

# Learning files (Reprint)

# Focus on infant food allergy

# Cow's milk protein allergy and other food hypersensitivities in infants

**Dr Carina Venter** reviews the diagnosis and management of food hypersensitivity, including cow's milk protein allergy, in infants and young children

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#### ABSTRACT

Food hypersensitivity (FHS) is the umbrella term used to describe both food allergy, which involves the immune system, and food intolerances, which do not. It is therefore important that the diagnosis is made by a specialist health care professional such as a paediatrician or allergist. Some experienced dietitians and health visitors may be able to assist in making a diagnosis.

The diagnostic work-up includes a medical history and blood tests/skin tests (where applicable). A food and symptom diary followed by a special test diet to identify the foods causing the infant's symptoms may also be needed. Once a diagnosis is made, dietary advice should be given to eliminate or reduce the intake of the offending foods. For cow's milk hypersensitivity in infants, this will include choosing the most appropriate specialised infant formula.

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#### Key words:

food allergy; food intolerance; cow's milk protein allergy; lactose intolerance; diagnosis; management

#### Introduction

It is not uncommon for parents to believe that their infants or children are allergic or intolerant to a food, which in the majority of cases will not be confirmed by a medical diagnosis. False negative diagnoses can lead to the risk of ongoing symptoms with further and possibly severe reactions. False positive diagnoses, on the other hand, can lead to unnecessary restrictions on lifestyle and possible diseases from nutrient restriction<sup>1.3</sup>. For some of those with a true diagnosis, these allergies or intolerances could be life-threatening or have a substantial impact on the quality of life. Appropriate dietary counselling and advice is needed to reduce the burden on the health system, as well as for the health and safety of the infant and child.

#### Nomenclature

In 2004 the European Academy for Allergy and Clinical Immunology (EAACI) and the World Health Organization (WHO)<sup>4</sup> published a guidance document for the nomenclature used in allergic diseases. This identifies food hypersensitivity as the umbrella term for food allergy and non-allergic food hypersensitivity (food intolerance). Food allergy is distinguished from other adverse reactions to food by a mechanism involving the immune system, whereas food intolerance does not involve the immune system. According to the type of reaction, children with food hypersensitivity will present with a specific clinical picture. In the case of cow's milk hypersensitivity, for example, they may present with immunoglobulin E (IgE)-mediated symptoms such as urticaria or angiodema, and also with non-IgE-mediated gastrointestinal symptoms including food protein enteropathy or non-allergic FHS such as lactose intolerance (see *Figure 1*).

#### **Prevalence**

Food hypersensitivity (FHS) usually manifests in early childhood and is caused mainly by eight foods: cow's milk, hen's egg, soy, peanuts, tree nuts, wheat, fish and shellfish.

The prevalence of FHS in 0–3 year olds ranges between 2.1–  $4.2\%^{6-8}$ . The few studies looking at FHS as a result of cow's milk consumption as a single food show that about 2.5% of children suffer from cow's milk protein allergy<sup>6,9-14</sup>, with 2.0–2.5% in the UK<sup>6,14</sup>.

The prognosis of cow's milk protein allergy is good, with about 45–50% of children having outgrown their allergy at one year of age, 60–75% at two years and 75–90% at three years<sup>6,15</sup>. It is most likely to persist in those with a strong family history of atopy, IgE-mediated reactions, and other food allergies such as to egg, soy, peanut or citrus fruits<sup>15,16</sup>.

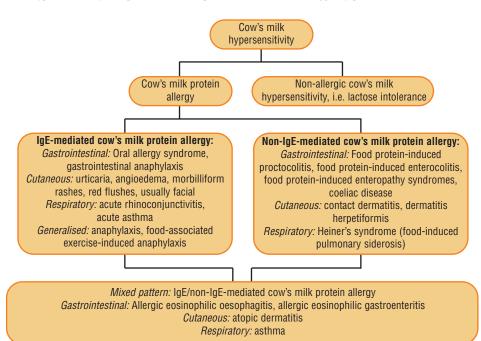


Figure 1: Definition of cow's milk protein allergy (adapted from Venter<sup>5</sup>)

Very little data on the prevalence of lactose intolerance is available, but it is estimated that lactose intolerance affects 6-12% of Caucasians and up to 60-90% of other races<sup>17</sup>. Lactose intolerance is least common among Caucasians and most common among populations in the Far East and Africa<sup>18</sup>.

#### Burden on the health system

Allergic diseases across all ages costs the NHS an estimated \$900 million a year<sup>19</sup>, mostly through prescribed treatments in primary care, representing 10% of the GP prescribing budget. The Health Economy Data as presented by Professor Julian Guest<sup>20</sup>, lecturer in Pharmaceutical Medicine at The University of Surrey, indicates that it costs the NHS \$23.6 million per year to manage cow's milk protein allergy in children. Treating one infant with an extensively hydrolysed formula for one year is estimated to cost \$1,000. Using an amino acid-based formula is estimated to cost \$2,500.

#### **Diagnosis of FHS**

There are many routes to a diagnosis (or false diagnosis) of food allergy and intolerance, such as taking a clinical history, tests and food challenges, and food reintroduction<sup>21</sup>. *Figure 2* summarises the roles of different health care professionals in

the diagnosis and management of FHS.

#### 1. Clinical history

The clinical history is relevant in the diagnosis of IgE-mediated FHS, non-IgE-mediated FHS and non-allergic FHS. Careful history taking and physical examination form the basis of diagnosis of FHS and are explained in *Table 1*.

#### Table 1: The usefulness of a clinical history<sup>21</sup>

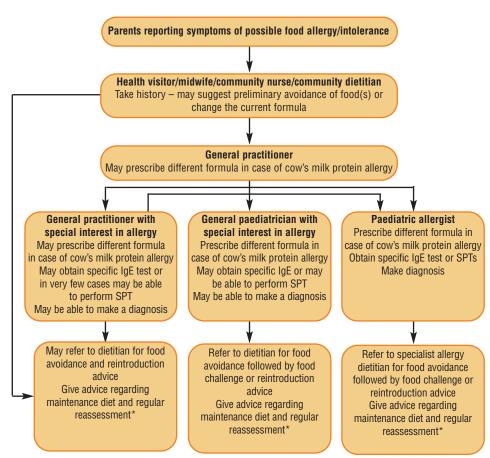
Taking a history can give useful information to the health care professional regarding:

- 1. Which diagnostic tests should be used, e.g. skin prick tests, blood tests or patch tests?
- Whether a food and symptom diary is needed (although it is not always possible to identify the offending food(s) from these diaries alone)
- 3. Which foods should be avoided during the diagnostic test diet?
- 4. Whether a food challenge at home/hospital or gradual introduction of the food(s) may be required

#### 2. Diagnostic tests

#### Skin prick tests and specific IgE tests

Both skin prick tests (SPT) and specific IgE tests are useful in the diagnosis of IgE-mediated food allergy, but not for non-IgE-mediated food allergy or non-allergic FHS. However, in most cases a health care professional cannot make a diagnosis of food allergy based on SPT or blood test alone



\* In some cases emergency medication will need to be discussed with appropriate training by a nurse/allergy nurse/clinician. Allergy nurses/paediatric nurses in some hospitals/centres may perform food challenges.

Figure 2: The role of health care professionals in the diagnosis of food hypersensitivity

(see below). There are now more specific clinical decision measures known as cut-off points for both SPT and specific IgE levels<sup>21</sup> available in the literature. This indicates to clinicians whether a food challenge is needed, and the likelihood of the outcome being positive.

#### Patch tests to food

This test is used in the USA in the diagnosis of allergic eosinophilic disease<sup>22,23</sup> (see *Glossary*) and in Europe for the diagnosis of atopic dermatitis<sup>22,23</sup>, but not generally in the UK. Although there are a few centres where this diagnostic procedure is used, the usefulness of the test is still debated and hence it is not widely used in the UK. The diagnosis and management of eosinophilic disease and food protein enter-opathies are usually dealt with in tertiary centres.

#### 3. Diagnostic exclusion diets followed by a food challenge or food reintroduction

For many patients, particularly those suffering from non-IgE-mediated allergy or non-allergic FHS, diagnosis can only be made by means of a combination of clinical history and dietary investigations (diagnostic exclusion diets) followed by a food challenge or food reintroduction.

Generally, all patients with either a history of immediate symptoms or positive SPT/specific IgE tests should be invited to a controlled setting, i.e. under a doctor's supervision and in the presence of resuscitation equipment, for a food challenge<sup>21</sup>. A diagnostic diet could involve exclusion of a single food such as cow's milk, excluding a number of foods such as cow's milk, hen's egg and wheat for allergic eosinophilic disease<sup>23</sup>, a few foods diet or a specialised infant formula (see *Table 2*).

Dietetic expertise is of particular importance when dealing with infants' and children's diets and progress should be monitored. Food exclusion diets are usually followed for a period of 2–3 weeks, but in diseases with fluctuating patterns such as eczema it may be necessary to continue for up to six weeks.

## Diagnosis of cow's milk hypersensitivity

An international task force has recently published guidelines for the diagnosis and management of cow's milk protein allergy (CMPA) in both breast-fed and formula-fed infants. These need to be adjusted for local use taking into account the health care system and health care provision in each country<sup>24</sup>. For a detailed discussion of this topic, see Meyer<sup>25</sup>.

Current guidelines for the UK are in progress, and are expected to include recommendations on the allergy care pathway including appropriate usage of amino acid-based formula and extensively hydolysed formula. Meanwhile, in the absence of specific guidelines, the decision to use one of these formulae for diagnostic purposes is a clinical one and may differ between different centres, depending on individual clinical preference.

#### Table 2: Different hydrolysed/amino acid-based formulae available in the UK

Formula	Hypoallergenic characteristics	Diagnostic use	ОТС	Prescription
Partially hydrolysed formulae				
Comfort 1 and Comfort 2 (Cow & Gate)	Partially hydrolysed whey	Not recommended for diagnosis or management of cow's milk protein allergy/intolerance	Y	Ν
Easy Digest (Aptamil)	Partially hydrolysed whey	Not recommended for diagnosis or management of cow's milk protein allergy/intolerance	Y	N
Extensively hydrolysed formulae				
Pepti (Aptamil)	Extensively hydrolysed whey Contains prebiotics Contains almost 40% lactose and therefore more palatable – suitable for most children with secondary lactose intolerance, but could be a problem with primary lactose intolerance as it is not lactose-free	To be used in diagnosis and management of CMPA in infants with IgE- or non-IgE-mediated allergy who first presented with symptoms upon introduction of a cow's milk formula without acute, severe reactions and/or growth faltering	Ν	Y
Pepti Junior (Cow & Gate)	Extensively hydrolysed whey Clinically lactose-free Contains 40% medium chain triglycerides	To be used in diagnosis and management of CMPA in infants with IgE- or non-IgE-mediated allergy who first presented with symptoms upon introduction of a cow's milk formula without acute, severe reactions and/or growth faltering Suitable for children with secondary lactose intolerance	N	Y
Nutramigen 1 and 2 (Mead Johnson)	Extensively hydrolysed casein Clinically lactose-free	To be used in diagnosis and management of CMPA in infants with IgE- or non-IgE-mediated allergy who first presented with symptoms upon introduction of a cow's milk formula without acute, severe reactions and/or growth faltering	Y	Y
Pregestimil (Mead Johnson)	Extensively hydrolysed casein Contains 54% medium chain triglycerides (fat malabsorption) Clinically lactose-free	To be used in diagnosis and management of CMPA in infants with IgE- or non-IgE-mediated allergy who first presented with symptoms upon introduction of a cow's milk formula without acute, severe reactions and/or growth faltering	Y	Y
Amino acid-based formula				
Neocate (SHS) Neocate Advance and Neocate Active (over 1 year)	Elemental formula	To be used in diagnosis and management of CMPA in infants with IgE-mediated-allergy:	N N	Y Y
Nutramigen AA		<ol> <li>Who reacted to cow's milk protein in breast milk</li> <li>With history of acute, severe reactions</li> <li>With growth faltering</li> <li>Whose symptoms continued on an extensively hydrolysed formula</li> <li>With multiple food allergies</li> <li>And in infants with non-IgE-mediated allergy:</li> </ol>	N Y	Y N
		<ol> <li>Who reacted to cow's milk protein in breast milk</li> <li>With growth faltering</li> <li>Whose symptoms continued on an extensively hydrolysed formula or despite maternal avoidance of cow's milk</li> <li>Infants suffering with food protein enteropathy syndrome with severe symptoms may also benefit from an amino acid formula (AAF)</li> <li>Infants and children with multiple food allergies</li> <li>Gut impairment conditions requiring an elemental diet, e.g.:         <ul> <li>Short bowel syndrome</li> <li>Maldigestion/malabsorption</li> <li>Intractable diarrhoea</li> <li>Inflammatory diseases of the bowel</li> </ul> </li> </ol>		

#### **Management of FHS**

The input of a dietitian is paramount in the management of food hypersensitivity (see *Table 3* for details of a typical dietary consultation).

#### **Avoidance**

A commonly presenting dilemma in clinical practice is whether to advise patients to strictly avoid the identified food or allow them to have small amounts on a regular basis when tolerated. Blanket advice of complete avoidance is difficult to follow, has a huge impact on quality of life and may not be essential for those children who tolerate small amounts. It could also lead to even more serious reactions in some children if accidental ingestion occurs<sup>26</sup>. Further evidence for the best approach of managing this common problem is needed.

## Table 3: Dietary management of food hypersensitivity

A dietary consultation will include:

- Assessment of height, weight and dietary intake
   Avoidance advice (*Table 4*), including understanding
- food labels
- Advice to ensure the diet is nutritionally adequate by providing information on substitute foods, "free from" lists and special dietary products
  - Advice on practical aspects such as: crosscontamination, eating in restaurants, going on holiday etc. When travelling abroad, translation sheets and useful information can be obtained from www.allergyaction.co.uk or www.allergyuk.org or www.anaphylaxis.org.uk
- 4. Advice on suitable recipes, recipe books and adaptation of family recipes
- 5. Follow-up and reassessment to determine development of tolerance

#### Levels of avoidance

Levels of avoidance required are currently based on:

- 1. The type of FHS from which the patient suffers.
  - Most people with IgE-mediated food allergy need to avoid the food completely, including trace amounts. However, some people are able to tolerate cooked egg even though they react to partially cooked egg (e.g. in lightly cooked scrambled egg) or raw egg (e.g. in mayonnaise)<sup>27</sup>. Some people are also able to tolerate heated milk products (e.g. in waffles and muffins) although they react to drinking pasteurised milk<sup>28</sup>
  - Some people with non-IgE-mediated food allergy may be able to tolerate small amounts of the food to which they are allergic

#### Table 4: Checklist of foods and ingredients to avoid when suffering from food hypersensitivity to a particular food. Source: www.infantandtoddlerforum.org

#### Milk

Butter, Casein, Cheese, Cow/Sheep/Goat milk, Evaporated or Condensed milk, Cream, Curd, Ghee, Lactoglobulin, Lactose, Milk solids, Whey, Yoghurt

#### Egg

Albumin, Dried egg, Egg powder, Egg protein, Egg white and yolk, Frozen egg, Globulin, Lecithin (E322), Livetin, Ovalbumin, Ovoglobulin, Ovomucin, Ovovittellin, Pasteurised egg, Vitellin

#### Wheat

Bran, Cereal filler, Farina, Flour, Starch, Vegetable protein, Wheat, Durum wheat, Semolina

#### Fish

Anchovy (Worcestershire sauce), Aspic, Caviar **Nuts** (peanut or tree nuts)

Pean ut, Peanut oil which could also be called Arachis oil/Hypogeaia, Peanut flour, Peanut protein or any of the tree nuts: Almond, Hazelnut, Walnut, Cashew, Pecan nut, Brazil nut, Pistachio nut, Macadamia nut and Queensland nut

#### Soya

Hydrolysed vegetable protein, Soya lecithin, Soya sauce, Miso, Soya albumin, Soya beans, Soya flour, Soya milk, Soya nuts, Soya oil, Soya proteins, Soya sprouts, Tempeh, Texturised vegetable protein, Tofu

It is important that labels are checked every time a product is bought as manufacturers may change the recipes from time to time. (For more on advising patients how to interpret food labels, see "Frequently Asked Questions" *Box* on p.133.)

- Most people with non-allergic food hypersensitivity (lactose intolerance) will be able to include small amounts of the food in their diet with no adverse effects (see *Table 4*).
- 2. The characteristics of the particular food protein and its degree of allergenicity, e.g. all children with nut allergies need to avoid the food completely, whereas some people with egg allergy may be able to tolerate small amounts of cooked egg
- 3. The natural history of the particular FHS, e.g. most children will outgrow their milk allergy, but only a few will outgrow their peanut allergy (see "Frequently Asked Questions" *Box* on p.133).

## Management of cow's milk hypersensitivity

In addition to management of other FHS, management of cow's milk protein allergy requires the health care professional to choose the appropriate formula (see *Table 2*, *Figure 3* and *Figure 4*).

The European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society of Pediatric Allergy and Clinical Immunology (ESPACI) stipulate that a hypoallergenic formula should be tolerated by 90% of infants with CMPA, with a 95% confidence interval<sup>29</sup>. This means that a formula can be considered as "hypoallergenic" if the vast majority of children with cow's milk protein allergy (about 90%) will tolerate the formula and improve when using it. However, a small percentage (about 10%) may still be symptomatic and will therefore need an amino acid-based formula.

#### Advice for breast-feeding mothers

The first advice to the breast-feeding mother should always be to try avoiding cow's milk or foods containing cow's milk in her own diet. If the maternal elimination diet does not lead to any improvement of symptoms despite very strong evidence of cow's milk protein allergy in the infant, the only alternative may be to advise the mother to stop breast-feeding and to recommend the use of an amino acid-based formula<sup>30</sup>.

## Choosing the most appropriate specialised infant formula

- The choice of product depends on:
  - the age of the infant
  - the level of sensitivity to cow's milk
  - the presence of co-existing allergies
  - the immune mechanism involved (IgE-mediated or non-IgE-mediated)
  - the nutritional status of the infant<sup>31</sup> (see *Table 1*).

#### Extensively hydrolysed formulae and amino acidbased formulae

As already mentioned, there are no clear guidelines in the UK regarding which formula (see *Glossary*) to choose. It is, however, recommended that an amino acid-based formula should be used when dealing with children with growth faltering<sup>32</sup>, severe IgE-mediated cow's milk allergy (history of anaphylaxis or breathing difficulties), severe eczema, or in children suffering from any type of eosinophilic disease or food protein enteropathy.

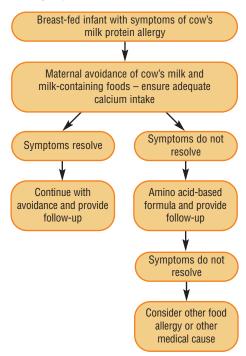


Figure 3: Managing cow's milk protein allergy in a breast-fed infant

For all other types or presentations of cow's milk protein allergies, an extensively hydrolysed formula can be used (see *Figure 3* and *Figure 4*).

## Extensively hydrolysed whey and extensively hydrolysed casein formulae

It is widely accepted that the palatability of extensively hydrolysed whey (eHF-w) formulae (Aptamil Pepti) is superior to extensively hydrolysed casein formulae (eHF-c)<sup>33</sup> (Nutramigen). This is because hydrolysation of the whey protein produces a more palatable product than hydrolysation of the casein protein. (For more on palatability, see "Frequently Asked Questions" *Box* on p.133.)

In addition, prebiotics have recently been added to the eHF-w (Aptamil Pepti), and two studies using this prebiotic mixture indicate an increase in probiotics (bifidobacteria and lactobacilli), reduced growth of potentially harmful bacteria as well as a reduced allergic response and reduced recurrent episodes of upper respiratory tract infection during the first year of life<sup>34,35</sup>. These two industry-funded studies, published in creditable peer-reviewed journals, are accepted as convincing despite being on small numbers of infants. Although the eHF-c may be less allergenic than the eHF-w, both these formulae have been used successfully in clinical trials in infants suffering from: IgE-mediated cow's milk allergy (without a history of anaphylaxis)<sup>36,37</sup>, colic and/or inconsolable crying, and eczema38-40 (see Figure 3 and Figure 4).

#### Soya formulae

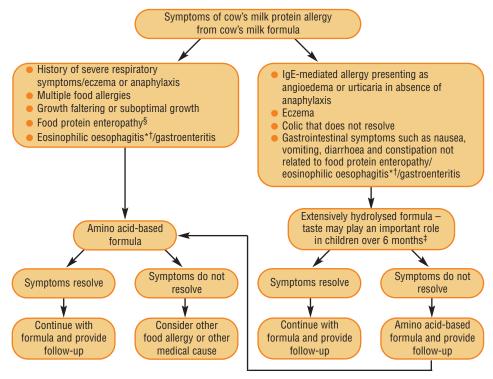
Soya formulae are not recommended for infants under six months of age, due the amount of isoflavones that will be consumed per kg of body weight in this age group and the risk of developing peanut or soya allergy, though these risks may be small<sup>41</sup>. Soya formulae can therefore be used in infants not allergic to soya after the age of six months, although soya is not considered to be the first choice of formula in many allergy centres. This is because infants who are allergic to cow's milk often react to soya as well<sup>41</sup>. Despite these guidelines, the use of soya in the UK is still inappropriately high<sup>20</sup>. Soya formulae, e.g. Infasoy (Cow & Gate); Nurture Soya (Heinz); Isomil (Abbott); Prosobee (Mead Johnson); and Wysoy (SMA) may, however, be given to those infants who refuse extensively hydrolysed formulae.

#### Milk alternatives for children over two years of age

For children over two years of age with a nutritionally sound diet and sound nutritional status, cow's milk alternatives include: soya milk; chufa milk derived from a succulent and trading under the brand name of Tiger White; almond milk; oat milk; coconut milk; quinoa drink (a milk derived from the quinoa plant); or potato milk. Rice milk is no longer recommended for children under the age of four-and-a-half years because of concerns about the arsenic levels in these milks<sup>42</sup>.

#### Cautionary note: goat's and ewe's milk

The use of goat's milk and ewe's milk in the management of cow's milk protein allergy is not



\* Could present as reflux that does not resolve with conventional treatment

† Some clinicians may prefer to use an eHF-c

‡ Some clinicians may choose to use an amino acid-based formula as first-line treatment and then revert to a hydrolysed formula § Often presenting with blood and/or mucus in stools or iron deficiency anaemia

Figure 4: Managing cow's milk protein allergy in a formula-fed infant

recommended because of the high level of crossreactivity between these milks and cow's milk, i.e. about 90% of children allergic to cow's milk will react to goat's milk and ewe's milk as well.

#### Lactose intolerance

Lactose is a carbohydrate present only in mammalian milk (7.2 g/100 ml in mature human milk and 4.7 g/100 ml in cow's milk). Lactose is hydrolysed by lactase to glucose and galactose<sup>43</sup>. Inadequate

## Table 5: Advice on a lactose-free diet<sup>31</sup>. Additional source: www.lactofree.co.uk

- Sources of lactose in pharmaceutical preparations must be avoided if total exclusion is required, which may not apply to the majority of cases
- Butter and hard cheeses can usually be included because their lactose content is either very low or they do not contain lactose at all. In a recent UK study, researchers found undetectable quantities of lactose in Gruyère, Emmental, Jarlsberg, Parmigiano Reggiano and Grana Padano Italian Parmesan, and mature Cheddar cheese from the UK West Country Farmhouse Cheesemakers Association only. Lactosecontaining cheeses include other mature Cheddar cheeses, Gouda and Edam<sup>44</sup>
- Yoghurt and other fermented milk products may also be tolerated by some people who are able to tolerate small amounts of lactose
- Commercially available lactose-reduced milks may be useful for those with temporary or partial lactose intolerance. However, they are not suitable for those with congenital alactasia or infants under two years of age

levels and/or absence of lactase in the gut leads to an inability to break down lactose effectively. This leads to symptoms such as flatulence, bloating, diarrhoea and abdominal pain. Tests for lactose intolerance include the lactose tolerance test or the hydrogen breath test. An elimination diet followed by re-introduction is also a feasible way of diagnosing lactose intolerance; see www.lactofree.co.uk for a regimen that has been reviewed by the British Dietetic Association (BDA) (*Table 5*).

In summary, FHS is an adverse reaction upon ingestion of food which can either be immune mediated or non-immune mediated. The diagnosis of FHS can be difficult as mechanisms are often not completely understood by scientists and health care professionals. Multiple symptoms (which may be of immediate and/or delayed onset) and triggers can also be involved. Furthermore, there is no ideal diagnostic test.

Health care professionals often have different opinions about the use of tests and food challenges, which may be further complicated by the involvement of non-professionals performing nonvalidated tests. (For more on tests advocated by some complementary and alternative medicine sources, see "Frequently Asked Questions" *Box* on p.133.)

A number of health care professionals are involved in the management of FHS, and specialist health care professionals could provide key inform-

ation to ensure appropriate avoidance strategies, while ensuring a nutritionally sound diet.



#### References

 Christie L, Hine RJ, Parker JG, Burks W. Food allergies in children affect nutrient intake and growth. *Journal of the American Dietetic Association* 2002; 102(11): 1648-1651

 Eggesbø M, Botten G, Stigum H. Restricted diets in children with reactions to milk and egg perceived by their parents. *Journal of Pediatrics* 2001; 139(4): 583-587

3. Sicherer SH. Diagnosis and management of childhood food allergy. *Current Problems in Pediatrics* 2001; 31(2): 35-57

 Johansson SG, Bieber T, Dahl R *et al.* Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *Journal of Allergy and Clinical Immunology* 2004; 113(5): 832-836

5. Venter C. Classification and Prevalence of Food Hypersensitivity. In: Skypala I, Venter C (eds). Food Hypersensitivity: Diagnosing and Managing Food Allergies and Intolerance. Oxford: Blackwell Publishing (Wiley-Blackwell), 2009, pp 3-21

 Venter C, Pereira B, Voigt K *et al.* Prevalence and cumulative incidence of food hypersensitivity in the first 3 years of life. *Allergy* 2008; 63(3): 354-359

7. Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. *Pediatric Allergy and Immunology* 2005; 16(7): 567-573

8. Roehr CC, Edenharter G, Reimann S *et al.* Food allergy and nonallergic food hypersensitivity in children and adolescents. *Clinical and Experimental Allergy* 2004; 34(10): 1534-1541

 Bock SA. Prospective appraisal of complaints of adverse reactions to foods in children during the first 3 years of life. *Pediatrics* 1987; 79(5): 683-688

10. Eggesbø M, Botten G, Halvorsen R, Magnus P. The prevalence of CMA/CMPI in young children: the validity of parentally perceived reactions in a population-based study. *Allergy* 2001; 56(5): 393-402

 Gerrard JW, MacKenzie JW, Goluboff N, Garson JZ, Maningas CS. Cow's milk allergy: prevalence and manifestations in an unselected series of newborns. *Acta Paediatrica Scandinavica Supplement* 1973; 234: 1-21

12. Høst A, Halken S. A prospective study of cow milk allergy in Danish infants during the first 3 years of life. Clinical course in relation to clinical and immunological type of hypersensitivity reaction. *Allergy* 1990; 45(8): 587-596

 Schrander JJ, van den Bogart JP, Forget PP, Schrander-Stumpel CT, Kuijten RH, Kester AD. Cow's milk protein intolerance in infants under 1 year of age: a prospective epidemiological study. *European Journal of Pediatrics* 1993; 152(8): 640-644

14. Hide DW, Guyer BM. Cows milk intolerance in Isle of Wight infants. *British Journal of Clinical Practice* 1983; 37(9): 285-287

 Høst A, Jacobsen HP, Halken S, Holmenlund D. The natural history of cow's milk protein allergy/intolerance. *European Journal of Clinical Nutrition* 1995; 49 Suppl 1: S13-S18

16. Iacono G, Cavataio F, Montalto G, Soresi M, Notarbartolo A, Carroccio A. Persistent cow's milk protein intolerance in infants: the changing faces of the same disease. *Clinical and Experimental Allergy* 1998; 28(7): 817-823

 Monsbakken KW, Vandvik PO, Farup PG. Perceived food intolerance in subjects with irritable bowel syndrome – etiology, prevalence and consequences. *European Journal of Clinical Nutrition* 2006; 60(5): 667-672
 Sahi T. Hypolactasia and lactase persistence. Historical review and the terminology. *Scandinavian Journal of Gastroenterology Supplement* 1994; 202: 1-6

19. Allergy: The Unmet Need. A Blueprint for Better Patient Care. A Report of the Royal College of Physicians Working Party on the Provision of Allergy Services in the UK. London: Royal College of Physicians, 2003

20. Guest JF. Resource Implications and Budget Impact of Managing Cow Milk Allergy in the UK. 2008. (Report.) Northwood: Catalyst Health Economics Consultants Ltd UK and Guildford: Postgraduate Medical School, Surrey University

21. Venter C, Vlieg-Boerstra BJ, Carling A. The diagnosis of food hypersensitivity. In: Skypala I, Venter C (eds). Food Hypersensitivity: Diagnosing and Managing Food Allergies and Intolerances. Oxford: Blackwell Publishing (Wiley-Blackwell), 2009, pp. 85-106

22. Niggemann B, Reibel S, Wahn U. The atopy patch test (APT) – a useful tool for the diagnosis of food allergy in children with atopic dermatitis. *Allergy* 2000; 55(3): 281-285

 Spergel JM, Beausoleil JL, Mascarenhas M, Liacouras CA. The use of skin prick tests and patch tests to identify causative foods in eosinophilic esophagitis. *Journal of Allergy and Clinical Immunology* 2002; 109(2): 363-368

24. Vandenplas Y, Koletzko S, Isolauri E *et al.* Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Archives of Disease in Childhood* 2007; 92(10): 902-908

25. Meyer R. New guidelines for managing cow's milk allergy in infants. *Journal of Family Health Care* 2008; 18(1): 20-24

26. Flinterman A E, Knulst A, Meijer Y, Bruijnzeel-Koomen C, Pasmans SG. Acute allergic reactions in children with AEDS after prolonged cow's milk elimination diets. *Allergy* 2006; 61(3): 370-374

 Lemon-Mulé H, Sampson HA, Sicherer SH, Shreffler WG, Noone S, Nowak-Wegrzyn A. Immunologic changes in children with egg allergy ingesting extensively heated egg. *Journal of Allergy and Clinical Immunology* 2008; 122(5): 977-983

 Nowak-Wegrzyn A, Bloom KA, Sicherer SH *et al.* Tolerance to extensively heated milk in children with cow's milk allergy. *Journal of Allergy and Clinical Immunology* 2008; 122(2): 342-347

 Høst A, Halken S. Hypoallergenic formulas – when, to whom and how long: after more than 15 years we know the right indication! *Allergy* 2004; 59 Suppl 78: 45-52

 Restani P, Gaiaschi A, Plebani A *et al*. Evaluation of the presence of bovine proteins in human milk as a possible cause of allergic symptoms in breast-fed children. *Annals of Allergy, Asthma and Immunology* 2000; 84(3): 353-360

 Wright T, Meyer R. Milk and eggs. In: Skypala I, Venter C (eds). Food Hypersensitivity: Diagnosing and Managing Food Allergies and Intolerance. Oxford: Blackwell Publishing (Wiley-Blackwell) 2009, pp. 117-135

32. Niggemann B, Binder C, Dupont C, Hadji S, Arvola T, Isolauri E. Prospective, controlled, multi-center study on the effect of an aminoacid-based formula in infants with cow's milk allergy/intolerance and atopic dermatitis. *Pediatric Allergy and Immunology* 2001; 12(2): 78-82

 Mabin DC, Sykes AE, David TJ. Nutritional content of few foods diet in atopic dermatitis. *Archives of Disease in Childhood* 1995; 73(3): 208-210
 Arslanoglu S, Moro GE, Schmitt J, Tandoi L, Rizzardi S, Boehm G.

Early dietary intervention with a mixture of prebiotic oligosaccharides reduces the incidence of allergic manifestations and infections during the first two years of life. *Journal of Nutrition* 2008; 138(6): 1091-1095

35. Moro G, Arslanoglu S, Stahl B, Jelinek J, Wahn U, Boehm G. A mixture of prebiotic oligosaccharides reduces the incidence of atopic dermatitis during the first six months of age. *Archives of Disease in Childhood* 2006; 91(10): 814-819

 Giampietro PG, Kjellman NI, Oldaeus G, Wouters-Wesseling W, Businco L. Hypoallergenicity of an extensively hydrolyzed whey formula. *Pediatric Allergy and Immunology* 2001; 12(2): 83-86

 Cooke SK, Sampson HA. Allergenic properties of ovomucoid in man. Journal of Immunology 1997; 159(4): 2026-2032

 Høst A, Samuelsson EG. Allergic reactions to raw, pasteurized, and homogenized/pasteurized cow milk: a comparison. A double-blind placebo-controlled study in milk allergic children. *Allergy* 1988; 43(2): 113-118

 Lothe L, Lindberg T. Cow's milk whey protein elicits symptoms of infantile colic in colicky formula-fed infants: a double-blind crossover study. *Pediatrics* 1989; 83(2): 262-266

40. Verwimp JJ, Bindels JG, Barents M, Heymans HS. Symptomatology and growth in infants with cow's milk protein intolerance using two different whey-protein hydrolysate based formulas in a Primary Health Care setting. *European Journal of Clinical Nutrition* 1995; 49 Suppl 1: S39-S48

41. British Dietetic Association. Paediatric Group Position Statement on the Use of Soya Protein for Infants. Birmingham: British Dietetic Association 2003, updated 2009.

http://www.bda.uk.com/resources/statements/SoyaStatement0309.pdf. Electronic citation, accessed 18 June 2009

 Food Standards Agency. Arsenic in rice research published. http://www.food.gov.uk/news/newsarchive/2009/may/arsenicinriceresear ch. 2009. (Electronic citation accessed 18 June 2009)

43. Lomer MC, Parkes GC, Sanderson JD. Review article: lactose intolerance in clinical practice – myths and realities. *Alimentary Pharmacology and Therapeutics* 2008; 27(2): 93-103

44. Portnoi PA, Macdonald A. Determination of the lactose and galactose content of cheese for use in the galactosaemia diet. *Journal of Human Nutrition and Dietetics* 2009; Apr 16. (Epub ahead of print)

45. European Union. Directive 2007/68/EC of the European Parliament amendment of Directive 2000/13/EC. *Official Journal of the European Union* 2007; L310: 311

 Hourihane JO, Roberts SA, Warner JO. Resolution of peanut allergy: case-control study. *British Medical Journal* 1998; 316(7140): 1271-1275
 Fleischer DM, Conover-Walker MK, Christie L, Burks AW, Wood RA. The natural progression of peanut allergy: Resolution and the possibility of recurrence. *Journal of Allergy and Clinical Immunology* 2003; 112(1): 183-189

48. Isolauri E, Sutas Y, Salo MK, Isosomppi R, Kaila M. Elimination diet in cow's milk allergy: risk for impaired growth in young children. *Journal of Pediatrics* 1998; 132(6): 1004-1009 49. Krop J, Lewith GT, Gziut W, Radulescu C. A double blind, randomized, controlled investigation of electrodermal testing in the diagnosis of allergies. *Journal of Alternative and Complementary Medicine* 1997; 3(3): 241-248

 Pothmann R, von Frankenberg S, Hoicke C, Weingarten H, Lüdtke R. [Evaluation of applied kinesiology in nutritional intolerance of childhood]. Forschende Komplementärmedizin und Klassische Naturheilkunde 2001; 8(6): 336-344

51. Zuo XL, Li YQ, Li WJ *et al.* Alterations of food antigen-specific serum immunoglobulins G and E antibodies in patients with irritable bowel syndrome and functional dyspepsia. *Clinical and Experimental Allergy* 2007; 37(6): 823-830

52. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial. *Gut* 2004; 53(10): 1459–1464

#### Further information Infant and Toddler Forum

Introduction to food hypersensitivity. (Factsheet 4.2.) http://www.infantandtoddlerforum.org/article\_42+An+ Introduction+to+Food+Hypersensitivity\_id-23.html

#### General guidelines on the management of food

hypersensitivity. (Factsheet 4.3.) http://www.infantandtoddlerforum.org/article\_43+General+ Guidelines+on+the+Management+of+Food+Hypersensitivity\_ id-24.html

#### **British Dietetic Association**

http://members.bda.uk.com/groups/paediatric/paedstatements oyaprotein.pdf

#### Food challenge guide

Ball H. Food Challenges for Children. A Practical Guide. Leicestershire: Nutrition and Dietetic Service, 11/12 Warren Parkway, Enderby, Leics, 2005.

#### Books

Wright T; Clough J (ed). Food Allergies. (2nd edn.) London: Class Publishing, 2007

Skypala I, Venter C (eds). Food Hypersensitivity: Diagnosing and Managing Food Allergies and Intolerance. Oxford: Blackwell Publishing (Wiley-Blackwell), 2009: pp. 3-21

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The information was correct at the time of publication (July/August 2009) but please note that developments occur rapidly in this field as new evidence becomes available.

The next Learning File will cover upper respiratory tract infections including the role of infant feeding, and will be published in the September/October issue of *JFHC*.

#### **Box: Frequently Asked Questions**

#### 1. Do children outgrow peanut allergy?

It has been assumed that peanut allergy is for life, but latest research indicates that between 10–20% of children could outgrow their allergy<sup>46,47</sup>. However, it is important that the development of tolerance to peanut should be established by means of the appropriate tests and food challenges. To assume that the patient has developed a tolerance without the appropriated testing could potentially lead to severe and even fatal reactions

# 2. Can we trust the information provided in the "allergen box" or "allergen statement" on a food label?

It is a legal requirement to include allergen information in the ingredient list. However, manufacturers are not legally required to list allergen information such as milk-free, egg-free etc. on the label, although some do. Therefore, health care professionals should always advise patients to read and take note of the ingredient list and not to rely on the information box, as this may not give all the pertinent information

**3. Which formula is indicated in infants with food allergies who suffer from growth faltering?** *An amino acid-based formula is the one that is usually recommended*<sup>48</sup>

#### 4. How should we deal with children who refuse

**an infant formula – primarily due to taste?** A major problem in the use of hypoallergenic formulae is their poor taste<sup>31</sup>. However, this is less of an issue for younger infants (less than six months of age) due to their relatively "naïve" taste perception. In addition, research has shown that eHF-w is more palatable than eHF-c<sup>33</sup>. Older infants, and infants who were previously breastfed, commonly reject the introduction of hypoallergenic formula. Therefore:

- Introduce the hypoallergenic formula as soon as possible, or if breast-feeding continue to breast-feed. In addition, make the transition gradual by the incremental mixing of the milks
- 2. Offer the hypoallergenic formula as the only fluid source
- If the infant is above six months, introduce the formula in a feeder beaker that has good flow (avoid beakers with valves as this prolongs contact of the fluid with teeth and could cause dental caries or decay)
- 4. Mask the smell with vanilla essence (a few drops only)
- 5. Commercial milkshake powders should be used as a last option as they could create preference for a "sweet taste". If used, their concentration should be reduced over time until the formula is taken neat.

#### 5. How do we deal with tests advocated by complementary and alternative medicine sources?

Alternative testing for food hypersensitivity can be divided into two main groups<sup>21</sup>:

- Tests which use the body's "energy" such as Vegatesting (electrodermal testing), hair analysis, applied kinesiology, and the pulse test
- 2. Blood analysis tests include IgG testing, Antigen Leukocyte Cellular Antibody Test (ALCAT) and Food Allergen Cellular Test
  - (ALCAT) and Food Allergen Cell (FAC-test)

Scientific literature does not support the use of any of these tests<sup>49,50</sup>. With reference to IgG testing, more research is required to see whether this also relates to food hypersensitivity<sup>51,52</sup>.

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and job title to sarah.monger@keywayspublishing.com.

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#### Answers

- nustard, sesame seed, lupin, sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre expressed as SO2<sup>45</sup> hen's egg, soy, peanuts, tree nuts, wheat, fish and shellfish. Other foods (not mentioned in the text) that are considered a problem in older children and adults include: mussels, celery,
- substances in food other than food proteins, with no involvement of the immune system caused by a protein interacting with the immune system and non-allergic FHS is caused by 2. The main difference between food allergy and non-allergic FHS is that food allergy is
- allergy centres. I his is because intants who are allergic to cow's milk often react to soya as vince of a set of the set of the
- Parmesan, and mature Cheddar cheese from the UK West Country Farmhouse are: Gruyère, Emmental, Jarlsberg, Parmigiano Reggiano and Grana Padano Italian 4. Most people with a lactose intolerance should be able to tolerate butter and hard cheeses as their lactose content is very low. Some cheeses are considered to be lactose-free. These
- yhteen esiwrahto ni seussi evitsepib ronim pnisee te bemie ere bne eonerelotni/yprelle 5. These products are not recommended for diagnosis or management of cow's milk protein

#### Glossarv of definitions used<sup>5</sup>:

Allergic eosinophilic gastroenteritis. Eosinophilic gastroenteritis is characterised by the infiltration of eosinophils of the gastrointestinal tract. Eosinophils can infiltrate either the mucosa (gut wall) or the muscle. The stomach is the organ most commonly affected, followed by the small intestine and the colon.

Allergic eosinophilic oesophagitis. Eosinophilic oesophagitis is an allergic inflammatory condition of the oesophagus, caused by an infiltration of the eosinophils. Symptoms are swallowing difficulty, food impaction, and heartburn.

Amino acid-based formula. Amino acid-based formulae are made up from single amino acids derived from various sources depending on the formula used.

Food allergy and food intolerance. Food allergy is caused by a protein interacting with the immune system, e.g. peanut proteins causing hives and swelling of the lips. Food intolerance is caused by substances in food other than food proteins with no involvement of the immune system, e.g. lactose in

Food protein-induced proctocolitis/enterocolitis syndrome (FPIES). FPIES is a disease of infants and young children that mimics food allergies. Inflammation is caused by the intestinal food proteinactivated lymphocytes and results in increased intestinal permeability, malabsorption, dysmotility, emesis, diarrhoea, pain, and failure to thrive. Hospitalisation for possible severe infection is common in children with FPIES and most children outgrow it by the age of three years.

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characterised by atrophy of the villi, caused by proteins other than gluten and with less extensive villous atrophy than is seen in coeliac disease. It is usually characterised by diarrhoea, mild-to-moderate steatorrhoea and weight loss.

ability to digest lactose. Food protein-induced enteropathy. This is a disease seen in the small bowel of patients, mainly

milk causing diarrhoea due to an inability or reduced

Learning files

These amino acids act as the individual building blocks that make up a protein and are highly unlikely to cause an allergic reaction.

Extensively hydrolysed formula. These formulae are based on cow's milk, soya or pork proteins. The proteins are broken down by means of enzyme splitting and filtration to provide a product with smaller protein segments (called peptides) that are less likely to cause an allergic reaction, i.e. the proteins are basically "chopped up" to provide peptides that are too short to cause allergic reactions in the majority of children with cow's milk

allergy.

#### **Learning Files:** Self-assessed learning Cow's milk allergy and other food hypersensitivities in infants

After reading this Learning File, test your knowledge by answering the questions below and comparing these with the answers (printed upside down on right).

#### Questions

- 1. Which foods are most likely to cause FHS in young children?
- 2. What is the difference between a food allergy and a food intolerance?
- 3. From what age can soya formula be used?
- 4. Should all types of dairy products be avoided on a lactose-free diet?
- 5. Are partially hydrolysed formulae such as Comfort or Easy Digest appropriate to be used for infants with suspected cow's milk protein allergy?

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