Proceedings of the Nutrition Society (2010), **69**, 11–24 doi:10.1017/S0029665109991832
 First published online 15 December 2009

A Meeting of the Nutrition Society, hosted by the Irish Section, was held at Queen's University Belfast on 17–19 June 2009

Symposium on 'Dietary management of disease'

Session 1: Allergic disease
The challenges of managing food hypersensitivity

Carina Venter[1]* and Rosan Meyer[2]
[1]*School of Health Sciences and Social Work, University of Portsmouth, Portsmouth PO1 2RF and The David Hide Asthma and Allergy Research Centre, Newport, Isle of Wight, UK*
[2]*Department of Paediatrics, Imperial College, London, UK*

Food hypersensitivity (FHS) is the umbrella term used for food allergies that involve the immune system and food intolerances that do not involve the immune system. FHS has a huge impact on quality of life and any dietary advice given should aim to minimise this effect. Despite many advances made in diagnosing and managing patients with FHS, the cornerstone of management still remains avoidance of the relevant food. However, a commonly-presenting dilemma in clinical practice is deciding to what extent the food(s) should be avoided. The level of avoidance required is currently based on the type of FHS the patient has, characteristics of the particular food protein and the natural history of the particular FHS. In addition to management of other FHS, management of cow's milk allergy requires the healthcare professional to choose the appropriate formula. Information required by the patient also includes understanding food labels and issues surrounding cross-contamination. In order to ensure that the diet is nutritionally sound, advice should be given about suitable food choices and following a healthy balanced diet, whilst taking into account the dietary restrictions. Practical issues that need to be addressed include going on holiday, travelling and eating away from home. The dietitian plays a crucial role in this process. At present, there are no standardised documents or protocols for the management of FHS and practices differ within and between countries. If adrenaline auto-injectors are prescribed, correct administration should be demonstrated and reviewed on an ongoing basis.

Dietary management: Food allergy: Food intolerance

In 2004 the European Academy for Allergy and Clinical Immunology and WHO published the revised nomenclature for food hypersensitivity (FHS) as guidance for the management of allergic diseases[1]. This guidance publication identifies FHS as the umbrella term for both immune- and non-immune-mediated reactions to food. Food allergy is distinguished from other adverse reactions by an immune-mediated mechanism, whereas food intolerances do not involve the immune system. If the allergic response involves serum IgE, it is classified as an IgE-mediated food allergy, which usually occurs within 2 h of allergen consumption[2]. A non-IgE-mediated food allergic response is thought to be a T-cell-mediated reaction and is often referred to as a delayed food allergy[3] (Fig. 1).

Symptomatology varies according to the type of hypersensitivity reaction (Table 1), and determining the type of reaction, i.e. immunological mechanisms involved[2], assists in the diagnostic work-up, management strategies and the prognosis of the FHS. For example, cow's milk-protein allergy may present with IgE-mediated symptoms such as urticaria or angioedema or non-IgE-mediated gastrointestinal symptoms such as protracted diarrhoea and marked abdominal discomfort[4]. Treatment and prognosis of these two immune responses to cow's milk differ.

FHS usually manifests in early childhood and is mainly caused by eight foods: cow's milk; hen's egg; soyabean; peanuts (*Arachis hypogaea*); tree nuts; wheat; fish; shellfish. The prevalence of FHS in 0–3 year olds ranges

Abbreviations: AAF, amino acid-based formulas; eHF, extensively-hydrolysed formulas; FHS, food hypersensitivity.

***Corresponding author:** Dr Carina Venter, fax +44 2392 844402, email carina.venter@port.ac.uk

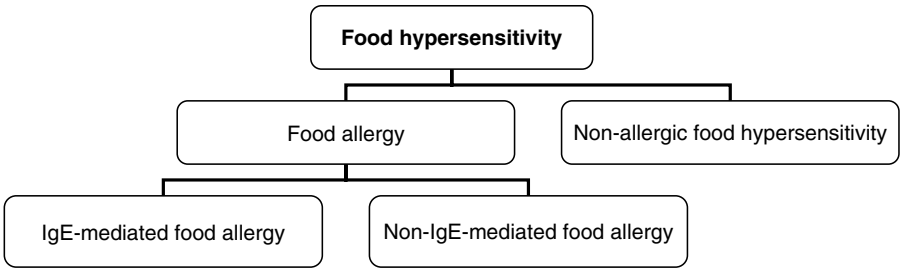

Fig. 1. Proposed nomenclature for food hypersensitivity[1].

Table 1. Clinical presentation of food hypersensitivity (adapted from Venter[28])

	Gastrointestinal	Cutaneous	Respiratory	Generalised
IgE-mediated food allergy	Oral allergy syndrome Gastrointestinal anaphylaxis	Urticaria, angioedema Morbilliform rashes Red flushes	Acute rhino-conjunctivitis Acute asthma	Anaphylaxis, food-dependant exercise-induced anaphylaxis
Non-IgE-mediated food allergy (cell-mediated FHS)	Food-protein-induced proctocolitis, food-protein-induced enterocolitis Food protein-induced enteropathy Coeliac disease	Contact dermatitis, dermatitis herpetiformis	Heiner syndrome (food-induced pulmonary haemosiderosis)	
IgE- and/or non-IgE-mediated (cell-mediated)	Allergic eosinophilic esophagitis, allergic eosinophilic gastroenteritis	Atopic dermatitis	Asthma	
Non-allergic food hypersensitivity	Lactose or disaccharide intolerance, galactosaemia, alcohol intolerance Pharmacological reactions caused by caffeine (jitteriness), biogenic amines such as histamine, tyramine, phenylethylamine, serotonin and tryptamine, alcohol, histamine Additives: monosodium glutamate, artificial colours and some preservatives Substances naturally occurring in foods: benzoates, salicylates and Ni			

between 2·1% and 4·2%[5–7]. The reported prevalence of true food allergies in adults varies between 1·8% and 4%[6,8–12]. The foods implicated in adulthood include wheat, cow's milk, egg, soyabean, citrus, fish and shellfish, pork, alcohol, menthol, additives and glucose, chocolate and cocoa, fruit and vegetables and peanuts and tree nuts.

The annual fiscal burden of allergic disease in the UK is estimated to be £900 × 10[6][13], mostly through prescribed treatments in primary care, which represents 10% of the general practitioners prescribing budget. The diagnosis of FHS is facilitated by a medical history, blood tests, skin prick test or a targeted elimination diet[2]. The use of blood tests and skin prick tests are helpful in the diagnosis of IgE-mediated food allergy and require careful interpretation. The best method for diagnosing IgE-mediated allergy and the only method for non-IgE-mediated allergy and food intolerances (non-allergic FHS) is an elimination diet followed by re-introduction of the relevant food or a food challenge. Dietetic expertise is of particular importance in advising and monitoring of elimination diets[14]. The use of elimination diets for the diagnosis of FHS has previously been discussed[15].

Dietary management of food hypersensitivity

The main goals in the management of FHS are to prevent the occurrence of acute and chronic symptoms. In children it is important to maintain optimal nutrition for growth and development[16]. Conversely, for adults the emphasis is on preventing micronutrient deficiencies and excessive weight loss[17]. These management objectives require regular dietary assessment and monitoring. Whilst the mainstay of treatment is allergen avoidance, more severe reactions may require the use of antihistamines and/or adrenaline. Other novel treatment and management modalities include oral and sublingual immunotherapy[18], anti-IgE treatments[18], Chinese herbal medication[18] and the use of pre- and probiotics[19,20]; however, their routine use requires further research. The present review will focus only on the dietary management of FHS and its challenges.

The EU considers cereals containing wheat and gluten, shellfish, eggs, fish, peanuts and tree nuts, cow's milk, celery, mustard, sesame seeds (*Sesamum indicum*), molluscs, soyabean, lupin (*Lupinus* spp.) and SO_2 as the most common food allergens[21]. Table 2 shows information on the major food allergens.

https://doi.org/10.1017/S0029665109991832 Published online by Cambridge University Press

Table 2. The fourteen major food allergens according to the EU: their sources, terminology used, nutrients, alternatives, mechanisms involved and level of avoidance required

	Sources	Other terms	Nutrients involved	Alternatives	Mechanisms	Level of avoidance
Milk[17,58]	Butter and most fat spreads, cheese, cow's, sheep and goat's milk, evaporated and condensed milk, cream, ghee, yoghurt, ice creams, custard, dairy desserts and manufactured foods using milk or butter in their ingredients	Casein, caseinates, curd, lactoglobulin, lactose, milk solids, whey, buttermilk, milk sugar, whey sugar, whey syrup sweetener	Vitamin A, vitamin D, riboflavin, pantothenic acid, cyanocobalamin, Ca, Mg, phosphate[90]	<6 months: eFH, AAF <2 years: eFH, AAF, soya-based formula >2 years: rice milk†, soya milk, oat milk, chufa milk, potato milk, almond milk, coconut (*Cocos nucifera*) milk, pea (*Pisum sativum*) milk Other foods: milk-free versions of spreading fats, cheese, yoghurts, ice cream and cream	IgE-mediated, non-IgE-mediated or both[29,91]	Range from strict avoidance to tolerance of small amounts, especially extensively heated
Lactose[58]	Similar to cow's milk	Mainly lactose, but some foods may be contaminated	Vitamin A, vitamin D, riboflavin, pantothenic acid, cyanocobalamin, Ca, Mg, phosphate[90]; unless lactose-free milk and yoghurts are used	<1–2 years: lactose-free formulas >1 year: lactose-reduced milk >2 years: lactose-reduced or lactose-free milk, rice milk†, soya milk, oat milk, chufa milk, potato milk, almond milk, coconut milk, pea milk	Non-allergic FHS	Range from strict avoidance to tolerance of small amounts§
Egg[58]	Egg white and yolk, cakes, biscuits, speciality breads, mayonnaise	Albumin, dried egg, egg powder, egg protein, frozen egg, globulin, lecithin (E322), livetin, ovalbumin, ovomucin, ovovitellin, pasteurised egg, vitellin	Riboflavin, biotin, protein, vitamin A, cyanocobalamin vitamin D, vitamin E, pantothenic acid, Se, iodine, folate[90]	Egg replacers Adjust recipes with extra liquid or fruit purees‡ Variety of egg-free products such as mayonnaise, cakes, muffins, puddings and omelette mix	IgE-mediated and/or non-IgE-mediated	Range from strict avoidance to tolerance of certain amounts, especially in cooked or baked form[58]
Wheat[92]	Bread, breakfast cereals, pasta, cakes, biscuits, crackers, cold cooked meat, pies, batter, flour, semolina, cous cous, bottled sauces and gravies	Bran, cereal filler, farina, starch, wheat, durum wheat, semolina, spelt, kamut, wheat bran, wheat gluten, wheat starch, wheat germ oil, hydrolysed wheat protein, triticale, bulgar wheat	Fibre, thiamine, riboflavin, niacin, Ca, Fe, folate if fortified[90]	Maize, rice, potato, cassava (*Manihot esculenta*), yam, quinoa (*Chenopodium quinoa*), millet, gram (chickpea; *Cicer arietinum*), sago, tapioca, amaranth, buckwheat (*Fagopyrum esculentum*) Wheat- and/or gluten-free foods Barley, rye and oats may be tolerated by some individuals with wheat allergy or intolerance Oats may be tolerated by some individuals with coeliac disease[93,94] Use of alternative grains should be individualised and based on tolerance as determined by clinician and/or dietitian	IgE-mediated and non-IgE-mediated wheat allergy Non- allergic FHS Coeliac disease	Range from strict avoidance to tolerance of certain amounts Coeliac disease: strict avoidance of gluten

Table 2 (Continued)

	Sources	Other terms	Nutrients involved	Alternatives	Mechanisms	Level of avoidance
Fish[95]	All types of white and fatty fish, anchovy (Worcester sauce), aspic, caviar, surimi, Caesar salad, Gentleman's Relish, kedgeree, Caponata, fish sauce, paella, bouillabaisse, gumbo Some individuals may tolerate canned fish Fish oil capsules may cause reactions in highly-sensitised individuals		All fish: protein, iodine Fish bones: Ca, P, fluoride Fatty fish: vitamins A and D, *n*-3 PUFA[90]		IgE-mediated food allergy Some individuals may react to high levels of histamine in spoiled fish, e.g. scromboid poisoning or ciguatera poisoning or to the *Anasakis* worm	Usually strict avoidance and reactions may occur in some on inhalation of fish vapours
Shellfish[95]	Crayfish, crab, lobster, shrimp, prawns		Similar nutrients to white fish Crab and mussels: good sources of *n*-3 PUFA Se, Zn, iodine and Cu[90].		IgE-mediated food allergy	Usually strict avoidance
Molluscs[95]	Clams, mussels, oysters, octopus, squid, snails, scallop	Health food preparations such as green-lipped mussel extract, oyster sauce	Varying amounts of protein (scallop), Ca (clam), Zn (oysters) and Fe (clam)		IgE-mediated food allergy	Usually strict avoidance
Peanut (*Arachis hypogaea*)[17,29]	Peanuts, peanut oil, peanut flour, peanut butter, some sprouts, confectionery, frozen desserts, Asian dishes (Indonesian, Malaysian, Thai and Chinese), peanut snacks, trail mix, some rice crackers, some cereal bars, some cookies, some brownies, nut toppings on ice cream, vegetarian and vegan foods, satay sauce, some breakfast cereals, pesto sauce may sometimes contain peanut	Arachis oil, hypogeaia, peanut protein, groundnut, earth nut, monkey nut	Vitamin E, niacin, Mg[90]		IgE-mediated food allergy	Usually strict avoidance
Tree nut[17,29] Almond, hazelnut, walnut, cashew nut, pecan nut, Brazil nut, pistachio nut, macadamia nut, Queensland nut*	Similar foods to peanut, Amaretto contains almond flavour, Worcester sauce (walnuts), korma sauce (almonds)	Hazelnut: filbert, cob nut Macadamia: Queensland nut, candle nut Pecan: hickory nut (Nutmeg, coconut, pine nut and palm nut are not classified as nuts)	Depends on type of nut		IgE-mediated food allergy	Usually strict avoidance
Sesame seed (*Sesamum indicum*)[29]	Sesame seeds, sesame oil e.g. halva, tahini, hummus, seeded bread and rolls, gomashio, Asian foods using sesame oil, Greek, Iranian, Lebanese and Turkish food, Aqua libra		Protein, fats, Vitamin E, Ca, K, P, vitamin B and Fe Avoidance has no marked effect on nutrition		IgE-mediated food allergy	Usually strict avoidance
Celery (*Apium graveolens* var. dulce) and celeriac (*Apium graveolens* var. rapaceum)[96]	Primary allergy: celery and celeriac in its raw, cooked, juiced, canned and dried (celery spice) form[96] Oral allergy syndrome: dried celery and celeriac may be tolerated		Fibre[90] Avoidance has no marked effect on nutrition		IgE-mediated food allergy: primary food allergy or associated with oral allergy syndrome	IgE mediated

Mustard[29]	Mustard, mustard seed, curry powder, pizza, sauces		Mainly fat and protein Avoidance has no marked effect on nutrition		IgE-mediated food allergy	Usually strict avoidance
Sulfite[98]	Present in dried fruits and vegetables, dehydrated potatoes, wine and beer, jams, jellies, pickles, relishes, fruit drinks (cordials, lime, lemon, grape juice), seafood, salads, wine vinegar, beefburgers, sausages[99,100]	(E220–E228) SO_2, potassium bisulfite, potassium metabisulfite, sodium bisulfite, sodium metabisulfite, sodium sulfite		Organic dried fruit, non-prewashed salads, premium-range jams and jellies	Non-allergic FHS	Individual tolerance levels
Soyabean[29]	Soya sauce, soya products, meat substitutes, breads, vegetarian and vegan foods, processed meat e.g. hot dogs, foods labelled as 'diet' and 'high-protein'	Soyabeans, soya flour, soya protein soya gum, soya starch, texturised (or hydrolysed) vegetable protein, soya flavouring, soya lecithin (E322)	Thiamin, riboflavin, pyridoxine, folate, Ca, P, Mg, Fe, Zn, protein, fibre[90]	Cow's milk, rice milk†, oat milk, chufa milk, potato milk, almond milk, coconut milk, pea milk	IgE- or non-IgE mediated or both	Range from strict avoidance to tolerance of certain amounts
Lupin (*Lupinus* spp.)[29]	Often used in mainland Europe in pastries, bread, pizza and lupin seeds in seeded breads		Protein, fat, fibre, thiamin, riboflavin and vitamin E Avoidance has no marked effect on nutrition		IgE-mediated	Usually strict avoidance

eFH, extensively-hydrolysed formula; AAF, amino acid-based formula; FHS, food hypersensitivity.

*Almonds, *Amygdalus communis L.*; hazelnuts, *Corylus avellana*; walnuts, *Juglans regia*; cashews, *Anacardium occidentale*; pecan nuts, *Carya illinoiesis Wangenh. K. Koch*; Brazil nuts, *Bertholletia excelsa*; pistachio nuts *Pistacia vera*; Queensland nuts, *Macadamia ternifolia*.

†Rice milk is not recommended in the UK for children <4·5 years of age[101].

‡One to two teaspoons fruit puree for binding; 1·5 teaspoons water, 1·5 teaspoons oil, one teaspoon baking powder; one teaspoon baking, powder, one teaspoon liquid, one teaspoon vinegar; one packet gelatine, two teaspoons warm water; one teaspoon yeast dissolved in 0·25 cup warm water[58].

§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 have found undetectable quantities of lactose in Gruyere, Emmental, Jarlsberg, Parmigiano Reggiano and Grana Padano Italian Parmesan and mature Cheddar cheese from the UK West Country Farmhouse Cheese Makers Association only and lactose in other mature Cheddar cheeses, Gouda and Edam[103]. Yoghurt and other fermented-milk products may also be tolerated by some individuals who are able to tolerate small amounts of lactose. Commercially-available lactose-reduced milks may be useful for individuals with temporary or partial lactose intolerance; however, they are not suitable for individuals with congenital alactasia or infants <12 months of age.

Many of these foods contribute substantially to dietary adequacy in patients and pose major nutritional challenges in the management of allergic disease. These challenges include: (1) determining the level of food avoidance required; (2) appropriate avoidance of the food; (3) ensuring adequate nutritional intake; (4) assessing and monitoring nutritional status; (5) determining development of tolerance.

Challenge 1: determining the level of avoidance required

The mainstay of treating FHS is the avoidance of the relevant food(s) from the individual's diet. However, a common dilemma in clinical practice is the extent of dietary avoidance. Complete avoidance, including traces of the allergen, is difficult to follow and has a major impact on quality of life[22,23]. This advice may not be essential for those who already tolerate small amounts of the relevant foods; strict avoidance in these patients may lead to serious reactions when accidentally ingested[24].

Levels of avoidance required are currently based on: type of FHS involved; characteristics of the particular food protein; natural history of the particular FHS; the nutritional status of the patient.

Type of food hypersensitivity involved

This level of avoidance relates to the immunological mechanisms involved. Most individuals with IgE-mediated food allergy need to completely avoid the food and even trace amounts of the food. However, some patients are able to tolerate small amounts of the allergen, e.g. extensively-heated egg or milk (i.e. biscuits, cakes), despite reacting to other forms of these foods such as raw egg or pasteurised milk[25,26]. The decision to allow small amounts in food should be made on an individual basis together with an allergist.

In the majority of severe cases of non-IgE-mediated allergy such as severe eczema, food-protein-induced enteropathies and eosininophilic disease complete avoidance of the allergen will be required[27]. However, some individuals with non-IgE-mediated food allergy (i.e. moderate gastrointestinal presentations) may be able to tolerate small amounts of the food to which they are allergic. Tolerance of trace amounts in non-IgE-mediated food allergies has not been defined by published research and should also be managed on an individual basis.

Most individuals with non-allergic food hypersensitivity will be able to include small amounts of the food or substance in their diet with no adverse effects. In these individuals the adverse reactions depend not only on the presence of the food, but also the amount ingested. For example, reactions to histamine-containing foods could be caused by several factors such as: amount of histamine produced and released intrinsically; histamine production by gut bacteria; dietary intake of foods containing or releasing histamine; catabolic enzymes not able to reduce excess histamine within the body[28].

Characteristics of the particular food protein

Individuals with nut allergies are advised to completely avoid all nuts in any form[29], whereas some individuals with egg allergy may be able to tolerate small amounts of well-cooked egg[25].

Natural history of the particular food hypersensitivity

Most children will outgrow their milk allergy at some point during childhood[5,30,31], but only about 20 %[32] will outgrow their nut allergy.

Nutritional status of the patient

Unnecessary avoidance of food allergens can further impair nutritional status.

Challenge 2: appropriate avoidance of the food(s)

Avoidance advice

Healthcare professionals should give patients and/or carers clear guidance about food avoidance to prevent both unnecessary restrictions and accidental exposure to allergens. Table 2 provides a checklist of foods and ingredients to avoid when suffering from food hypersensitivity.

Preventing cross-contamination. In order to prevent cross-contamination individuals should be advised to wash cooking utensils thoroughly, take special care when washing chopping boards or work surfaces and wash hands thoroughly[33]; also, they should not use the same oil for cooking different foods and not to use the same spoon for serving different food[34].

Eating away from home. Eating away from home can be problematic as individuals will not always have reliable ingredient information to assess allergen exposure. It is crucial to ask questions about ingredients and food preparation or possible cross-contamination. If possible, individuals should call ahead and ask to speak with the individual who prepares the food (e.g. chef when going to a restaurant) who can give information about the menu and discuss alternative safe options.

It is quite common for individuals with allergies to carry a 'chef card'[35,36] that outlines the foods that require avoidance; when eating in a restaurant such cards can be very useful. They are available from a variety of distributors across Europe.

The nutritional burden of food avoidance can be important in the growing child[37,38]. It is essential that suitable alternatives or supplements are provided to ensure normal growth. Carers of children with food allergies also benefit from practical advice (i.e. suitable snacks, birthday cakes) for nursery, for school and for children's birthday parties. Carers should also be advised on how to minimise the effect of ostracising the child and how to use emergency medication if prescribed[34]. The dangers of children exchanging food items provided in lunch boxes should also be discussed and clarity should be provided on the exact meaning of specific 'food bans' at the playgroup or school.

https://doi.org/10.1017/S0029665109991832 Published online by Cambridge University Press

Table 3. Useful websites for healthcare professionals managing food hypersensitivity

US sites	UK and European sites
American Academy of Allergy Asthma and Immunology: www.aaaai.org	British Society for Allergy & Clinical Immunology: www.bsaci.org
The Food Allergy & Anaphylaxis Network: www.foodallergy.org	Food Standards Agency: www.foodstandards.gov.uk
Food Allergy Initiative: International Food Information Council: www.foodallergyinitiative.org www.ific.org	Allergy Action: www.allergyaction.co.uk www.allergyuk.org
	The Anaphylaxis Campaign: www.anaphylaxis.org.uk
	European Academy of Allergy and Clinical Immunology: eaaci.net

This approach will be similar for dealing with away-days and school trips.

For adults, managing FHS at work can be challenging. It is important to take suitable food to work to minimise the risk of becoming hungry and having to check foods and food labels at work. Special occasions at work should be dealt with in a similar way to eating away from home.

Going on holiday. Holidays should be an enjoyable occasion, but for those individuals needing to adhere to strict avoidance measures some planning is required. Whether holidays are in the country of origin or abroad, self-catering is in most cases the best option. Some hotels are happy to discuss dietary restrictions and may accommodate nutritional requirements.

For those going on holiday abroad it is advisable to obtain the following information beforehand: ingredients of foods served on the flight, train or boat; where the nearest emergency unit is and the contact details; translation cards can be obtained from a number of sources such as Allergy Action[39] or Allergy UK (British Allergy Foundation)[40]. These translation cards provide information on the patient's FHS in the local language in addition to food ingredients to look out for when travelling.

The Anaphylaxis Campaign (see Table 3) is also able to provide useful information to individuals with food allergies.

Finally, prescribed medication should be carried and a medical alert armband or necklace worn at all times[34]. A letter from a healthcare professional is useful for airlines when carrying these individuals onboard.

Understanding food labels

Food labelling legislation differs across the world and healthcare providers should obtain information relating to domestic food labelling laws, in particular the labelling of food allergens. Individuals should be shown how to read food labels to identify relevant ingredients.

In the EU the food labelling law for pre-packed foods effective from 25 November 2005 was updated in 2007[21]. This legislation requires that all pre-packed food, including alcoholic drinks, sold in the UK or the rest of the EU clearly list all ingredients, including any of the major allergens, even if only present in small amounts.

The '25% rule' has been abolished under the new legislation in which individual components of a compound ingredient making up <25% of the finished product do not have to be listed. However, the EU directive does not abolish 'may contain' statements on labels. Thus, even though an allergen (particularly used for nuts, seeds and milk) is not deliberately included in the food, the manufacturer cannot ensure that the product does not contain traces as a result of, for example, manufacturing other products within the same factory. The Food Standards Agency advises that these statements (advisory labelling) should only be used following a thorough risk assessment and if it is considered that there is a real risk of allergen cross-contamination[41]. Despite this guidance, it has been reported that many families consider the widespread use of 'allergen traces' labelling on pre-packed foods (particularly those aimed at or widely consumed by children) and everyday staples (bread, cereals and ordinary biscuits) to be the major obstacle to leading a normal life[42,43].

A further important point to note about labelling is that allergen statements such as milk-free, egg-free etc. are not compulsory to give, although it is given by some manufacturers[41]. It is therefore prudent not to assume that if there is no allergy statement present on the label that a product is free from the allergenic foods. Healthcare professionals should always advise patients to read and take note of the ingredient list and not to rely on the information box, as this source may not give all the information.

Lifestyle issues arising when avoiding certain foods

Research has indicated that 39% more time is spent on shopping in families with a member who has a food allergy[44]. More importantly, a study has indicated that the quality of life of children with peanut allergy is worse than that of children living with diabetes[22]. Living with dietary restrictions therefore requires substantial changes in lifestyle in order to ensure the appropriate level of avoidance, particularly if complete avoidance of the food(s) is needed. Healthcare professionals can help to minimise the effect on quality of life for both the patient and the family with the provision of information (as discussed earlier).

What can be learned from fatalities?

A report has indicated that only half the individuals who are known to have died from food allergy in the UK had been actually trying to avoid the food implied in their

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death[45]. Foods that have been reported to be associated with fatalities include milk, peanuts, nuts, fish, shellfish, snail, sesame, egg and tomato. It has not been possible to identify the foods in a number of cases. Most of the fatal reactions were found to have happened at home or at a friend's or relative's house, followed by work, school, nursery, in a restaurant, out and about, at camp and at a wedding reception. The food blamed for fatal reactions was reported to be catered, prepared at home, in a package and labelled, sold loose or unlabelled, whole nuts and in three cases unknown.

On the other hand, all fatalities in the USA since 2001 have been reported to have been caused by known allergens[46]. These reactions were reported to have happened at home, a friend's house, at school, restaurants and buffets or when camping. In some cases it was found that the individual did not ask for the ingredients, but in some cases they did ask and were wrongly informed. It was found that the foods involved in the fatalities involved a wide range of foods such as cakes, biscuits, sweets, sauces, ethnic foods and nut mixes or were caused by cross-contamination. Most fatality cases had presented only with mild symptoms in the past.

The most important messages from these two reviews are to always ask about ingredients, to insist that the ingredients are checked, to always carry emergency treatment and to treat any reaction immediately whenever possible.

Challenge 3: ensuring adequate nutritional intake

The nutritional implications of any avoidance diet will depend on a number of factors[17,47].

Frequency of normal consumption of the food(s) and avoidance of particular food group

Avoidance of a single food or type of food that is not eaten regularly (such as kiwi fruit (*Actinidia deliciosa*)) will be of little importance. In contrast, avoidance of a single food or food group that is considered to be a staple food and contributes substantially to nutritional adequacy (such as wheat in adults or cow's milk in children) will be of considerable importance (Table 2).

Frequency of ready-prepared food consumption

In the UK the tendency to cook at home from fresh ingredients has reduced, resulting in an increase in the reliance on ready-made meals and takeaways. This change, which is mainly related to convenience and cost[48], markedly complicates the exclusion of allergens, which often are present in only small amounts (i.e. nuts and soyabean) in manufactured foods. Wheat allergy poses a particular problem, as it is not only considered to be a staple food but is also used in a large number of commercial products such as bread, cereals, cakes and biscuits and pasta[49].

Additional food avoidance not related to food hypersensitivity

Patients requiring special attention are those who exclude foods for cultural, religious (e.g. kosher foods) or ethical reasons and those with particular food preferences in addition to their FHS. For example, a vegan who is allergic to nuts will need considerably more nutritional input to assure dietary adequacy.

The number of allergens avoided

The more foods that require to be avoided, the more the nutritional quality of the diet is affected[15]. This position is related to the limited availability of nutritionally-suitable alternatives, with a consequent adverse effect on dietary adequacy. Avoidance of a large number of foods increases the likelihood of the individual losing their interest in food, which may have an additional impact on food intake, particularly in children[17].

Period of elimination

The nutritional impact of a short-term exclusion diet (4–6 weeks) is likely to be minimal. However, if the exclusion diet is likely to last for a longer period, i.e. for life, the impact on a patient's nutritional status could more be important[17].

Nutrient content of major food allergens and how to ensure adequate intake

In order to ensure a nutritionally-adequate diet whilst avoiding some foods from their diets, individuals need the following information[17]: most important nutrients in the food or food group that are being avoided (Table 2); a list of alternative foods high in a particular nutrient(s) to substitute nutrients that are omitted from the diet as a result of the FHS; nutritional supplements, especially in the infant and growing child with an allergy[37,50].

Further points that need to be taken into account to ensure nutritional adequacy include: advice on suitable foods; special considerations for children with cow's milk-protein allergy.

Advice on suitable foods. There are a number of ways to identify suitable foods for an individual with an allergy[34]. Some retailers and manufacturers provide 'free from lists' for their own brands. This information is very useful and can often be obtained from the retailer or manufacturer. Although specifically-manufactured food products are available for patients with allergies, many everyday foods are suitable for individuals with FHS. Healthcare professionals, in particular dietitians, can assist patients to modify recipes suitable for their FHS or obtain an 'allergy-free' recipe book with trialled recipes. However, many family recipes will still be suitable for a restricted diet, possibly with minor adaptations. Table 3 summarises useful websites for healthcare professionals managing FHS.

Special considerations for children with cow's milk-protein allergy. The management of cow's milk allergy requires advice for breast-feeding mothers and/or assistance in choosing an appropriate hypoallergenic formula

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where mothers' choose not to breast-feed or need a supplement to breast milk[51].

Mothers who breast-feed should be encouraged to continue and a maternal cow's milk-exclusion diet is therefore the first line of treatment. If the maternal elimination diet does not lead to any symptom improvement, a normal diet should be resumed or other allergies need to be considered. Special attention should be given to infants with atopic dermatitis, proctitis and enterocolitis[27], as components other than bovine β-lactoglobulin or casein have been shown to induce allergic symptoms in children who are exclusively breast-fed and may therefore continue to exhibit allergic symptoms[52]. In some cases an amino acid-based formula (AAF) may be indicated despite careful avoidance of cow's milk or other relevant foods. This decision to stop breast-feeding should not be taken lightly as it is difficult to reverse. A discussion with the mother and an appropriately-qualified healthcare professional is indicated.

Formulas that are suitable for the management of cow's milk allergy are extensively-hydrolysed formulas (eFH) and AAF. The European Society of Paediatric Gastroenterology, Hepatology and Nutrition and the European Academy of Allergy and Clinical Immunology stipulate that 'dietary products for treatment of cow's milk protein allergy in infants should be tolerated by at least 90% (with 95% confidence) of infants with documented cow's milk protein allergy'[53].

A number of studies have evaluated the use of eHF based on casein and whey and AAF for the management of cow's milk allergy. A systematic review has indicated that eHF and AAF are equally effective in relieving the symptoms of cow's milk allergy in young children[27]. However, infants suffering from non-IgE-mediated food-induced gastro-enterocolitisproctitis syndromes with failure to thrive, severe eczema and severe reflux oesophagitis or with symptoms during exclusive breast-feeding are more likely to benefit from AAF than eHF. Infants on AAF also seem to have better longitudinal growth than infants on eHF[54,55]. It has also been recommended that infants presenting with severe manifestations of cow's milk-protein allergy such as failure to thrive, hypoproteinaemia and hypoalbuminaemia or Fe-deficiency anaemia should start with AAF[56]. Similarly, infants and children with multiple food allergies often have more severe features, with possible reactions even to small quantities of antigens, and are thus unresponsive to eFH and have a late acquisition of tolerance[57].

It is important to take the cost of different treatment options for cow's milk allergy into account against the cost of hospitalisation, investigation and increased morbidity in infants for whom effective treatment is delayed. Further health economic data are required to assist healthcare workers in this context[27].

A major problem with the use of hypoallergenic formulas is their poor palatability[58]. However, infants <6 months of age have a relatively 'naïve' taste perception and therefore usually accept these formulas without difficulties. Older infants and those who have been previously breast-fed commonly reject the introduction of hypoallergenic formula[59].

Thus, the hypoallergenic formula should be introduced as soon as possible or if the infant is being breast-fed continue to do so until 1 year of age when other more-palatable alternatives may be considered. Depending on the severity of the symptoms, transitional introduction may be considered with incremental mixing of the milks. The hypoallergenic formula can be offered as the main fluid source. If the infant is >6 months introduce the formula in a feeder beaker that has good flow (avoid beakers with valves). The smell can be masked with a good-quality vanilla essence (a few drops only; it should be noted that vanilla essence does contain alcohol and excessive addition is not indicated and can also make the formula bitter). Commercial milk-free 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.

In the UK soya formulas are not recommended for infants aged <6 months[60]. Although it is also not recommended as the first choice of formula for infants aged between 6 months and 12 months who are allergic to cow's milk, it can be useful for infants not allergic to soyabean who refuse hypoallergenic formulas[61,62]. The prevalence of concomitant soyabean allergy in infants with cow's milk allergy differs between IgE- and non-IgE-mediated disease[63]. It ranges between 10% and 14% in infants with IgE-mediated allergy[64,65], but in non-IgE-mediated cow's milk allergy it is markedly higher, especially in enterocolitis and enteropathy syndromes[63].

For children >2 years of age with a nutritionally-complete diet and good growth cow's milk alternatives include Ca-enriched soya, almond (*Amygdalus communis L.*), pea (*Pisum sativum*), oat, coconut (*Cocos nucifera*) and potato milks or the more rare alternatives such as quinoa (*Chenopodium quinoa*) drink and chufa milk made from tigernuts (*Cyperus esculentus*).

A number of factors play a role in the decision to move children from an infant formula to commercially-available milk substitutes including: the volume of formula that is consumed and amount of solid food eaten, e.g. a child with feeding issues who is still taking a substantial volume of formula may be left on the formula for much longer or a formula for older children may be chosen; the alternatives to cow's milk available locally and the nutritional profile of the milk substitute (Table 4); growth profile; energy requirements *v.* energy intake[66].

Food refusal is commonly seen during infancy. It is thought that 16·7% and 18·8% of 8-month-old and 12-month-old infants respectively have severe aversive feeding behaviour[67]. Research indicates that infants with reflux-type symptoms or colic, which are often related to non-IgE-mediated allergy to cow's milk and soyabean, are associated with major feeding problems that range from food refusal, gagging on introduction of lumpier textures and extreme anxiety during meal times[68,69]. Studies on the prevalence of feeding difficulties in children with IgE-mediated food allergies have not been conducted. Children with food allergies and concomitant feeding difficulties pose a major nutritional challenge, as food choices are often further limited because of important sensory hypersensitivity symptoms: texture aversion; colour specificity;

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Table 4. Comparison of the different milks (/100 ml)*

	Cow's milk (full fat)	Soya milk (enriched)	Rice milk (enriched)	Oat milk (enriched)	Nutramigen 2‡	Pepti§	Neocate Active‖
Energy (kJ)	268	180	197	188	301	276	418
Protein (g)	3·3	3·3	0·1	1	2·3	1·6	2·7
Ca (mg)	122	140	120	120	90	47	95
Vitamin D (μg)		0·75	†	0·5	1·08	1·3	0·83
Fe (mg)	0·08	†	†	†	1·3	0·5	1·3
P (mg)		†	†	†	55	26	74

*Values for cow's milk and soya milk are taken from Food Standards Agency[104] and values for all other milks are derived from information provided by manufacturers.
†Negligible amounts present.
‡Mead Johnson Nutrition, Uxbridge, Middlesex, UK; extensively-hydrolysed casein formula, suitable for infants >6 months of age.
§Nutricia Ltd, Trowbridge, Wilts., UK; extensively-hydrolysed whey formula, suitable from birth.
‖Nutricia Ltd; amino acid-based formula, suitable from 1 year of age.

temperature; smell; taste specificity. These feeding problems should ideally be managed within a multidisciplinary team and should address the following issues: ensure that the child does not have undiagnosed allergies leading to continuing discomfort; nutritional adequacy of the diet; meal-time routine and feeding times; sensory hypersensitivity; behavioural management.

Challenge 4: assessing and monitoring nutritional status

Initial assessment

A nutritional assessment can provide useful information that can be used as a baseline for monitoring the nutritional status and the impact of the avoidance diet[17]. More importantly, this information may affect the management (avoidance) strategy that will be implemented. For example, a young child with faltering growth related to multiple food allergies will require avoidance advice as well as advice on how to increase energy, protein and vitamin and mineral intake. If an adult with a history of an eating disorder is seen about irritable bowel syndrome less stringent advice may be given than when the same patient is seen with a history of anaphylaxis caused by peanut ingestion. It is therefore important to weigh up the nutritional implications of the diet against the severity and extent of the symptoms.

Monitoring nutritional status

Monitoring height and weight. When dealing with children the simplest way of monitoring for nutritional deficiencies is to assess growth velocity using the nationally-recognised growth curves[70]. Measuring the growth of infants, toddlers and children can help to detect growth-related concerns: excessive weight gain; weight faltering; wasting and stunting. It can also provide reassurance about normality[71].

In an adult population monitoring weight, height, BMI or other anthropometric measurements can be used to assess nutritional status[72,73].

Monitoring dietary intake. It is known that an individual can have a poor nutritional status despite having a normal BMI or even being overweight[49,72]. For individuals with FHS it is particularly important to assess the intake of micronutrients as well as that of macronutrients. A variety of dietary intake measures may be used, e.g. 24 h recall and 1–7 d food diaries, each of which have their own limitations[74]. Intakes may be analysed and compared against the national recommended nutrient intakes (for UK recommended nutrient intakes, see Department of Health[75]).

It has been suggested that for infants >6 months a 24 h recall may be used[49]. However, a 3 d diet record is necessary for a child aged ≥6 months and for adults because day-to-day intake is more varied. The interpretation of dietary intake data requires a qualified dietitian. In some cases it may also be necessary to consider the assessment of biochemical markers[49]. The combination of a dietary assessment and assessment of biochemical markers can aid the recommendation to supplement the intake of a particular vitamin and/or mineral.

Adverse outcomes of exclusion diets

The nutritional contribution of any allergenic foods that are being excluded and the number of foods excluded from the diet must be carefully considered[75,76]. A number of reports have documented inadequate energy intake that leads to growth faltering in children[50,77–81]. In particular, insufficient intake of vitamin D presenting as rickets[50,82], hypocalcaemia[50], Fe-deficiency anaemia[50], essential fatty acid deficiency[83] and kwashiorkor in conjunction with multiple nutrient deficiencies[84,85] have been reported.

Three studies have addressed growth in children with multiple food allergies[77,86,87]. A study of 100 infants (<12 months of age) with cow's milk-protein allergy has found that their length and weight-for-length indices are decreased compared with those of age-matched healthy controls[86]. Furthermore, age at the onset of symptoms and duration of the elimination diet are major contributors to growth impairment. An evaluation of the efficacy of AAF compared with eHF in children with cow's milk allergy has found improved growth (length) in those taking AAF despite similar energy intakes[87]. This finding has been confirmed by work showing that children with two or more food allergies are shorter, based on height-for-age percentiles, than those with one food allergy and their

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intakes of Ca, vitamin D and vitamin E are also lower than the recommended daily intakes[77].

These studies have identified maternal fears[50], no dietetic referral[84,87], alternative allergy testing[50], use of an inappropriate alternative formula[85] or palatability of the chosen formula[50] as important indicators of a poor nutritional status. This evidence reinforces the need for all food-avoidance diets to be supervised by an appropriate specialist healthcare professional with nutritional knowledge such as a registered dietitian[84,88].

Challenge 5: determining development of tolerance

Patients should be re-assessed frequently in order to determine development of tolerance to a food. There are a number of factors that play a role in determining the tolerance to food(s). The regular assessment of nutritional status during a period of food avoidance will assist in the decision as to whether to continue an elimination diet or consider food challenges in an attempt to broaden the scope of an individual's diet.

Cow's milk and egg allergy is often transitory and mostly is resolved by 5 years of age[5]. The timing of reintroduction will vary according to the clinical circumstances. If previous reactions have been severe IgE-mediated reactions or other food allergies have developed reintroduction may be delayed for longer. The decision to reintroduce food allergens should always be taken by an appropriately-qualified clinician and may require supervision in hospital. It is now also known that there is a possible risk of enhanced reaction after a period of withdrawal[24]; however, this outcome is specific to children with a history of delayed symptoms only, for whom a risk of developing immediate more-severe symptoms during a 'home challenge' does exist. It is therefore best clinical practice to repeat skin-prick testing or specific IgE levels before to a food challenge. When the size of the skin-prick test or specific IgE levels are the same or even greater the challenge should be postponed; this provision applies to all foods. In the case of cow's milk, persistence into childhood and adulthood necessitates permanent exclusion. It is often the case that following a negative challenge the child does not want to reintroduce the food into the diet[89] because of anxiety or dislike of the taste, and parents will need guidance on ways of incorporating these foods into the diet.

Very little is known about development of tolerance to either foods or ingredients in adults.

Conclusion

Avoidance of the relevant food is the mainstay of the management of FHS. Before any dietary avoidance is implemented the individual should be medically assessed and diagnosed appropriately. In some cases an elimination diet may be needed for diagnostic purposes. There is no validated tool or guide available for the management of FHS. In order to ensure appropriate avoidance of the food whilst the individual maintains a good nutritional status a dietary consultation should include: (1) assessment of height, weight and dietary intake; (2) avoidance advice including understanding food labels and lifestyle issues; (3) information on substitute foods, 'free from' lists and special dietary products; (4) follow-up and reassessment to determine development of tolerance.

Acknowledgements

The authors declare no conflict of interest. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. C. V. prepared a skeleton outline of the paper. C. V. and R. M. then prepared their allocated sections and edited each other's contributions.

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