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INFANT COWS' MILK ALLERGY AND INTOLERANCE

According to the World Allergy Organisation's (WAO) definition of adverse reactions to food, an allergic reaction is where the immune system is involved in the reaction. The WAO does not have a definition of food intolerance, but instead talks of non-allergic food hypersensitivity (1).

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Whilst we are encouraged to use these terms to help clarify adverse reactions to food, the general public and many healthcare professionals not working in the allergy field, still use the terms 'food allergy' and 'food intolerance'. In these circumstances, the term 'food allergy' is used to describe a reaction that is immediate, often severe and, if a blood test or skin prick test were to be carried out, they would give a 'positive' result, showing the presence of the allergy antibody IgE. The term 'food intolerance' would be used to describe all other reactions to food.

Whilst using terms in this way does have a certain degree of consensus, it makes it difficult to interpret research results and also to apply the information and direction found in position statements and diagnostic and treatment guidelines which use the WAO approved nomenclature.

In this article the term 'milk allergy' will be used to mean a reaction that involves the immune system (with or without the presence of IgE) and the term 'milk intolerance' will apply to all other reactions that can be caused by enzyme deficiencies, pharmacological agents and naturally occurring substances.

PREVALENCE OF COWS' MILK ALLERGY AND INTOLERANCE

As was explained in the article Adverse reactions to food in childhood in the February issue of NHD (page 9), the number of infants perceived to have an adverse reaction to food is much higher than the number who have been clinically diagnosed with such a condition and the same is true for milk allergy and intolerance. The only meta-analysis that looks at the results from a plethora of studies on milk reactions in pre-schoolers, puts the self-reported prevalence at between 1.0 and 17.5% with the prevalence of children with a food challenge confirmed milk reaction as between 0 and 3.0% (2).

There is a belief that rates of reactions to cows' milk in infants varies geographically (3) with increased prevalence in the Netherlands, UK, Spain and Germany compared to other countries. It is not clear, however, whether these differences reflect true prevalence or are a result of methodological differences between studies. To address this, the European commission launched the EuroPrevall project (www.europrevall.org) in 2005 and its first results will be the prevalence of self-reported and food challenge confirmed reactions to food (including milk) in infants up to the age of 36 months (4).

CLINICAL PREVALENCE OF COWS' MILK ALLERGY AND INTOLERANCE

The symptoms of infants reacting to cow's milk can be very varied. For those infants with a food allergy, the symptoms can be immediate or late onset. For immediate onset cow's milk allergy, the symptoms can involve the gastrointestinal tract and can include nausea, vomiting, diarrhoea, gastro-intestinal pain and possibly bloody stools. Reactions can elicit in other organs such as the skin (with urticaria, rashes, eczema, flushing and angio-oedema) and the respiratory tract (with rhinitis, wheeze and more seriously chest tightness). Immediate onset reactions can involve whole body systems which can result in anaphylaxis.

Late onset reactions are those that develop from one hour after ingestion up to a few days. They most commonly manifest in the gastrointestinal tract (with gastro-oesophageal reflux disease, eosinophilic conditions, chronic abdominal pain, constipation, diarrhoea, malabsorption and failure

Table 1: Clinical recommendations for which replacement formula to use for IgE mediated cows' milk allergy (3)

Recommendation 7.1	In children with IgE mediated cows' milk allergy, at high risk of anaphylactic reactions, amino acid formula should be used in preference to extensively hydrolysed milk formula	Conditional recommendation/ very low quality evidence
Recommendation 7.2	In children with IgE mediated cows' milk allergy, at low risk of anaphylactic reactions, extensively hydrolysed milk formula should be used in preference to amino acid formula	Conditional recommendation/ very low quality evidence
Recommendation 7.3	In children with IgE mediated cows' milk allergy extensively hydrolysed formula should be used in preference to soy formula	Conditional recommendation/ very low quality evidence
Recommendation 7.4	In children with IgE mediated cows' milk allergy extensively hydrolysed formula should be used in preference to extensively hydrolysed rice formula	Conditional recommendation/ very low quality evidence

to thrive), but cutaneous reactions also occur (most commonly eczema).

Food intolerance to cows' milk in infants again is most likely to manifest itself via the gastro-intestinal tract (specifically lactose intolerance), but as with early and late onset allergic reactions to cows' milk, they can cause cutaneous reactions by way of contact dermatitis.

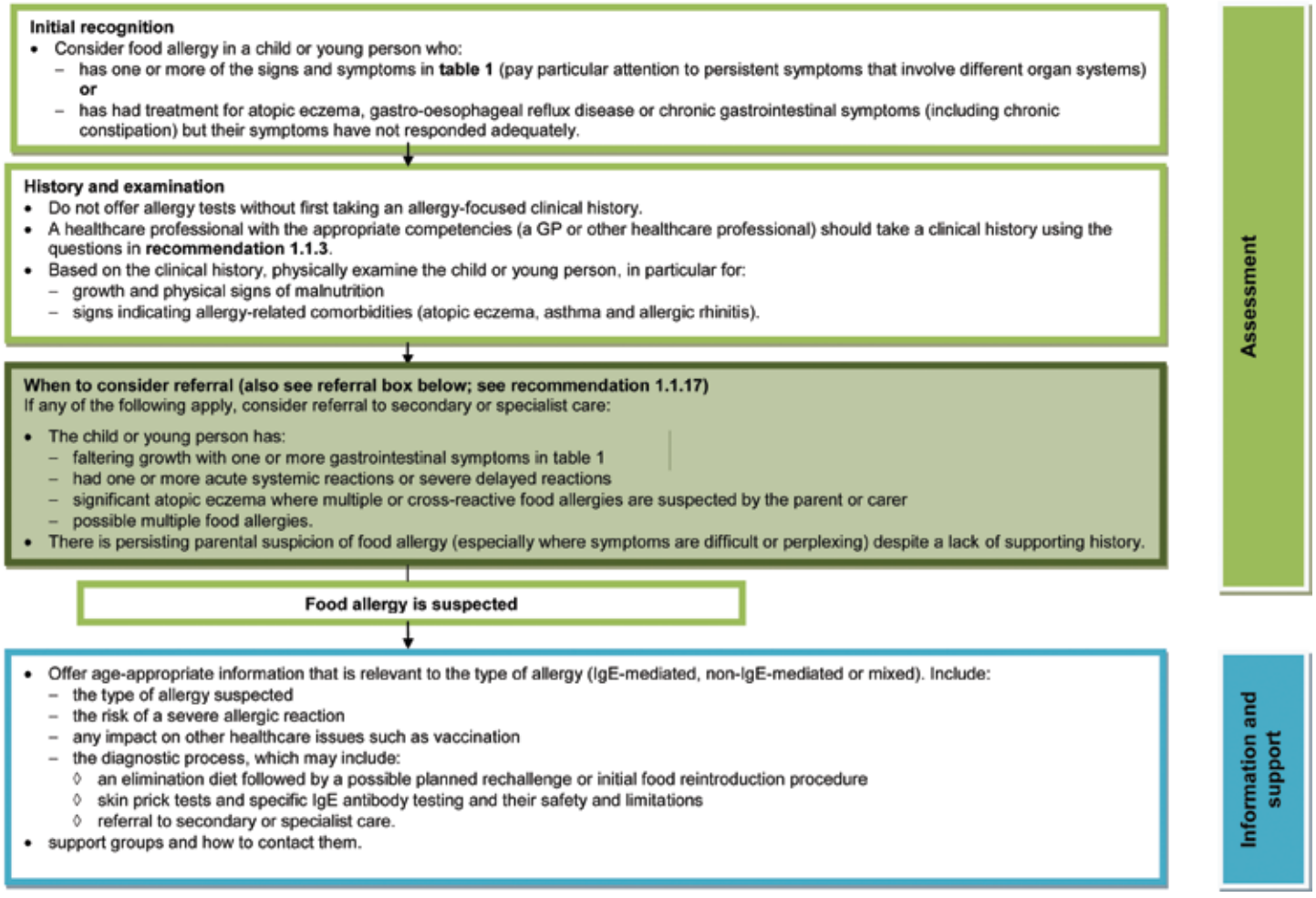
DIAGNOSIS

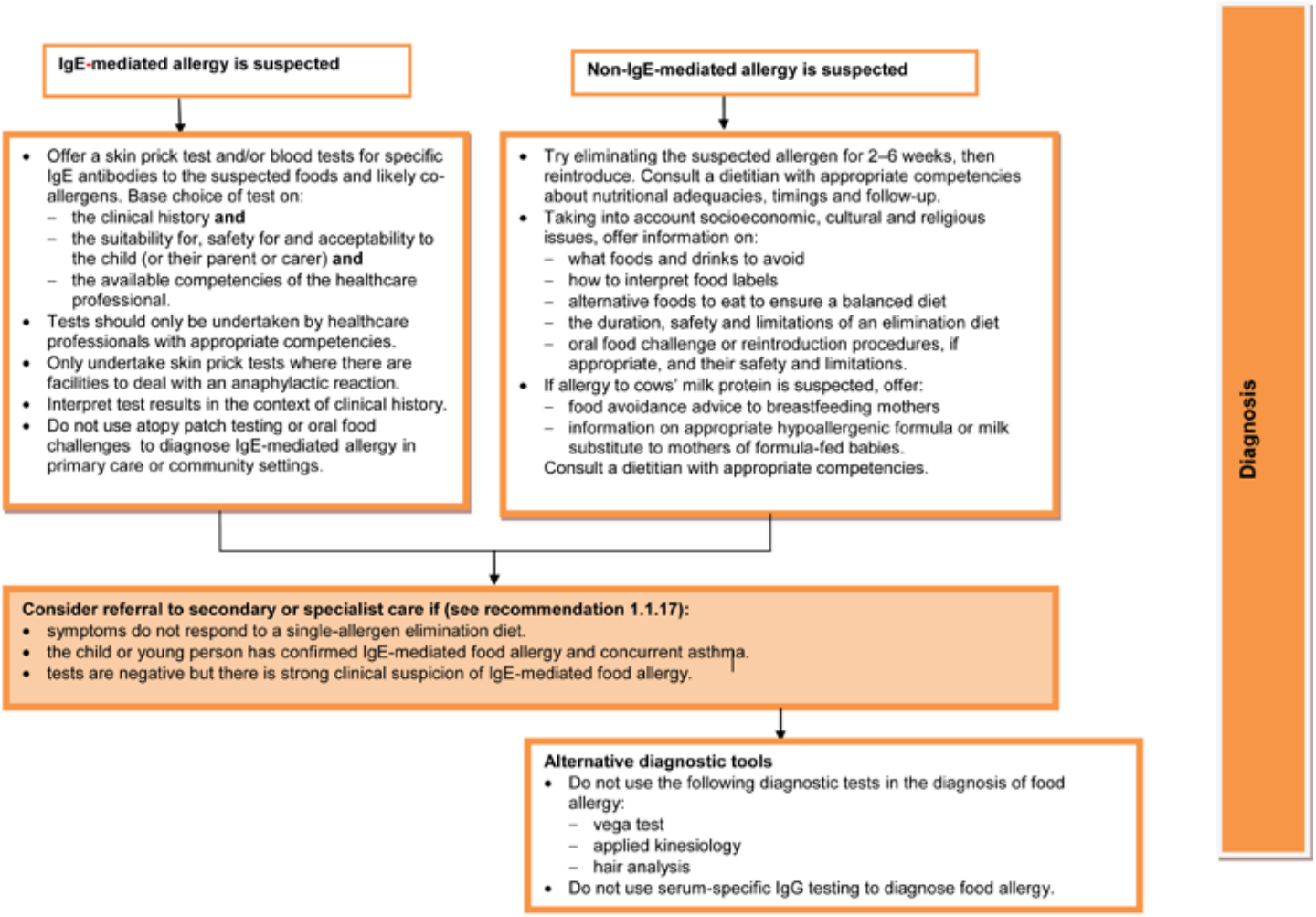
The diagnosis of an infant with food allergy starts with suspicion, with an accurate clinical history providing the required elements to progress towards a firm diagnosis. A full and detailed history is always the first stage in diagnosis and questions that elicit relevant details, such as the nature of the reaction, time between ingestion and symptoms, as well as the frequency of reactions, all paint a picture of the condition. Immediate reactions are most likely to be due to the actions of IgE and so blood tests and skin prick tests to demonstrate the presence of IgE to cow's milk are indicated. But in primary care, these facilities may not always be available, so a period of milk avoidance may be the quickest way to progress to a diagnosis.

Where the reaction is late onset, then a clinical history can also help ascertain whether the reaction may be due to an enzyme deficiency (specifically lactose deficiency), which can be confirmed by the presence of reducing substances in the stool. Often, when the symptoms are chronic, the only way to confirm a reaction to milk is to remove it from the diet to see if symptoms improve and then to reintroduce it to see if the symptoms return.

NICE guidelines on how to diagnose food allergy in children and young adults have recently been published and the steps outlined in the document are applicable to allergic reactions to cows' milk seen in infants. Their recommendations can be divided into three sections, the first step details the assessment, the second

Figure 1: Care pathway





what information and support should be offered in the diagnostic process and the third the actions needed to make the diagnosis (5). This care pathway is shown in Figure 1.

TREATMENT

Unfortunately, the NICE guidelines did not consider treatment options for food allergy. Treatment always involves the removal of the offending food and this is the case for cows' milk reactions. Under the age of two years, a cows' milk substitute of adequate nutritional value is required. Which type of cows' milk substitute should be used is dependent on the symptoms, the age of the infant and their current diet. There have been a number of recommendations and consensuses made for the treatment of cows' milk allergy and these are detailed in the WAO position paper on diagnosis and rationale in cows' milk protein allergy (3). As well as detailing these recommendations, this position paper made a series of clinical recommendations concerning which replacement formula should be used for infants with IgE mediated cows' milk allergy. These recommendations are made in Table 1 (shown on the previous page). No recommendations were made for which formulae should be used in non-IgE mediated food allergy or in food intolerances, but the paper did state that there was a need for 'rigorously designed and executed' randomised trials comparing different types of formula for the treatment of food allergy.

In addition to choosing the most appropriate replacement cow's milk product, it needs to be ensured that the infant receives a varied diet appropriate to its age and development and this information needs to be provided to the infant's carer by a registered dietitian with the appropriate clinical competencies to deliver individually tailored dietary exclusion advice.

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References: 1. Vandenplas Y *et al.* Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Arch Dis Child* 2007; 92:902–908. **2.** Taylor R *et al.* Cost-effectiveness of using an extensively hydrolysed formula compared to an amino acid formula as first-line treatment for cow milk allergy in the UK. *Pediatric Allergy Immunology* 2011: 1–10. **3.** MIMS, January 2012. **4.** Birch E *et al.* The DIAMOND (DHA Intake And Measurement Of Neural Development) Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. *Am J Clin Nutr* 2010; 10: 1–12. **5.** Drover J *et al.* Cognitive function in 18-month-old term infants of the DIAMOND study: a randomized, controlled clinical trial with multiple dietary levels of docosahexanoic acid. *Early human development* 2012.

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Questions relating to: *Infant cows' milk allergy and intolerance*
Type your answers below and then **print for your records.** Alternatively print and complete answers by hand.

Q.1	What reactions can be described as 'food allergy'?
A	
Q.2	In this article, what is the difference between 'milk allergy' and 'milk intolerance'?
A	
Q.3	What are the symptoms of immediate onset cows' milk allergy?
A	
Q.4	What late onset reactions can develop?
A	
Q.5	NICE guidelines on how to diagnose food allergy can be divided into three steps. Please describe these three recommendations.
A	
Q.6	What is the treatment for children under the age of two?
A	
Q.7	The type of cows' milk substitute used is dependent on what?
A	
Q.8	What is the WAO position paper recommendation for children with IgE mediated cows' milk allergy at high risk of anaphylactic reactions?
A	
Q.9	Within the assessment phase of the care pathway detailed in the NICE guidance, describe four considerations that may initiate a referral to secondary or specialist care.
A	

Please type extra notes here . . .