered). The important thing is NOT to do nothing. Based on current evidence, a more cautious avoidance approach is no longer acceptable. Timely communication with a specialist may help in a case where there is uncertainty about the right course to take regarding allergen introduction in a high-risk infant.

In cases of highest risk infants i.e. those with both egg allergy and severe or early onset eczema, where there was failure to introduce peanut early in the weaning diet, special considerations apply. If these infants are almost or just over one year of age, there is a greater likelihood that the window of prevention was missed. Therefore, discussion with a specialist is advisable before introducing peanut in such cases. Allergists in Ireland are available and keen to advise regarding such queries from primary care (see contact details for specialists).

2.2 Introduction of Complementary Foods/Solids in General

The age at which to advise introduction of any complementary foods or solids has been an area of change and debate in recent years. Guidance in recent years had suggested waiting until 5 or even 6 months of age, and as a result many healthcare professionals in Ireland have been advising parents to delay beyond the more traditional time of 4 months (or even 3 months, which despite being earlier than advisable was and still is quite common Irish practice). This guidance was mainly based on WHO guidance for exclusive breastfeeding for the first 6 months and, in some cases, parents felt they needed to wait until 6 months exactly. Updated HSE guidance on introduction of solids has reverted to a more sensible range of 4-6 months as an appropriate age, with the decision based on looking for signs that an infant is ready for solids[28].

There is increasing recognition that breastfeeding is not adversely affected by introduction of solid foods. All advice regarding allergen prevention is made in the context of both promotion and preservation of breastfeeding. However, in reality, the preservation of breastfeeding in relation to early introduction of allergenic foods currently only applies to a very small proportion of the Irish population, as we know that only 19% of infants in Ireland are exclusively breastfed at 3-4 months of age [29] and less by 6 months. Even with this small section of the population in mind, the EAT study provided adequate reassurance that early introduction of solid foods from 4 months, for the purpose of allergy prevention, did not interfere with breastfeeding [18].

Introduction of Egg

- Only cooked egg should be introduced to infants (raw egg, apart from posing a salmonella risk, is also the most allergenic form and therefore has a higher chance of a more severe reaction) [30].
- If eczema is present, an attempt to obtain control should be made with topical steroids and emollients prior to introduction (and on an ongoing basis) [31]. This reduces the risk that itching and redness related to the eczema will be misinterpreted as an allergic reaction.
- As with other food allergens, egg can first be given in a small amount to taste.
- Once tolerated, egg should be given regularly (several times a week), especially for high risk infants. If there is a mild-moderate reaction to lightly-cooked egg, small amounts of egg in baked form (which is less allergenic) should be tried and the IFAN Egg Ladder[16] used to test for and promote tolerance. If a diagnosis of egg allergy is made in primary care, even if the reaction was mild-moderate, referral to a specialist should be made in addition to using the Egg Ladder in the community because these infants are high risk for other food allergies and need assessment in an allergy clinic.
- See section on Egg Allergy for more detail on how to proceed following severe reactions.

Introduction of Peanut [22 32]

- Whole nuts or coarse nut pieces should never be given to infants or small children due to choking risk, infants can be given smooth forms. “Natural” peanut butter is now readily available with no added ingredients (salt, sugar, palm oil etc.) other than blended peanuts.
- Small amounts can be given to start. It may be thinned with milk or water or added to pureed fruit, cereals or yoghurt.
- Eczema control should be optimised before introducing peanut.
- To achieve the aim of allergy prevention, peanut should be given regularly (several times a week).
- For high risk infants, once they have tolerated a small amount, an approximate total of 2 teaspoons a week should be ingested regularly and on an ongoing basis. Discontinuation runs the risk of allowing peanut allergy to emerge. If any reaction occurs that is thought to be an allergic response to peanut (or other nut) ingestion, both peanut and all nuts not yet eaten safely should be avoided until the infant is assessed by a specialist.

Questions Parents may ask if Nervous about Early Introduction

Could s/he be allergic already?

Yes, it is possible but, the earlier you give the suspected allergen to him/her, and the less likely it is. The longer you wait, the higher the chance of an allergic reaction whenever s/he does encounter it.

Could my child have anaphylaxis with first ingestion of peanut?

In theory, yes, it is possible. However, so far there have been no reported cases of fatal anaphylaxis to peanut on early introduction. Anaphylaxis typically happens when peanut is introduced later, which is what we are trying to prevent.

“I’d prefer to just avoid peanut or nuts long-term as they are not in my diet anyway and I don’t want the chance of a bad reaction”.

In reality it doesn’t work that way. As children get older, and go to other houses and parties, they will inevitably encounter peanut unless they are identified as peanut allergic and steps have already been taken to eliminate peanut. Logic indicates it is better for a young child to eat small amounts of peanut deliberately at home under parental supervision than to casually eat unknown amounts elsewhere when parents are not around.

2.3 Eczema and Food Allergy

Eczema is not caused by food allergy. The cause is an underlying skin barrier defect that leads to trans-epidermal water loss, altered skin pH and reduced antimicrobial defence. This disruption to normal skin function results in dryness, pruritus, waxing and waning cutaneous inflammation and dysregulated skin microbiome.

There is, however, a strong association between eczema and food allergy. Eczema is a significant risk factor for development of IgE mediated food allergy [7 33]. Foods should not be removed from the diet with the aim of improving eczema in primary care. Removal of foods from infant diets may prevent natural acquisition of tolerance. Focus of care should be on optimising skin care with adequate bathing, copious application of emollients and topical steroids as appropriate. Infants and children with eczema that are not responding to such treatment will need specialist dermatological input. If these infants and children also have food allergies, they may need input from both a dermatologist and an allergy specialist.

Section 3: Specific Food Allergies: Diagnosis and Management in General Practice

3.1 Cow's Milk Protein Allergy

- Cow's milk protein allergy (CMPA) first presents in infancy. It does not develop de novo in childhood or adolescence [26]. It is present in approximately 1% of children under two years [1].
- Resolution of the allergy can be expected in 75 – 90% of cases before 5 to 6 years of age i.e. the majority of children develop tolerance to cow's milk[26].
- CMPA can be IgE mediated or Non IgE mediated. This guidance document deals primarily with the Non IgE mediated type because it can be managed exclusively in primary care in most cases. At present, IgE mediated CMPA requires specialist management.
- Tolerance to milk by 5 years of age is less likely with IgE CMPA than with Non IgE CMPA (about 50% with IgE) [26, 34].

History

Table 3 describes the features of IgE mediated and Non IgE mediated CMPA which can be elicited from the clinical history. Key questions relate to the infant's feeding history regarding breast milk or formula. In an infant already taking solids, ask regarding any intake of dairy in solids (e.g. infant weaning porridge powders often contain milk powder).

Table 4: Features of IgE mediated and Non IgE mediated CMPA which can be elicited in the history

IgE mediated CMPA	Non IgE mediated CMPA
Symptoms usually occur within minutes of ingestion and typically involve an urticarial rash or erythema around the face and neck. Severe symptoms including anaphylaxis are possible.	Symptoms occur more than 2 hours after ingestion by definition, but often occur at 24-48 hours, and even up to 72 hours post ingestion. Symptoms are primarily gastrointestinal and include: • Vomiting with back arching and screaming • Feed refusal • Dysphagia and food impaction • Diarrhoea often protracted with propensity to faltering growth • Constipation or more typically, straining with defecation, but producing soft stools • Blood and or mucus in stools (proctocolitis) • Unwell child: delayed onset protracted vomiting and diarrhoea (enterocolitis) Other symptoms • Failure to thrive or poor weight gain • Pallor and tiredness • Colic

	• Non-specific skin symptoms such as erythema and eczema flares may also occur (milk should not be removed from the diet on the basis of skin symptoms alone) • FPIES

Differential Diagnosis of Non-IgE CMPA

Many of the symptoms associated with Non IgE CMPA are common features of infancy in the absence of allergy, making it complex to diagnose. Posseting, effortless vomiting and a certain degree of gastro-oesophageal reflux are all normal phenomena in infancy and colic (excessive crying) alone is not an indicator of CMPA.

In any infant with irritability and vomiting particularly if the child appears unwell, sepsis and other medical causes must be considered. With gastrointestinal (GI) symptoms such as blood in stools, other intestinal or surgical conditions should be considered. CMPA is the likely diagnosis, the longer GI symptoms persist in an infant and the more they progressively worsen over time.

Presentation of CMPA in Formula-Fed Infant's versus Breastfed Infants

Non-IgE Mediated CMPA

- Will usually present very early, even within the first few weeks in infants where standard infant formula (which is made with cow's milk) has been used as the sole food source.
- Can also present soon after birth in exclusively breastfed infants whose mothers have dairy in their diet.

IgE Mediated CMPA

- Is less common in infants established on formula milk from birth.
- Rarely presents while infants remain exclusively breastfed, never having been given formula or dairy-containing solids.
- However, as breastfed infants wean to formula or dairy-containing foods, CMPA tends to reveal itself. It is likely that these infants were sensitised early in infancy.
- There is some evidence that formula top ups in the new-born period is a risk factor for the development of IgE CMPA in infants subsequently exclusively breastfed. For mothers who are initiating breastfeeding following birth, formula top-ups for new-borns should be discouraged unless clearly medically indicated, with every support provided to the nursing mother to achieve effective breastfeeding [35].

Investigations

No tests should be done if Non IgE mediated CMPA is suspected because there is no reliable test for this type of allergy[36]. Instead, the diagnosis is confirmed by improvement on exclusion of milk and, crucially, recurrence of symptoms on reintroduction[36].

Management

IgE-Mediated CMPA

If IgE mediated CMPA is suspected (i.e. if there is rapid onset of symptoms, urticaria, angioedema etc.), it is currently not recommended to perform reintroduction of milk in the community [37].

Non-IgE Mediated CMPA

In infants presenting with a multitude of abdominal symptoms only (reflux, poor feeding, diarrhoea, irritability etc), where Non-IgE mediated CMPA is suspected, a period of exclusion, followed by trial reintroduction, is usually advised. This involves excluding cow's milk from the infant's diet for a defined period, usually 4-6 weeks, followed by a trial of reintroduction. During the exclusion period ensure there is complete avoidance of cow's milk, not a reduction, otherwise the response will not be clear [36].

Exclusion of Cow's Milk

Exclusion of milk for formula fed infants: replace cow's milk-based formula with Extensively Hydrolysed Formula (EHF) on prescription. In EHF, the cow's milk proteins have been broken down into short segments. In more severe cases of allergy, amino acid formula can be used (protein broken into individual amino acid components) [5]. Partially hydrolysed formula available over the counter is not a suitable alternative to EHF. EHF is used in the management of suspected or confirmed CMPA but does not have a role in prevention of CMPA and should not be used for this purpose. Soya formula is not usually recommended in infants with Non IgE CMPA as it often triggers the same symptoms profile.

Note: in contrast, in IgE CMPA, soya formula can be used in infants from around 6 months of age.

Exclusion of milk for breastfed infants: a trial period of complete exclusion of dairy from the mother's diet for a defined period (4-6 weeks) should be tried. As for formula fed infants it must be absolute exclusion for this period. The mother's breastfeeding plans should be supported and encouraged [37].

Reintroduction

Trial Introduction: The first reintroduction of milk is a trial reintroduction that follows the trial period of absolute exclusion. The purpose is to make a diagnosis of CMPA which, if confirmed, leads to a longer exclusion period being required. If the symptoms do not recur with trial reintroduction, continue cow's milk in the diet as tolerated.

Remember: If IgE mediated CMPA is suspected (i.e. if there is rapid onset of symptoms, urticaria, angioedema etc.), reintroduction in the community is currently contraindicated.

Later reintroduction of cow's milk to establish resolution of the issue

Later reintroduction of cow's milk following diagnosis and a longer period (typically several months) of excluding cow's milk from the infant's diet serves to establish whether the issue is resolved after that period. In Non IgE mediated CMPA reintroduction can be progressed in the community without guidance or evaluation by a specialist.

The Cow's Milk Ladder [38] [37] can be used to assist with reintroduction. The Cow's Milk Ladder is a model by which to determine the amount of dairy that an infant is ready to tolerate.

The timing of cow's milk reintroduction depends on the particular case. In cases where the diagnosis has been reached quite late with associated weight loss, food aversion etc., it may be appropriate to defer any attempts at dairy reintroduction until parents and infant have had time to recover from what can be a traumatic period.

Typically, infants will still display symptoms in response to whole milk (the most allergenic form) but are able to tolerate baked forms, which are less allergenic. Thus, reintroduction should follow the Cow's Milk Ladder[38], which starts with smaller amounts of baked milk. Parents should be encouraged to follow the Cow's Milk Ladder themselves. It is important that the infant is well-established on a variety of solids before trying reintroduction. Ideally home factors such as sleep routine should be favourable at the time, although of course this is not always possible.

If symptoms occur with reintroduction or when moving up the Cow's Milk Ladder

If symptoms such as vomiting, loose stools or distress with feeding recur with reintroduction of cow's milk or with moving up a rung of the Cow's Milk Ladder, it is advisable to wait 2-3 months before attempting again. Any form of cow's milk (e.g. small amounts in baked goods) that they are tolerating without adverse effects can be continued. It is important that parents are not advised to "push through" difficult gastrointestinal symptoms with the aim of inducing tolerance. Infants do not have to earn tolerance of cow's milk by experiencing symptoms regularly, they should just move up the Cow's Milk Ladder as tolerated using each move up a rung as a way to "test the waters" and see if tolerance is improving.

Referral to a Dietician

Any exclusion of cow's milk for more than the limited trial period should involve input from a dietician to avoid potentially serious nutritional deficiency for the infant [36]. Unfortunately, this service is lacking in many parts of Ireland. In areas where it is not possible to refer to a dietician service for infants, GPs must ensure that infants and (breastfeeding mothers) are receiving adequate Vitamin D/Calcium supplementation if necessary.

Exceptions to Reintroduction of milk in the community

Exceptions to reintroduction of milk in the community are IgE CMPA, where currently specialist input is required or, in the rare cases of Non IgE CMPA where severe enterocolitis or FPIES occurred.

Formulas in CMPA [5]

Table 5: Formulas in CMPA

Formulas used in infants with CMPA	**Formulas and "Milks" not advised** *(no role in the management of CMPA)*
Extensively hydrolysed formula Amino acid formulas *Soya formula is a reasonable option in infants with IgE mediated CMPA. However, in infants experiencing mostly abdominal symptoms it is usually not well tolerated.*	Hungry formulas Staydown formulas Lactose free formulas Partially hydrolysed formulas Colic or comfort formulas Goat's milk formula The following milks should not be used as a cow's milk alternative: Other mammalian milk (goat, sheep) Plant or grain based "milks" (oat, almond, rice, coconut although small amounts can be used for a milky taste for children over 1 year.

Table 6: Non-IgE mediated CMPA

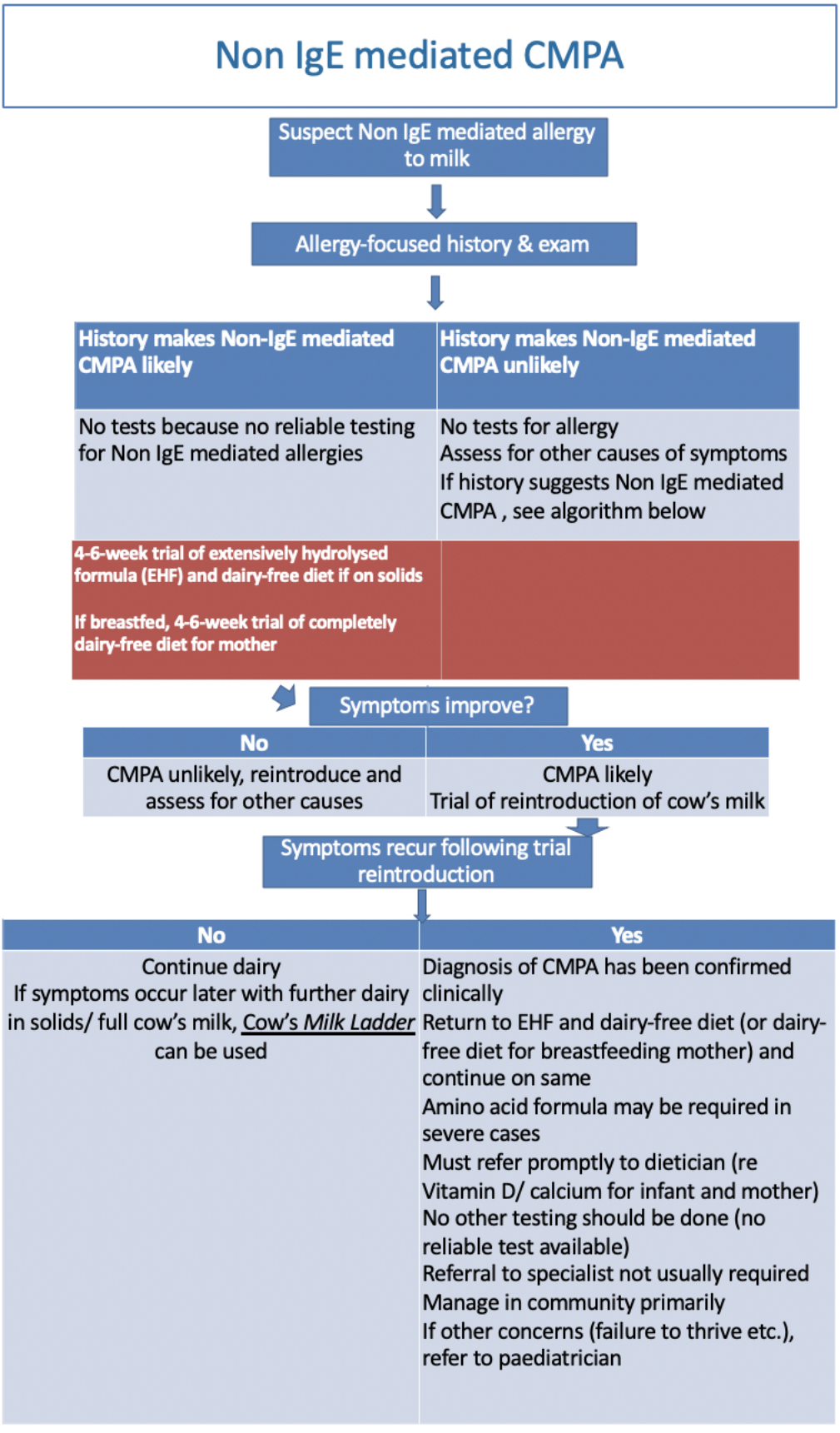


Table 7: IgE mediated CMPA

IgE mediated CMPA

•Rapid onset of symptoms (usually minutes) after ingestion of cow's milk
•Typically urticaria, but severe symptoms/ anaphylaxis possible
If clinical picture suggests IgE :mediated CMPA

If the history is in keeping with IgE mediated reaction (immediate type) AND cow's milk is clearly the precipitating allergen, make a clinical diagnosis

testing not advised in primary care.

•If the history is in keeping with IgE mediated reaction BUT there is doubt about which allergen precipitated it, then specific IgE to cow's milk (and possibly another suspected allergen) can help to confirm the diagnosis or the source allergen.

•Do not delay management of a clinical diagnosis if clinically likely while awaiting specific IgE result.

•Never advise a trial of another cow's milk-based formula or goat's milk formula if an infant has reacted with urticaria to cow's milk (significant cross-reaction to proteins).

•Reassure breastfeeding mother that cow's milk does not need to be removed from mother's diet (that only applies in Non IgE mediated CMPA).

•If there is a plan to introduce formula to a breastfeeding infant with IgE mediated CMPA, prescribe Extensively Hydrolysed Formula (EHF).

•Parents should be advised to continue to introduce solids as normal (with avoidance of dairy and vitamin D / calcium supplementation) but with specific emphasis on introduction of peanut and egg (see Allergy Prevention).

•Urgent referral to a specialist is key; indicate clearly on referral why you believe this is IgE CMPA. There should be no delay in referral. Avoid cow's milk until reviewed by an specialist; do not attempt reintroduction or the Cow's Milk Ladder in the community.

•If severe symptoms or anaphylaxis occurred to cow's milk, an adrenaline autoinjector may be required, but in the case of CMPA, these are usually initiated in specialist clinics. Discuss with an specialist if in doubt; these infants need to be seen most urgently see *Adrenaline Autoinjectors*.

3.2 Egg Allergy [39]

- Egg allergy occurs in 3% of Irish children [1].
- It is usually an immediate type (IgE mediated) allergy but can be Non IgE mediated.
- Egg allergy usually presents in infancy, coinciding with the introduction of egg in the diet.
- Strict avoidance of all forms of egg is rarely necessary and not routinely recommended.
- Well-cooked egg is less allergenic than raw or lightly cooked egg.
- Reaction is usually dose dependant: small amounts may be tolerated but larger amounts may provoke a reaction.
- Most infants and children with egg allergy (70-90%) can tolerate baked egg.
- Ingestion of baked egg may promote tolerance of lightly cooked egg.
- The majority of children outgrow their egg allergy.
- Most children with egg allergy do not require adrenaline auto injectors unless they have had a severe (i.e. anaphylactic) reaction.
- Most children with egg allergy can work up the IFAN Egg Ladder in the community, with primary care input as needed.
- However, in addition to primary care management, all infants with egg allergy should be referred at the time of diagnosis to a specialist (or paediatrician with a special interest), even if they are progressing on the Egg Ladder. This is because egg allergy is a strong marker for other food allergies, therefore these children need specialist assessment and input.
- Children with egg allergy are at greater risk of developing other food allergies, especially peanut allergy [40]
- Eczema is a risk factor for egg and other food allergies. However, egg allergy is not a cause of eczema and exclusion of specific foods should not be used in primary care to treat eczema.

History

Diagnosis is essentially based on clinical history (as outlined in Allergy-focused Assessment).

In addition to the key allergy questions, additional questions relating to the suspected reaction to egg include the following:

- The form of eggs that provoked a reaction – lightly cooked, well cooked, baked with wheat.
- The type of reaction – timing, symptoms, severity.
- Any form of eggs previously tolerated.
- Presence of eczema – indicates a significantly higher risk of egg allergy particularly if eczema is severe or early onset (< 3months of age).
- Reaction to ingesting or tolerating peanut – egg allergy indicates a significant risk of having or subsequently developing a peanut allergy.

Suspect IgE mediated allergy if the reaction to ingestion of or contact with eggs is within minutes up to 2 hours.

Examination

Examine an infant for the presence of eczema and, if present, determine the severity and the need for better topical treatments to optimise control.

Investigations

Egg Allergy is the likely diagnosis no tests required

Investigations are often not needed when managing egg allergy in primary care. If the diagnosis seems LIKELY from the history, a clinical diagnosis of egg allergy without tests can be made and the child managed accordingly.

Egg Allergy is an unlikely diagnosis no tests required

If the diagnosis seems UNLIKELY from the history, laboratory testing is not required. For example, if symptoms such as urticaria occur but egg is tolerated in the diet, and there is not a repetitive relationship between ingesting egg and symptoms, the diagnosis can be ruled out on history. An alternative diagnosis should be sought (e.g. idiopathic urticaria).

Uncertain diagnosis consider testing

In a case where the diagnosis is UNCERTAIN i.e. cannot be confirmed on the history but there is reasonable suspicion, there may be a role for serology testing with specific IgE to egg.

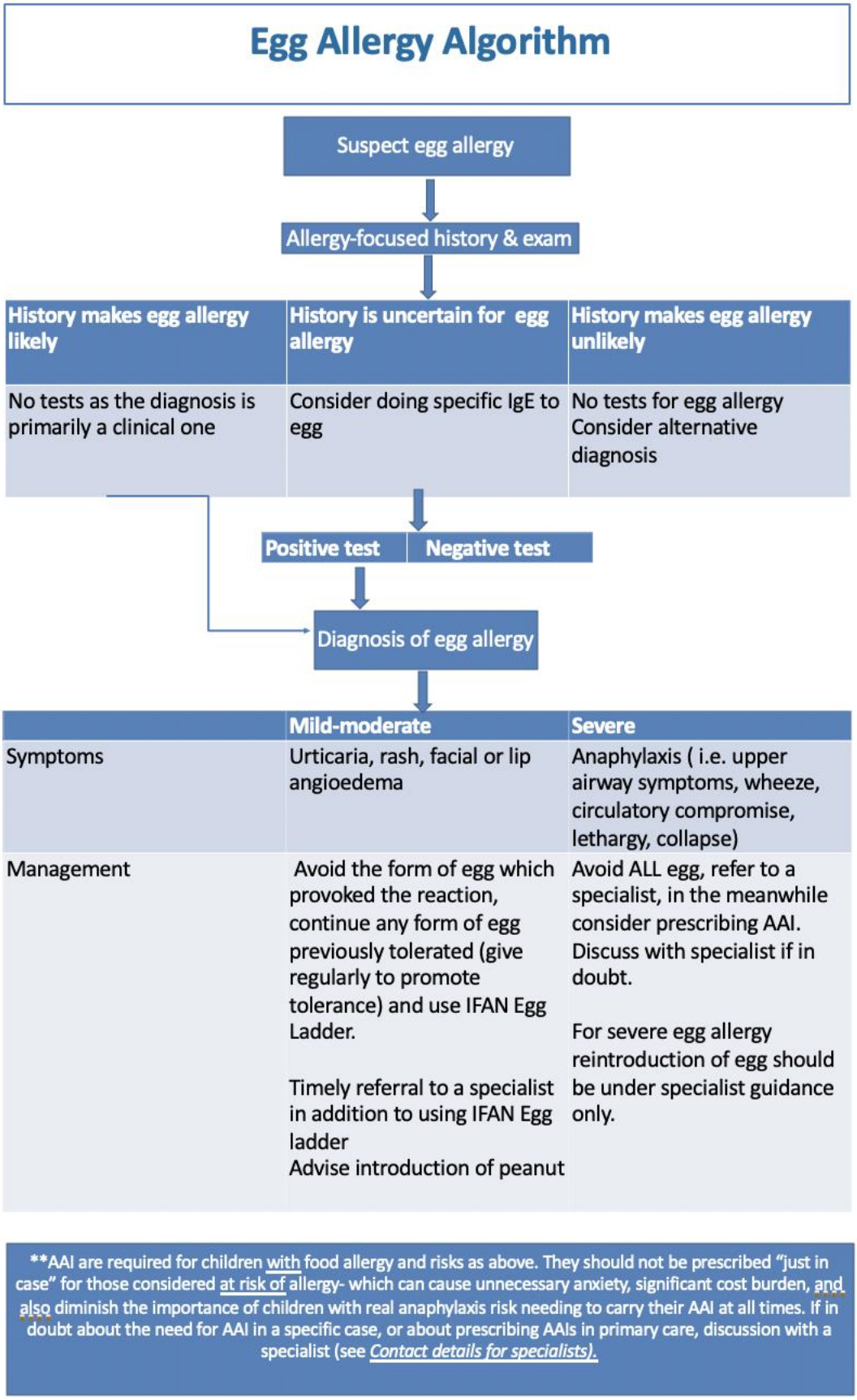
- If testing is negative for egg, consider an alternative diagnosis and advise reintroduction of egg.
- If testing is positive for egg, the diagnosis is confirmed. Management and dietary advice regarding egg depends on the severity of the reaction and whether asthma co-exists (see next section).

Skin prick testing is an alternative test to specific IgE serology for IgE mediated allergy but performance and interpretation of this test should be done in specialist centres only (including some GPs with special interest).

Management

See Egg allergy algorithm [40] Management depends on the severity of the reaction.

Table 8: Egg allergy algorithm



Evaluation of Risk

Allergy to egg can be categorised as either mild, moderate or severe. Urticaria and angioedema are common presenting symptoms of egg allergy and are considered mild-moderate [39]. Vomiting is also very common in egg allergy. Severe reactions including wheeze or other respiratory or cardiovascular compromise are less common but can occur [39]. Any severe reaction equates to anaphylaxis.

Severe Reactions

Any severe reaction (anaphylaxis) is an indication to avoid ALL egg until specialist review has taken place or advice has been sought. Any child with severe egg allergy or anaphylaxis must be referred urgently to a specialist. Include all information listed in the Allergy-focused Assessment on the referral, making it clear why it is urgent to allow appropriate triage. If the GP is comfortable, it is acceptable to prescribe an Adrenaline AutoInjector (AAI) in primary care and instruct regarding use [6] (Grade B) if the indication is clear (history of or high risk of anaphylaxis). If the indication is in doubt or the GP has any uncertainty, they should consult an specialist before prescribing. AAIs are overprescribed for mild reactions 'just in case'.

Mild-Moderate Reactions

If an infant had a mild-moderate reaction to egg, parents should be advised to initially avoid the form of egg that provoked the reaction and to start on the Egg Ladder. This begins with the slow introduction of well-cooked egg baked with wheat (or alternate grains) i.e. buns, cakes. Generally, it is recommended to start with tiny pieces, increasing every few days as tolerated until a full serving is eaten (1 bun, 1 sponge finger). Once tolerated, baked egg should continually be provided to infants as more lightly cooked forms are simultaneously trialled.

When progressing up the Egg Ladder, it is important that parents choose a good time to progress. This means ensuring the child is well with no concurrent illness. Any co-existing eczema should be optimised by skin care (topical steroids and emollients) and asthma should be well-controlled. If there is a reaction having moved up the Egg Ladder, they should just move back down to the previous rung that was tolerated and continue this for a period before trying again. Oral antihistamines are useful for treating the mild-moderate reactions which may occur to egg.

All egg allergic infants, irrespective of severity or progress along Egg Ladder, should be referred to a specialist or paediatrician with a special interest in allergy as part of overall management.

Recognising the Presence of Egg

Parents must learn to recognise the presence of egg in order to avoid it and learn how to read food labels. Unlabelled food e.g. from the bakery should be avoided. Uncooked egg is hidden in many foods, mayonnaise, some types of ice cream, pastry glazes and some marshmallows. It is also possible to inhale vapour from eggs cooking or even uncooked cracked eggs. Contact with eggshells and other birds' eggs should be avoided.

Raw egg is often present on egg boxes used in art and crafts. This should be considered in schools, preschools, crèches where there is a child with a significant egg allergy. These institutions should consider avoiding baking with eggs or

using such materials when they have such a child in their class; altering activities in favour of including that individual is preferable to excluding them, from a quality of life and even a human rights point of view. See Table 5 for a description of the egg content of foods.

Table 9: Egg content of food

Well-cooked egg (least allergenic)	Lightly cooked egg	Almost raw egg (most allergenic)
Sponge Muffin Cake Pancake	Egg pasta Hardboiled or fried egg Omelette	Scrambled egg Meringue Marshmallow (including Milky Way®, Snowball®) Mayonnaise Some ice cream (Haagen Dazs®, homemade)

Peanuts and Egg Allergy

Egg allergy is an indicator of a significant risk of other food allergies, especially peanut. Infants with both egg allergy and either severe or early onset eczema are at highest risk of developing peanut allergy.

For younger infants with egg allergy without severe eczema, the key aim is to introduce peanuts promptly into the diet to prevent peanut allergy developing. This is because the egg allergy still indicates a high risk for this occurring subsequently (see Allergy Prevention).

Eczema and Egg Allergy

Although there is a significant association between eczema and food allergy, eczema is not caused by food allergy. In fact, it is considered more likely that the causal link is actually eczema causing food allergy (See Section Eczema and Food Allergy).

Vaccines and Egg Allergy

MMR Vaccine

The MMR vaccine does not contain egg and should be given to egg allergic infants and children in the usual manner in the community [39] [41].

Yellow Fever Vaccine

Yellow fever vaccine contains small amounts of egg and specialist input should be sought before administering to an egg allergic child [39] [42]. The Tropical Medicine Bureau is familiar with protocols for egg-allergic children.

Flu Vaccine

In egg allergic children where the allergy was not severe and there is not severe or uncontrolled asthma, flu vaccine can be given in the community in the usual manner. For infants and children with egg allergy that is severe, unresolving or with a history of anaphylaxis, or with egg allergy and severe asthma, it is best to discuss with the child's paediatrician or specialist before proceeding or refer to the current HSE guideline[43].

3.3 Peanut Allergy

Peanut allergy occurs in 2% of children[1] and often presents with first exposure to peanut. Peanut allergy is IgE mediated. Most children do not grow out of their peanut allergy, with peanut allergy persisting in 80% of children[44]. Severe reactions in peanut allergy are more common than with other food allergies. The severity of future reactions is hard to predict but subsequent reactions are not automatically more severe.

Refined peanut oil or oil of arachis does not pose a risk to children with peanut allergy. This oil is used in some aural preparations to soften ear wax and can be used safely in the case of peanut allergy. It is also present in roaccutane, which is used for acne, and in testosterone injections for primary hypogonadism and is safe for these uses in peanut allergic children.

History (see Allergy-Focused Assessment)

- Most peanut allergic children (80-90%) will have other atopic conditions.
- Severe reactions and anaphylaxis occur in 30-40% of first reactions on accidental exposure.
- Severe reactions usually occur only through ingestion.
- Contact reactions with peanut will occur but tend to be mild.
- Overlap with other nuts (tree nuts) is common (50% will develop tree nut allergy).

Management (see algorithm)

- The management of anaphylaxis is covered here (Anaphylaxis).
- Any case of suspected peanut allergy must be referred promptly to a specialist, specifying severity of symptoms.
- Testing is not essential in primary care, but specific IgE serology to peanut can be considered especially if the diagnosis is uncertain.
- Do not delay referral waiting for test results, although forwarding results once available is useful for triage in the allergy services.
- Complete avoidance of peanut and all nuts not already eaten and tolerated in the diet is indicated until they are assessed by a specialist.
- If there was a clear history of anaphylaxis following peanut ingestion, Adrenaline Autoinjector (AAI) can be initiated in primary care. However, if there is any doubt regarding the indication, the case should be discussed with a specialist. Most children with peanut allergy will require an AAI eventually but not all require it immediately.

Living with Peanut Allergy

- The specialist can perform a skin prick test and advise on the introduction of those nuts with negative results, thereby preventing subsequent sensitisation caused by unnecessary avoidance[45] .
- Living in a completely peanut free environment (at home or in school/ crèches) is neither possible nor necessary.
- Removal of peanut and peanut butter from the household entirely is not necessary; in line with our allergy prevention advice, peanut should be introduced early in the diet to infant siblings. Care must then be taken about keeping it out of reach of toddlers and small children with peanut allergy. Parents must carefully read food labels and avoid any unlabelled goods e.g. from the bakery.
- Handling nuts e.g. on nature tables, in schools or during outdoor activities should also be avoided and schools should be made aware of this risk [46].
- Contact reactions to peanut allergy are easily treated with antihistamine.
- Desensitisation to peanut is not currently available in a clinical setting. Research models are however at a late stage of development and FDA/EMA-licenced products will come to market in the next few years.

Peanut Allergy Prevention

Early introduction of peanut can prevent development of peanut allergy. See Allergy Prevention.

Table 10: Algorithm for Peanut Allergy

Suspect peanut allergy

1.If acute severe reaction – conduct emergency management as below
2.If non-acute presentation at time seen- perform full allergy-focused assessment regarding reaction which occurred previously

History makes peanut allergy unlikely	History is uncertain for peanut allergy	History makes peanut allergy likely
Peanuts are being tolerated in the diet If this is the case, seek alternative cause for symptoms . Continue peanut in diet. No allergy testing for peanut	Specific IgE to peanut may help Advice from specialist or advise peanut avoidance and refer if still reasonable suspicion	Avoid peanuts and any nuts not already eaten and tolerated. Refer to specialist (specify if severe symptoms for triage). Serology for specific IgE to peanut may be considered but is not essential prior to attending specialist clinic especially if clear diagnosis on history. If severe symptoms occurred, prescribe AAI and instruct re use. If in doubt re need for AAI consult with specialist.

Section 4: Anaphylaxis

Definition

Anaphylaxis is a severe, progressive multisystem allergic reaction usually of rapid onset with either airway involvement or hypotension typically with cutaneous features [6]. It is a medical emergency.

Symptoms and Signs

Any of the following are severe allergy symptoms and therefore represent anaphylaxis:

- Any involvement of the airway (tongue swelling, wheeze, shortness of breath or even sudden onset cough or hoarseness)
- Any circulatory compromise (pallor, clamminess, feeling faint or lethargy, hypotension, tachycardia or bradycardia)
- Collapse/loss of consciousness

The severe symptoms above are typically accompanied by cutaneous signs such as widespread flushing, urticaria and angioedema of face and lips.

Emergency Management in Primary Care[47]

Key features of emergency management of anaphylaxis are to

- Recognise that anaphylaxis is occurring
- Attend promptly to ABC (Airway Breathing Circulation)
- Administer appropriate dose of adrenaline 1/1000 IM without delay
- Call for help or ambulance early
- Remove the allergen if still present
- Oxygen, chlorphenamine IM/IV, nebulised salbutamol and hydrocortisone IV may also be necessary
- Transfer to the emergency department must always be made even if good response to adrenaline

In terms of adrenaline administration, for anaphylaxis it must always be 1/1000 strength and always as an IM injection (recommended site is anterolateral thigh).

Vials of adrenaline 1/1000 are recommended, the appropriate volume must be drawn up based on the child's age and weight (see HSE link). Keeping adrenalin in date along with all emergency drug supplies is key.

An alternative is to keep auto injector vials in the surgery or emergency bag for this purpose, however these are less cost effective and expiration is an issue.

Adrenaline Autoinjectors (AAIs)

Indications for prescribing[6]

- Food allergy with prior severe immediate-type allergic reaction or anaphylaxis (any food allergen).
- Food allergy AND asthma on more than minimal ICS, because considered high risk of anaphylaxis.
- Other risk factors such as remoteness from medical facilities or a reaction to a very small amount of allergen influence the decision to prescribe AAI.
- Most children with peanut allergy will require AAI eventually. However, if the reaction that has occurred was not severe, AAI should not be required immediately before being seen by a specialist.

It is appropriate for GPs to initiate AAI prescriptions in the primary care setting, if the GP is comfortable and if the above criteria apply [6] (Grade B).

AAIs are required for children with food allergy and risks are as described. They should not be prescribed "just in case" for those considered at risk of allergy, which can cause unnecessary anxiety, significant cost burden and diminish the importance of children with real anaphylaxis risk needing to carry their AAI at all times. If in doubt about the need for AAI in a specific case or about prescribing AAIs in primary care, discussion with a paediatric specialist or paediatrician with an interest in allergy is recommended (see contact details for specialists).

A risk assessment by a specialist is needed to determine the ongoing need for AAI prescription.

How to Prescribe AAIs in Primary Care

The dose of adrenaline autoinjectors is as follows:

- 150microgram for children 15-30kg
- 300microgram for children > 30kg
- 500microgram for those >50kg

Infants weighing < 15kg should not be prescribed in primary care; it is not common for AAIs to be indicated in small infants. If AAIs are required in an infant, this must be discussed with a specialist before prescribing.

AAIs contain adrenaline 1/1000 and are always given as an intramuscular injection into the anterolateral thigh (described as "outer thigh" to patients and carers). A child requiring AAI should have 2 devices with them at all times as a second delivery of adrenaline may be required [6].

There are 4 brands of AAI devices available on prescription currently in the Republic of Ireland: Anapen, Emerade, Epipen, Jext (these are all covered by GMS).

When any of the above are prescribed there must be a clear explanation to the patient's caregiver of when and how to use them. Method of delivery varies between brands. Each brand of AAI listed above has instructions for use in diagram or video format on their websites (see here) and will supply a demo pen to a GP practice on request.

A copy of the IFAN emergency management plan should be provided to the parents.
Parents should be reassured that adrenaline administration is safe, simple and lifesaving and that they should feel confident to deliver. The child prescribed an AAI must be referred to an allergy clinic where there will be further education, risk assessment and planning as appropriate. In addition to prescribing an AAI, non-sedating antihistamines should be prescribed to use in the case of milder reactions. Avoidance of the allergen must be reinforced as a preventative strategy.

Maintaining good control of asthma if present, is a key factor in reducing potential severity of reactions [6]. Short-acting bronchodilators should be available for patients with asthma and food allergy for use in the case of anaphylaxis in addition to adrenaline administration.

Compliance with carrying AAIs is known to wean over time. Every clinical encounter provides an opportunity to ensure that AAIs are being carried and that the parent/patient know how to deliver them.

Useful Links for Anaphylaxis

- IFAN Safety Plan
- IFAN Adrenaline Autoinjectors and Trainer Devices
- How to use Emerade
- Epipen user guide
- Jext video demonstrations
- Anapen patients

Section 5: Quality of Life and Food Allergy

Food allergy has been shown to have a negative impact on quality of life for patients and their families [20]. This can stem from many factors, including either the patient or parent profoundly fearing death (which in reality is a remote chance, even in severe allergy), exclusion from school, sport or social activities, bullying, feeling different, difficulties as family manage allergen avoidance or challenges with different caregivers varying in their stringency with emergency preparedness. Times such as starting a new school, or the teenage years pose particular issues.

It is important as GPs to be aware that young patients with food allergy and their families may need particular encouragement and support. It is helpful for GPs to think of screening for associated stress or mental health issues when the opportunity arises.

Also, be aware that the onus should be on schools and sporting or other institutions to be inclusive of children with food allergy, including the relevant staff or coaches etc. being instructed on how to administer AAI if required. In general children with food allergy are extremely unlikely to encounter a food allergen while playing sports or even in school, especially in cases where children bring prepacked lunches to school. Far too much focus is placed on fear of delivery of adrenaline and too little on developing practical preventions strategies. Click here for more information.

Section 6: Domiciliary Care Allowance, Incapacitated Child Tax Credit and Special Needs Assistants (SNA) in School

GPs are frequently asked to complete paperwork regarding the above schemes.

Eligibility for domiciliary care allowance and incapacitated child tax credit is based on a severe disability requiring care and attention, significantly over and above the care required for another child of similar age. There is no indication that food allergy alone meets these criteria. Food allergic children with other disabilities which do require substantially increased care levels may qualify but food allergy alone does not satisfy the criteria.

The SNA scheme in schools was put in place for children and young adults with special educational needs who, without support, would otherwise not be able to attend school. Food allergic children do not require an SNA to attend school. Food allergic children with significant care needs relating to other disabilities or medical conditions may require an SNA.

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Appendix 1: Useful Links

- National Pathology Handbook Guidance on laboratory testing for Total IgE and Specific IgE
- Eczema and Food Allergy
- IFAN Milk Ladder
- IFAN Egg Ladder
- IFAN advice for parents and carers
- Early Feeding Guidance from BSACI
- IFAN algorithm: managing an allergic reaction
- IFAN overview of medication in food allergy
- HSE guidance on treatment of anaphylaxis in the community
- How to use Emerade
- Epipen user guide
- Jext video demonstrations
- Anapen patients

Appendix 2: Contact Details Allergy Specialists

Please note that the following emails and phone numbers will not always be accessed on a daily basis, and during periods of annual leave they may be unread for longer periods. There is also a possibility of changes to contact details over time. Therefore do not rely on them for urgent queries- and if there is a delayed response, seek an alternative route.

County	Title	Name	Address	Telephone	Email
Dublin	Paediatric Allergist	Dr Aideen Byrne	Our Ladies Hospital for Sick Children, Crumlin	01 4096013	Aideen.byrne@olchc.ie
Dublin	Paediatric Allergist	Prof Jonathan Hourihane	Children's University Hospital, Temple Street/ CHI at Connolly/ Beacon for Kids, Beacon Hospital Dublin	01-6504665	beaconforkids@beaconhospital.ie
Dublin	Paediatrician with a special interest	Dr John Fitzsimons	Children's University Hospital, Temple Street	01-8784200	
Dublin	Paediatrician with a special interest	Dr David Coghlan	Tallaght University Hospital/ Beacon for Kids, Beacon Hospital Dublin	01-414 2408	beaconforkids@beaconhospital.ie
Dublin	Paediatrician with a special interest	Dr Cathryn O'Carroll	Children's Health Ireland (CHI) at Tallaght University Hospital	01-4142000	
Galway	Paediatrician with a special interest	Dr Edina Moylett,	University Hospital Galway	091-524411	edina.moylett@nuigalway.ie
Galway	GP with special interest	Dr Hilary Allen .	Spiddal Medical Centre, Spiddal, Co Galway/ Suite 36, Galway Clinic, Galway	091-553135	www.drhilaryallen.com

Cork	Paediatrician with a special interest	Dr Juan Trujillo	Cork University Hospital	021-4922000	
Cork	Paediatrician with a special interest	Dr Ioana Maris	Suite 2.2, Consultants Private Clinic, Wilton, Co Cork,	021-4941339	akelly@bonsecours.ie
Cork	GP with a special interest	Dr Ann-Marie McGinley	Weir Family Health Clinic Riverview Shopping Centre Bandon Co Cork	023-8852918	
Waterford	GP with a special interest	Dr Dermot Nolan	Tramore Medical Clinic Summerhill Centre Tramore Co. Waterford	051-386299	
Limerick	GP with a special interest	Dr Clodagh Buckley	Cedarville Medical Centre Abbeyfeale, Co. Limerick	068-32188	
Tipperary	GP with a special interest	Dr Jarlath Healy	Toomevara, Nenagh Co. Tipperary	067-26212