Allergy and intolerance in infants and children

The correct terms of allergy versus intolerance must be understood if we are to diagnose and correctly treat the condition in question, writes **Claire Cullinane**

ALLERGY and intolerance are terms often used interchangeably when infants and children display adverse reactions to a particular food. This article distinguishes between non-allergic (food intolerances) and allergic hypersensitivity reactions to cow's milk.

Adverse reactions to food or 'food hypersensitivity' are defined by reactions triggered by ingestion of food proteins. They can be divided into allergic reactions and food intolerances.

A food allergy occurs when the trigger food has been proven to elicit an abnormal immunological response. The resulting allergy can be immunoglobulin E (IgE) mediated or non-IgE mediated. Although any food can cause a reaction, few foods are responsible for the large majority of the symptoms (ie. milk, eggs, wheat, peanuts, nuts, fish and shellfish).

Food intolerances, on the other hand, may be triggered by a number of factors. Intolerances to food can be caused by a specific component of the food, such as pharmacological agents like monosodium glutamate or histamine found in scombroid fish, or non-specific mast cells activation by irritating foods such as strawberries or additives.[1]

Intolerance to cow's milk can occur for other reasons, such as a permanent or temporary reduction in lactase activity in the brush border of mucosal enterocytes. The resulting malabsorption of the lactose in cow's milk is intolerance, not an allergic reaction. This may cause excessive flatus, explosive diarrhoea, perianal excoriation, abdomen distention and pain. There is no involvement of the immune system.

Cow's milk protein allergy (CMPA) is not to be confused or incorrectly labelled as an intolerance or vice versa. They are two distinct separate disorders. Both fall under the remit of food hypersensitivity but have different pathophysiology and therefore follow a separate treatment pathway. Between 5-15% of infants show symptoms suggesting adverse reactions to cow's milk protein (CMP), while estimates of the prevalence of cow's milk protein allergy (CMPA) vary from 2-7.5%.[2]

The same trigger food can give rise to different symptoms, resulting in an allergic reaction in one patient and signs of intolerance in another. It is vital that those responsible for caring for children have a clear understanding of the difference between food allergy and food intolerance. *Table 1* demonstrates that food hypersensitivity can be divided into immune-mediated reactions (food allergy) and non-immune-mediated reactions (food intolerance).

Food allergic reactions can be broadly divided into IgE-mediated (immediate onset) reactions and non-IgE- mediated (delayed onset) reactions.

Diagnosis of an allergy or an intolerance

A good medical and symptom history in so important in diagnosing any food hypersensitivity whether it is a IgE cow's milk protein allergy, a non-IgE mediated cow's milk protein allergy or an intolerance.

Cow's milk allergy (CMA)

Diagnosing CMA is not always straightforward. The key to diagnosis rests on obtaining a good history backed by appropriate tests.

IgE-mediated CMA is diagnosed by a clear clinical history followed by skin prick testing and measurement of specific serum IgE levels(SpIgE). It must be remembered that laboratory investigations are not diagnostic but can support a diagnosis made on clinical grounds. So always start off the consult with taking that good history. It is very often the case that the clinical history will alert you as to whether you are dealing with an allergy (IgE or non-IgE mediated) or an intolerance. An elimination diet and a subsequent food challenge confirms diagnosis.

Unfortunately, there is no one symptom that is characteristic for CMPA. Symptoms can include pruritus, urticaria, angio-oedema, vomiting, diarrhoea, abdominal cramps, respiratory difficulty, wheezing, hypotension, syncope, shock. Symptoms will appear within the first 20 minutes to a maximum of two hours of eating the offending allergen.

Allergic-looking rashes can be caused by a viral infection, for instance, so the carefully taken history is crucial.

Non-IgE mediated CMA is somewhat more challenging. These are more associated with delayed gastrointestinal and skin symptoms.

Gastro-oesophageal reflux, gastritis, colitis, constipation and eczema fall under the heading of a non-IgE mediated food allergy. Skin prick tests and SpIgE will be negative. Therefore, an elimination diet is used as the main diagnostic tool. If the child improves on the elimination diet then that is your diagnosis. Unsupervised restrictive diets can result in nutritional deficiency so this needs to be undertaken in conjunction with a paediatric dietician.

Intolerance

The exact nature of an intolerance can be difficult to determine: the reaction may be transient – it may be triggered today and not tomorrow; it may depend on the amount of the food consumed. One such intolerance that we mentioned above is lactose intolerance.

A trial of a lactose-free diet is useful in primary lactose intolerance, but this is a very unusual condition. Lactose containing foods are eliminated and then slowly and incrementally reintroduced to test tolerance.

The key to diagnosis is in the history. Before any testing is to be considered a clear clinical history must first be undertaken. Points

Sponsored by an unrestricted grant from SMA Nutrition

in the history should include:

- Suspected foods
- Time between ingestion and reaction
- Amount of food needed to cause a reaction
- Frequency and reproducibility of reactions
- Signs and symptoms
- Could there have been any cross contamination of foods?
- The location of the reaction.

What to do next for CMPA infants

Treatment is the removal of the offending allergen and it should be clear that breast is best! In comparison to cow's milk formula-fed infants, exclusive breastfeeding during the first four to six months reduces the risk for CMPA and most severe allergic manifestations during early infancy. Despite the many advances in the modification of cow's milk formulae, human breast milk remains unchallenged as the 'gold standard' infant milk.[4]

The mainstay of treatment for CMPA infants (IgE and non-IgE mediated) is avoidance of all CMP (this includes CMP derived infant formulas and other dairy products). The requirement for complete milk avoidance is very much dependent on the nature of the individuals child's allergy.[5]

While the majority of children with either IgE or non-IgE- mediated reactions should avoid CMP completely, a significant number may tolerate a small amount of extensively heated (baked) dairy. This is dairy that is baked in the oven in a biscuit or a cake.

A small percentage of babies are affected by the cow's milk protein present in the breast milk due to the mother's diet. If this is the case, the mother is advised to avoid dairy products in her own diet while continuing to breastfeed. If there are no signs or symptoms present in the baby there is no reason for the mother to commence a dairy free diet.

In the absence of human milk, a hypoallergenic infant formula will need to be selected. Hypoallergenic formulas can be broken down into two types: an extensively hydrolysed formula (EHF), such as Nutramigen, Aptamil pepti, or an amino acid formula (AAF) such as Neocate, Nutramigen AA.

While an EHF is suitable for the majority of CMPA infants, 2-10% of CMPA infants with an IgE-mediated disease continue to react to EHF and will require an AAF.[6]

Use of other mammals milk

It is commonly believed that non-dairy mammalian milks such as goat's, ewe's, mare's and donkey's milk provide an acceptable alternate infant formula for use in CMPA infants. However virtually all cow's milk allergic patients suffer a cross reactivity to ewe and goat's milk and in addition, these milk varieties have an inadequate nutritional composition to suit the infant's needs and can cause for example, megaloblastic anaemia through folic acid deficiency.

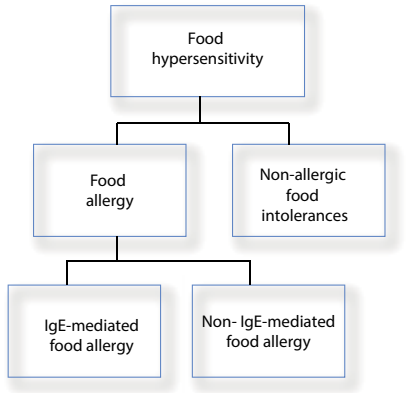
What about soy formula?

Before the availability of hypoallergenic formulae, the only alternative to CMP-based milk for infants with CMPA, were derived from soy. Soya milk is not recommended for primary prevention of CMPA or for nutritional support of CMPA infants under six months.

Recent concerns (based on animal studies) relate to the possible effects of soy on young infants due to phytoestrogens but current medical advice is that soya can be used as a cow's milk substitute after six months of age.[7]

Table 1

Classification of food hypersensitivity[3]



Treatment of IgE-mediated reactions

Reactions of a mild nature involving the skin or the upper respiratory tract, ie. rhinitis, typically settle spontaneously or with the administration of a non-sedating antihistamine. If the case of anaphylaxis, prompt administration of intramuscular adrenaline is the first line of treatment.

Follow up and development of tolerance

The natural history of both IgE and non-IgE- mediated reactions is for the development of tolerance during childhood. The follow up of cow's milk allergic patients is important to ensure a nutritionally complete diet, reinforce avoidance advice, to revise the management of allergic reactions and to assess for the development of tolerance.[8]

In the case of non-IgE- mediated allergy a history of uneventful dietary inclusion of the previous offending food confirms tolerance. In the case of IgE-mediated CMPA, the timing of reintroduction usually requires a hospital challenge.

Adverse reactions to food encompass a diverse range of conditions ranging from lactose intolerance to life threatening IgE-mediated anaphylaxis. A good medical and symptom history in so important in diagnosing any food hypersensitivity. The correct terms of allergy versus intolerance must be understood and adhered to if we are to diagnose and correctly treat the condition in question.

Management is avoidance of the offending food. This must be carried out in conjunction with careful dietary supervision to ensure that nutrition is not compromised. Parents and carers need to be educated and empowered to be able to recognise and respond appropriately to reactions when they occur.

Claire Cullinane is a paediatric allergy nurse with the Department of Paediatrics and Child Health in UCC

References

1. Sampson HA, Burks AW. Mechanisms of food allergy. Annu Rev Nutr 1996; 16: 161-77

2. Host A. Frequency of cow's milk allergy in childhood. Ann Allergy Immunol 2002; 89 (suppl 1): 33-7

3. Johansson SG, Hourihane JO, Bousquet J, Bruijnzee-Koomen C, Dreborg S, Haahtela T, et al. A revised nomenclature for allergy. An EACCI position statement from the EACCI nomenclature task force. Allergy 2001; 56(9): 813-24

4. Saarinen UM, Kajosaari M. Breastfeeding as prophylaxis against atopic disease: prospective follow up study until 17 years old. Lancet 1995; 346(8982): 1065-9

5. 75. Hill DJ, Bannister DG, Hosking CS, et al. Cow milk allergy within the spectrum of atopic disorders. Clin Exp Allergy 1994; 24: 1137-43

6. De Boissieu D, Matarazzo P, Dopont C. Allergy to extensively hydrolyzed cow's milk proteins in infants: identification and treatment with an amino acid based formula. J Pediatr 1997; 131: 744-7

7. Scientific Advisory Committee on Nutrition. Soy Based Infant Formula. SMCN/03/10.2003.

8. Zapatero L, Alonso E, Fuentes V, et al. Oral desensitization in children with cow's milk allergy. J Investig Allergol Clin Immunol 2008; 18: 389-96