



Guideline fever: an overview of DRACMA, US NIAID and UK NICE guidelines

Carina Venter^{a,b} and Syed H. Arshad^{b,c,*}

Purpose of review

It is well known that many aspects of food allergy are lacking sufficient research and publication. Practising evidence-based medicine in this field is, therefore, a particular challenge. Internationally, there is considerable variation in practices and no agreed treatment pathways. The time was right to review the evidence and seek the views of experts in the field, industry and food allergic individuals to develop guidance for clinical practice and to plan future research. The purpose of this review was to summarize points of agreement and discrepancy in the recently published Diagnosis and Rationale for Action against Cow's Milk Allergy, US NIAID and UK NICE guidelines.

Recent findings

The publication of the three guideline documents on food allergies gives clinicians, scientists, industry, governments and patients the opportunity to review the information in a concise format and appreciate the role of clinical expertise in decision making. The guidelines covered all aspects of food allergy: prevalence and natural history, diagnosis, management and treatment and other aspects such as vaccinations.

Summary

The guidelines summarized not only our current evidence base but also gaps in our knowledge. Use of these guidelines would facilitate high quality standardized care and indicate the direction of future research.

Keywords

Diagnosis and Rationale for Action Against Cow's Milk Allergy, food allergy diagnosis, food allergy guidelines, NIAID guidelines, NICE guidelines

INTRODUCTION

There is a dearth of sufficient high quality publications in many aspects of food allergy. Practising evidence-based medicine in this field is, therefore, a particular challenge. The UK, Department of Health review on food allergy services concluded in 2006 that there was considerable variation in practices and no agreed treatment pathways existed [1]. The time was therefore right to review the literature and seek the views of experts in the field, industry and food allergic individuals to develop guidance for clinical practices and to plan future research.

The years 2010 and 2011 have seen the publication of three international guidelines on food allergy, informing a number of other guidelines which are currently in development. The World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) guidelines was the first document to be published in April 2010 [2^{••}], followed by the National Institute of Allergy and Infectious Diseases (NIAID)

guidelines on the Diagnosis and Management of Food Allergy in the United States, published in December 2010 [3^{••}], and then the UK National Institute for Health and Clinical Excellence (NICE) guidelines: Food allergy in children and young people; diagnosis and assessment of food allergy in children and young people in primary care and community settings, published in February 2011 [4^{••}]. Some other guidance has also been published

^aNIHR Post Doctorate Research Fellow, University of Portsmouth, Portsmouth, ^bThe David Hide Asthma and Allergy Research Centre, Newport and ^cProfessor of Allergy and Clinical Immunology, III Research Division, University of Southampton, Isle of Wight, UK

Correspondence to Dr Carina Venter, The David Hide Asthma and Allergy Research Centre, Newport, Isle of Wight, PO30 5TG, UK. E-mail: carina.venter@port.ac.uk

*MP: 810, Level F, South Block, Southampton General Hospital, Tremona Road, Southampton, SO16 7JB.

Curr Opin Allergy Clin Immunol 2012, 12:000–000

DOI:10.1097/ACI.0b013e3283535893

KEY POINTS

- Guidelines on the diagnosis and management of food allergies are much needed in clinical practices.
- The clinical history is the key element in the diagnosis of food allergies.
- Any diagnostic test results should be reviewed in the context of the clinical history.
- The management of food allergy necessitate avoidance of the allergenic foods and a dietetic consultation is recommended.

in the past [5,6], a consensus document from Australia was published in 2009 [7], and European Guidelines on the Diagnosis and Management of Food Allergies are currently being developed.

This review will give a brief overview of the DRACMA guidelines [2^{••}], US NIAID guidelines [3^{••}] and the UK NICE guidelines [4^{••}], focusing on what these guidelines have to offer, points of consensus and points of discrepancy.

WHAT DO THE GUIDELINES OFFER US?

All three guidelines [2^{••}–4^{••}] were informed by a systematic review of the available literature, using the Grading of recommendations assessment, development and evaluation system where appropriate. Clinical expertise of leaders in the field of food allergy was sought. The evidence from the systemic reviews was then interpreted in the context of their clinical expertise to provide guidance for those dealing with food allergic individuals. Stakeholders such as industry, federal/government agencies, professional bodies or organizations for allergic patients either formed part of the guideline groups or were invited to comment on and review the documents.

The guidelines documents do, however, caution that any guidance should be interpreted in the context of each country and should not overrule clinical judgment when dealing with individual patients and that they should not be used as policy documents. The UK NICE guidelines in particular state that the patient's needs and preferences should always be considered in any decision making.

Diagnosis and Rationale for Action Against Cow's Milk Allergy

The DRACMA guidelines (Table 1) focused on Cow's Milk Allergy in infants, children and adults [2^{••}]. The expert panel included a range of clinicians, scientists and patient representatives across the

world, and focused on epidemiology and natural history of cow's milk allergy, allergens and immunological mechanisms involved in cow's milk allergy, symptoms involved in cow's milk allergy and how to take a clinical history, the diagnosis and management of cow's milk allergy and the role of immunotherapy in the treatment of food allergy. Research recommendations were also made.

The guideline panel used the term 'we recommend' for strong recommendations, that is, when they considered that most individuals should receive the intervention and that most individuals in that situation would want the diagnostic measurement or treatment/management option.

The term 'we suggest' was used for conditional recommendations, that is, that the clinician should realise that different choices may be appropriate for different patients and that the majority of individuals in a particular situation would want the diagnostic measure or treatment/management option.

These are important points to take into consideration, as clinicians should not blindly follow any guidance being given from these documents.

US NIAID guidelines

The US NIAID guidelines [3^{••}] (Table 1) covered food allergies in adults and children, focusing on advice for allergists and clinical researchers and practitioners in the areas of paediatrics, family medicine, dermatology, gastroenterology, emergency medicine, pulmonary and critical care medicine, and others dealing with patients in the clinical setting. It did not deal with areas outside of the clinical care setting, for example, schools or with public health. The document covered definitions of food allergy, epidemiology and natural history of food allergies, diagnosis of food allergies, management and treatment of acute and nonacute food allergies, allergy prevention and anaphylaxis. It also highlighted gaps in the evidence base and provided guidance on points of controversy.

The guideline expert panel, mainly consisting of American colleagues, used the term 'recommend/recommendation' when the expert panel strongly recommended for or against a particular course of action. The term 'suggest/suggestion' was used when the expert panel weakly recommended for or against a particular course of action. For any guideline to be incorporated in the document, more than 90% agreement between members of the expert panel was needed. The draft guideline was posted on the NIAID website for public review and comment, and the final guidance document incorporated these comments/suggestions where appropriate.

Table 1. The guidelines at a glance

	DRACMA [2 ^{••}]	NIAID [3 ^{••}]	NICE [4 ^{••}]
What does it cover?	Cow's milk allergy in all ages with a focus on IgE-mediated cow's milk allergy in the diagnosis section	All food allergies in all ages	All food allergies in infants and children up to 19 years
Expert panel	Worldwide	Mainly USA	UK only
Who is it for?	Physicians and healthcare professionals everywhere	Clinical specialists, family care physicians and other healthcare professionals (nurse specialists and dietitians)	Primary Care (UK); Community settings
What advice is given?	Nomenclature; Epidemiology and natural history; Allergens and immunological mechanisms; Taking a clinical history and the symptoms involved; Diagnosis (discussed as five questions); Management and treatment (discussed as two questions); Immunotherapy; Research recommendations; Plan of dissemination	Definitions of food allergy; Epidemiology and natural history (including comorbidities); Diagnosis (covered in 18 guidelines); Management and treatment of acute and nonacute food allergies, including immunotherapy and vaccinations (covered in 19 guidelines); Prevention (covered in five guidelines); Anaphylaxis (covered in three guidelines); Highlights gaps in the evidence base and provides guidance on points of controversy; Plan of dissemination; Summary document for clinicians/patients (www.niaid.nih.gov)	Brief introduction on definitions; Signs and symptoms (recommendation 1); Comorbidities (recommendation 2); Taking an allergy focussed clinical history (recommendation 3); Physical examination (recommendation 4); Diagnosis of IgE-mediated allergies (recommendation 5–10); Diagnosis of non-IgE-mediated allergies (recommendation 11); Providing information and support (recommendation 12–16); When to refer to secondary care (recommendation 17); Alternative testing (recommendation 18–19); Research recommendations; Plan of dissemination; Quick reference guide for ease of implementation (http://guidance.nice.org.uk)
Advice given as:	'We suggest' or 'we recommend' with clear definitions for each; High (~80%), average (~40%) and low (~10%) pretest probabilities with clear definitions	'We suggest' or 'we recommend' with clear definitions for these	We recommend

DRACMA, Diagnosis and Rationale for Action Against Cow's Milk Allergy; NIAID, National Institute of Allergy and Infectious Diseases; NICE, National Institute for Health and Clinical Excellence.

UK NICE guidelines

The UK NICE guideline [4^{••}] (Table 1) expert panel included clinicians (allergists, paediatricians, general practitioners, nurses and dietitians) and patient representatives from the UK only and dealt with the diagnosis of food allergy in primary care and community settings. The main emphasis and real strength of the document are to elucidate how to take an allergy focused clinical history. The guideline is applicable to the care of children and young people up to their 19th birthday and summarize its guidance as 19 recommendations covering signs and symptoms of food allergy, comorbidities, taking an allergy focused clinical history, physical examination, diagnosis of IgE-mediated allergies, diagnosis of non-IgE-mediated allergies, providing information and support, when to refer to secondary care and the role of alternative testing. It only

briefly covered the management of food allergies as this was outside the scope of the document. Research recommendations with particular reference to the UK situation were also made.

Advice was given as 'we recommend', with no definition of the term.

NOMENCLATURE

The DRACMA guidelines [2^{••}] and the UK NICE guidelines [4^{••}] used the definition of food hypersensitivity as defined by the WAO in 2001 (Fig. 1) [8]. The term food hypersensitivity was not used in the US NIAID document [3^{••}], apart from referring to immediate gastrointestinal hypersensitivity. In these guidelines, we see yet another definition of food allergies (Fig. 2). None of the documents discussed food intolerances/nonallergic food hypersensitivities.

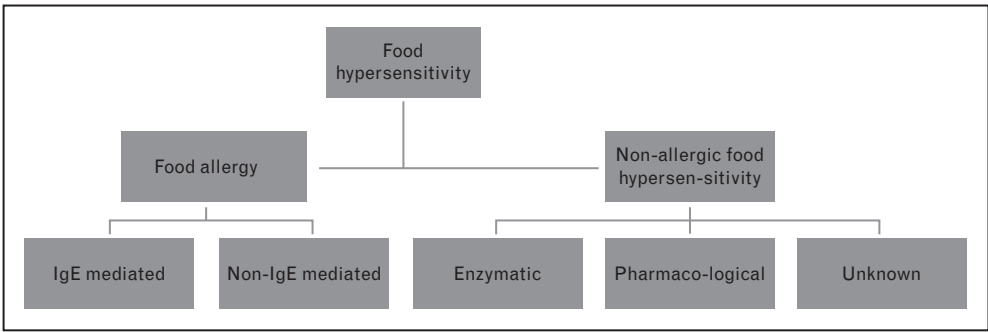


FIGURE 1. Definition of Food Hypersensitivity according to Diagnosis and Rationale for Action Against Cow’s Milk Allergy [2²²] and the UK NICE [4²²] guidelines – Adapted from World Allergy Organization nomenclature [8].

PREVALENCE, NATURAL HISTORY OF FOOD ALLERGIES AND BACKGROUND INFORMATION

All three of the guideline documents [2²²–4²²] allude to the fact that reported rates of food allergy/hypersensitivity is higher than that of objectively diagnosed food allergy/hypersensitivity as also summarized in a recent systematic review [9].

Diagnosis and Rationale for Action Against Cow’s Milk Allergy

The DRACMA guidelines [2²²] summarized the information regarding the prevalence of cow’s milk allergy in detail, stating this to be a problem in 1.9–4.9% of children and acknowledged that food allergies show geographical trends.

Allergens in cow’s milk

There is a detailed discussion of the allergens in cow’s milk, once again confirming that sheep and goat’s milk are not suitable for the majority of cow’s milk allergic individuals. The DRACMA guidelines [10] also stated that there is no clear relationship between digestibility and protein allergenicity and

that milk allergens are known to preserve their allergenicity even after boiling, pasteurization, ultra-high temperature processing, or evaporation for the production of powdered infant formula. However, there is now some evidence to show a reduction in the allergenicity of conformational whey epitopes following extensive heating with some clinical relevance in terms of increased tolerance [11].

Immunological mechanisms

The immunological mechanisms involved in the different presentations of CMA are also discussed and the DRACMA guidelines [2²²] summarized that type I reactions represent the classic immediate allergic reactions, whereas the three other types, described as non-IgE-mediated allergy, are less well understood, although an immunological basis is clearly present.

Natural history

DRACMA [2²²] concluded that the natural history of CMA indicate that the majority of children will outgrow their CMA, but this is dependent on a number of factors such as immediate versus delayed

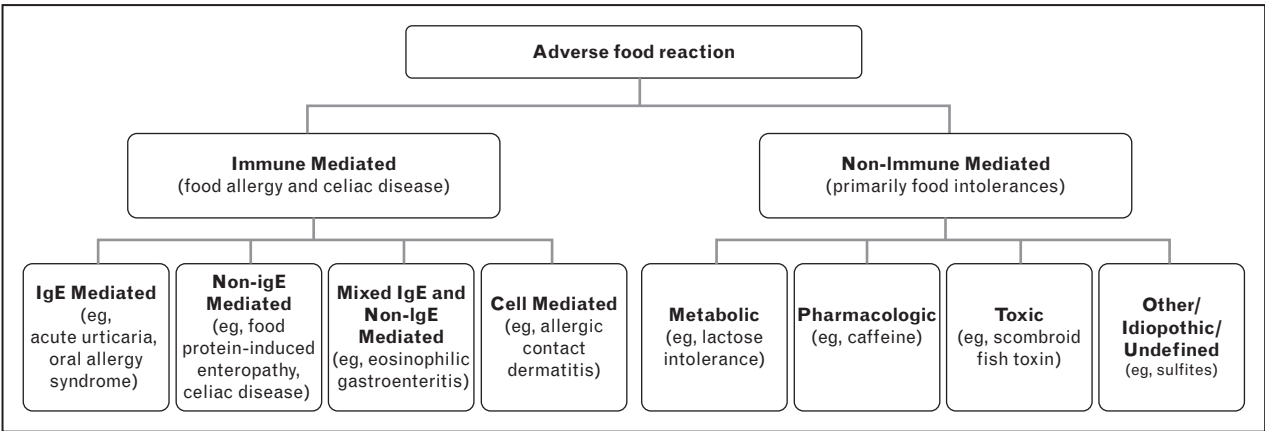


FIGURE 2. Definition of adverse reactions to food according to the US NIAID guidelines [3²²].

type CMA, sensitization levels at diagnosis, respiratory symptoms at diagnosis, presence of other food allergies, dose at which reaction is observed during food challenge, family history of allergic diseases and genetics.

US NIAID guidelines

The prevalence of food allergies and their natural history was summarized focusing on the most common food allergens in adults and children, also highlighting the co-occurrence of food allergy with other allergic diseases [3¹¹].

Natural history

The natural history of food allergies indicate that most children with food allergies will become tolerant to cow's milk (as in DRACMA), egg, and wheat and fewer children will become tolerant to tree nuts and peanut [3¹¹]. The time taken for the development of tolerance varies by food, and some children may only become tolerant as teenagers [3¹¹]. As with DRACMA they stated that a high initial sensitization level to a food is associated with a lower rate of developing clinical tolerance over time. Very little is known about the development of tolerance in adult onset food allergies, although it seems that these allergies persist.

Coexisting allergic conditions

The guidelines [3¹¹] then focused on other co-existing allergic conditions stating that:

- (1) Coexistence of asthma and food allergy may predispose to acute severe asthma.
- (2) Food allergy is commonly seen in children with atopic dermatitis but once the food allergy is outgrown it will not affect the atopic dermatitis any more.
- (3) Food allergy is often seen in eosinophilic esophagitis (EoE), a chronic relapsing condition, but the role of food allergies in the natural history of EoE is not known.
- (4) Foods may be involved in exercise-induced anaphylaxis in a third of patients.
- (5) Allergic rhinitis seems to have less of an association with food allergy.

Risk factors for the development of food allergies and predicting severe reactions

The only risk factors identified that may play a role in the development of food allergy is atopic dermatitis and a family history of allergy [3¹¹].

The severity of a reaction cannot be accurately predicted by the severity of past reactions. However,

co-existing asthma is the most reliable indicator of possible severe reactions to food.

UK NICE guidelines

A Systematic review of the literature was not undertaken regarding the prevalence and natural history of food allergy or comorbidities [4¹¹].

DIAGNOSIS

All three guideline documents [2¹¹–4¹¹] acknowledge that food allergy is associated with a wide range of symptoms and highlight the importance of the clinical history in the diagnosis of food allergy as summarized in Table 2.

We have summarized a number of points (Table 3) regarding the diagnosis of food allergy, but do advise the reader to refer back to the original documents [2¹¹–4¹¹] for exact wording used.

The elimination diet and the role of food challenges

The guidance documents [2¹¹–4¹¹] agree that the oral food challenge plays an important role in the diagnosis of food allergy and that it should be preceded by an elimination diet. However, the role of the dietitian in this very important step is mentioned only by the UK NICE guidelines [4¹¹]. The UK NICE guidelines [4¹¹] and DRACMA [2¹¹] clearly indicate that oral food challenge for IgE-mediated allergies should not be conducted out of clinical care settings, but that challenges for diagnosing less severe non-IgE-mediated food allergies may be conducted at home under the guidance of a dietitian (as per NICE). In case of any suspicion of more severe reactions either indicated by history or sensitization status, challenges should always be conducted in the clinical setting.

Diagnosis of IgE-mediated food allergy

There is some disparity on the role of specific IgE testing and skin prick test (SPT) in the diagnosis of IgE-mediated allergy, with the UK NICE guidelines [4¹¹] and the US NIAID guidelines [3¹¹], indicating that these tests should be performed in all patients when indicated by history. The DRACMA guidelines [2¹¹] gave a more complex overview of this decision as summarized in Table 3.

Non-IgE-mediated food allergy

The UK NICE guidelines [4¹¹] and DRACMA [2¹¹] recommend a period of elimination followed by

Table 2. Taking an allergy focused history

Guidance by DRACMA [2 ^{***}]	Guidance by NIAID [3 ^{***}]	Guidance by NICE [4 ^{***}]
Obtain information on:	The guidance document recommends taking an allergy focussed history and doing a physical examination:	Obtain information on:
Age at onset	Critical questions should include the following:	Any personal history of atopic disease (asthma, eczema or allergic rhinitis)
Nature of symptoms	What are the symptoms of concern?	Any individual and family history of atopic disease (such as asthma, eczema or allergic rhinitis) or FA in parents or siblings
Frequency of their manifestation	What food precipitates the symptoms?	Details of any foods that are avoided and the reasons why
Timing between ingestion and onset of symptoms	What quantity of food was ingested when the symptoms occurred and in which format was the food consumed (cooked/baked/raw)?	Presenting symptoms and other symptoms that may be associated with food allergy:
Quantity of milk necessary to provoke symptoms	When do they occur in relation to exposure to a given food?	The age of the child or young person when symptoms first started
Reproducibility of the reaction	Can the food ever be eaten without these symptoms occurring?	Speed of onset of symptoms following food contact
Interval of time since last reaction	Have the symptoms been present at times other than after exposure to a given food?	Duration of symptoms
Influence of external factors on the manifestation (e.g. exercise, hormonal changes, or emotional stress)	What treatment was given and how long did the symptoms last?	Severity of reaction
Other important information:		Frequency of occurrence
Food diary		Setting of reaction (for example, at school or home)
Growth records		Reproducibility of symptoms on repeated exposure
Early feeding details (duration of breast-feeding, type of infant formulas, introduction of weaning solids)		What food and how much exposure to it causes a reaction
Effect of elimination diets (soy, treatment formulas, diet of the mother during breast-feeding)		Cultural and religious factors that affect the foods they eat
Therapeutic interventions		Who has raised the concern and suspects the food allergy
		What the suspected allergen is
		The child or young person's feeding history, including the age at which they were weaned and whether they were breastfed or formula-fed – if the child is currently being breastfed, consider the mother's diet
		Details of any previous treatment, including medication for the presenting symptoms and the response to this; any response to the elimination and reintroduction of foods
		Physical examination:
		Pay particular attention to:
		growth and physical signs of malnutrition signs related to allergy-related comorbidities (atopic eczema, asthma and allergic rhinitis)

DRACMA, Diagnosis and Rationale for Action Against Cow's Milk Allergy; FA, food allergy; NIAID, National Institute of Allergy and Infectious Diseases; NICE, National Institute for Health and Clinical Excellence.

Table 3. Summary of guidance on Diagnosis by Diagnosis and Rationale for Action Against Cow's Milk Allergy, NIAID, NICE

	DRACMA [2 ^{***}]	NIAID [3 ^{***}] Recommendations	NICE [4 ^{***}]
Symptoms of FA	Individuals with CMA can present with a range of symptoms. Knowledge and understanding of these are important to make a correct diagnosis	Consider food allergies in individuals who show symptoms of allergic disease, children with non-IgE-mediated diseases e.g. FPIES, AEG or EoE, and adults with EoE	Consider the possibility of FA in children and young people who have one or more of the signs and symptoms of FA, particularly persistent symptoms and symptoms who do not respond to other treatment Pay particular attention to persistent symptoms that involve different organ systems
Medical history	An accurate medical history can help to facilitate the diagnostic process	Obtain a detailed medical history and perform physical examination, but confirm suspected FA with a proper diagnostic work-up	Take an allergy-focused clinical history tailored to the presenting symptoms and age of the child or young person Do a physical assessment focusing on: Growth and any signs of malnutrition Signs indicating allergy-related co-morbidities
Elimination diet	Should be prescribed for most patients Optimal duration of diagnostic elimination phase unclear but could be shorter for immediate CMA and longer for delayed symptoms	Suggestion: Elimination of one or a few specific foods from the diet may be useful in the diagnosis of FA, especially in identifying foods responsible for some non-IgE-mediated disorders	
IgE-mediated food allergies			
Skin test	Should skin prick tests be used for the diagnosis of IgE-mediated CMA?	Use SPT to identify foods that may be causing IgE-mediated FA – however, SPT alone cannot diagnose FA Do not use intradermal testing	If IgE-mediated allergy suspected: Offer SPT and/or specific IgE tests to the
	Recommendation: If OFC is required for diagnosing CMA – use OFC as the only test to diagnose FA Suggestion:		Suspected foods and likely co-allergens Tests should only be undertaken by healthcare professionals with the appropriate competencies to select, perform and interpret them
	If OFC is not required for the diagnosis in patients with high pretest (~80%) probability (pp): use a SPT ≥ 3 mm to make diagnosis		SPT should only be performed where HCP have the facilities to deal with an anaphylactic reaction

Table 3 (Continued)

	DRACMA [2 ^{***}]	NIAID [3 ^{***}] Recommendations	NICE [4 ^{***}]
	Where OFC is required in patients with a medium pp (~40%): use an OFC as the only test to diagnose or refute FA		
	Where OFC is required in patients with low pp (~10%) of CMA: use a SPT of <3 mm to refute the diagnosis		
Specific IgE test	Should specific IgE test be used for the diagnosis of CMA?	Total serum IgE should not be used to make a diagnosis of FA	Choose between a SPT and a specific IgE test based on:
	Recommendation:	Use specific IgE tests for identifying foods that potentially lead to IgE-mediated food allergic reactions, but alone these tests are not diagnostic of FA	The clinical history and
	If OFC is required for the diagnosis—use OFC only		whether the test is suitable, safe and acceptable to individual and
	Suggestion:		the healthcare professional have the competencies to perform the test and interpret the results
	If OFC is not required in patients with a high pp – use specific IgE ≥ 0.7 IU/l to diagnose FA		Any allergy testing should be preceded by and interpreted in the context of the allergy focused clinical history
	If OFC is required, in patients with an average pp – do only food challenge to diagnose or rule out FA		
	If OFC is required in patients with low pp – use specific IgE < 0.35 IU/l to rule out FA		
	Should in vitro specific IgE determination be used for the diagnosis of CMA in patients suspected of CMA and a positive result of a skin prick test?		
	Suggestion:		
	In patients with a low initial probability		
	who have a positive SPT (≥ 3 mm), use OFC rather than specific IgE to diagnose FA		
	In patients with a an average or high initial probability who have a positive SPT – use specific IgE ≥ 0.35 IU/l to diagnose FA		
	Should in-vitro specific IgE determination be used for the diagnosis of CMA in patients suspected of CMA and a negative result of a skin prick test?		

Table 3 (Continued)

	DRACMA [2 ^{***}]	NIAID [3 ^{***}] Recommendations	NICE [4 ^{***}]
	Recommendation:		
	In patients with a low initial probability who have a negative SPT, use specific IgE <0.35 IU/l to rule out FA		
	In patients with a high initial probability who have a negative SPT use OFC to diagnose or rule out FA		
	Suggestion:		
	In patients with an average initial probability who have a negative SPT, use OFC to diagnose or rule out FA		
Micro-array analysis/ component resolved diagnosis	More research is needed	More research is needed	No comment
Food challenge	Use OFC to diagnose or refute CMA, monitor development of tolerance or assess possible cross-reactions	DBPCFC is the 'gold standard,' for diagnosing FA – single-blind and open challenges can be used in a clinical setting	Do not use OFC to diagnose IgE-mediated food allergy in primary care or community settings
	If IgE-mediated allergy is suspected, either by history OR by sensitisation status, a physician-supervised OFC is needed		
Non-IgE-mediated food allergies			
Non-IgE-mediated food allergies	No specific recommendations regarding non-IgE-mediated allergy is made, but the guidance document refers to food elimination followed by food reintroduction or an OFC upon improvement of symptoms	Disease specific advice given:	Following from the clinical history, if non IgE-mediated FA is suspected, try an elimination diet of the suspected allergen(s) (normally for between 2–6 weeks) and reintroduce after the trial
		Suggestion:	Seek advice from a dietitian with appropriate competencies, about nutritional adequacies, timings of elimination and reintroduction, and follow-up
		SPTs, sIgE tests and APTs may be considered to help identify foods that are associated with EoE, but these tests alone are not sufficient to make the diagnosis of FA	
		Use medical history and OFC to diagnose FPIES – OFC not needed in case of hypotensive episodes or multiple reactions to the same food	
		Use elimination diet and OFC to diagnose allergic proctocolitis – repeat OFC to look for resolution by 1–2 years	

Table 3 (Continued)

	DRACMA [2 ^{***}]	NIAID [3 ^{***}] Recommendations	NICE [4 ^{***}]
Food challenge/ reintroduction	When non-IgE-mediated CMA is suspected, gradual home introduction of milk is recommended	See above	See above
Specific conditions	No comment	Suggestion: Use clinical history, positive sIgE or SPTs and positive immediate epicutaneous skin tests to diagnose food-induced contact urticaria Use clinical history and positive patch tests to diagnose systemic contact dermatitis Use clinical history and positive patch tests to diagnose Allergic Contact Dermatitis	No comments
Atopy patch test	No specific recommendation	Suggestion: APT should not be used to diagnose noncontact FA. Do not use a combination of SPTs, sIgE levels, and APTs for the diagnosis of FA	Do not use APT testing to diagnose IgE-mediated FA in primary care or community settings
Alternative testing	No recommendation	Advises against the use of these nonstandardised tests	Do not use alternative diagnostic tests in the diagnosis of food allergy

APT, atopy patch tests; CMA, Cow's Milk Allergy; DRACMA, Diagnosis and Rationale for Action Against Cow's Milk Allergy; FA, food allergy; HCP, Health Care Professional; NIAID, National Institute of Allergy and Infectious Diseases; NICE, National Institute for Health and Clinical Excellence; OFC, oral food challenge; SPT, skin prick test.

reintroduction of the food. The US NIAID guidelines [3^{***}], although in agreement with this, give, however, more specific advice based on the different presentations of non-IgE-mediated food allergies (Table 3).

In general the guidelines admit that more data are needed on the role of the atopy patch test, component resolved diagnosis and microarray analysis and these tests are not currently recommended for the routine diagnosis of food allergy.

Both the UK NICE guidelines [4^{***}] and the US NIAID guidelines [3^{***}] advise against the use of alternative diagnostic tests.

MANAGEMENT OF FOOD ALLERGIES

Management of food allergies is briefly summarized in Table 4. The UK NICE guidelines [4^{***}] did not focus on the management of food allergies, but most of the information provided during the initial elimination diet is also of relevance in the long-term management of food allergies. In brief, the guidelines [2^{***}–4^{***}] agree that avoidance advice, which includes labelling information, should be given to

individuals with or carers of children with food allergies. Nutritional considerations of food avoidance should be taken into account and regular follow-up of patients is required, partly to determine development of tolerance.

The DRACMA guidelines [2^{***}], boldly advised on the much needed topic of 'Which formula?' for which they should be congratulated, while acknowledging that advice and choice of formula may differ from country to country [7]. The DRACMA guidelines and the US NIAID guidelines [3^{***}] further give advice on immunotherapy. The UK NICE guidelines give advice on onwards referral as the document is aimed at primary care.

In addition to the information listed in Table 4, the US NIAID guidelines [3^{***}] addressed the difficult question of 'allergy testing' and dietary management of those at risk of reactions/general population. The panel suggested that patients at risk for developing food allergies 'do not limit their exposure to other (nonfood) allergens such as dust-mites or pollen, and do not need to limit exposure to cross-reactive foods, as the risk of a reaction is very low'.

Table 4. Management of food allergies

	DRACMA [2 ^{***}]	NIAID [3 ^{***}]	NICE [4 ^{***}]
Summary of advice given	Factors to consider when managing CMA: Elimination diet Labelling information and legislation Beef allergy versus milk allergy Nutritional considerations Dietary compliance Periodical review Immunotherapy	In general the guidelines address: Food avoidance Nutritional counselling Growth monitoring and follow-up Food labelling Pharmacological treatment Immunotherapy	Recommendation: Offer information on: type of allergy suspected risk of severe allergic reaction potential impact of the suspected allergy on other factors such as vaccination diagnostic processes and the type of food allergy they suffer from when to refer to secondary/specialist care
Food avoidance	Cow's milk and cow's milk containing foods should be avoided Special advice should be given to breast feeding mothers to avoid cows milk and a calcium supplement recommended	Recommendation: Avoid ingesting the food allergen(s) that the patient is allergic to Provide age- and culturally-appropriate information on food avoidance and management of anaphylaxis Provide education and training on how to read and interpret food labels	Recommendation: Provide avoidance advice taking into account socioeconomic status, cultural and religious issues – provide information on: what foods and drinks to avoid food labels adequate nutritional intake safety, limitations and duration of an elimination diet oral food challenge or food reintroduction support groups
Role of the dietitian	Not mentioned	Recommendation: Nutritional counselling and regular growth monitoring for all children with FA	Seek the advice of a dietitian with the appropriate competencies
Follow-up	Regular follow-up recommended	Suggestion: Regular follow-up is necessary. Intervals of repeated testing depend on the food(s), age of the individual, and the clinical history	Regular follow-up recommended
Hypoallergenic formulas	Which formula should be used in children with IgE-mediated CMA?	In infants – use a hypoallergenic formula if not breast fed If breast fed – eliminate the food from the mother's diet or feed the baby a hypoallergenic formula until the allergenic food is identified	Recommendation: For babies and young children with suspected allergy to cows' milk protein, offer:

Table 4 (Continued)

	DRACMA [2 ^{***}]	NIAID [3 ^{***}]	NICE [4 ^{***}]
	Suggestion:		avoidance advice to breastfeeding mothers
	In infants/children at high risk of anaphylaxis, use an amino acid formula		information on the most appropriate hypoallergenic formula or milk substitute to mothers of formula-fed babies
	In children with IgE-mediated CMA at low risk of anaphylactic reactions, use an extensively hydrolyzed milk (EhF) formula		Seek advice from a dietitian with appropriate competencies
	In children with IgE-mediated CMA, use an EhF rather than soya formula		
	In children with IgE-mediated CMA, use EhF rather than extensively hydrolysed rice formula		
	More data is needed on rice formulas		
Other suitable milk substitutes	In the developed world, other milks could be considered if formulas cannot be used	No comment	See above
	Other milks can be used based on the clinical picture and individual situation		
	Goat's, ewe's and buffalo's milks should not be used		
	Camel's milk can be used for children after 2 years		
	Equine milks can be considered for children with delayed-onset CMA		
	The use of a suitable infant formula is particularly important before 2 years of age for nutritional reasons		
Pharmacological treatment		There are no medications recommended to prevent IgE-mediated or non-IgE-mediated FA reactions	
Nutritional implications	Nutritional implications of a CM free diet mainly include malnutrition and rickets	Food avoidance may put the individual at nutritional risk and appropriate advice is required	Seek advice from a dietitian regarding nutritional issues and follow-up
	More information is needed on pre, pro- and symbiotic preparations and polyunsaturated fatty acids and traditional Chinese herbal remedies		
Immunotherapy	At this stage, oral immunotherapy should only be done as part of clinical research	Aller Recommendation: Allergen specific immunotherapy or immunotherapy with cross-reactive allergens is not recommended to treat FA in clinical practice	No comment

7. Allen KJ, Davidson GP, Day AS, *et al.* Management of cow's milk protein allergy in infants and young children: an expert panel perspective. *J Paediatr Child Health* 2009; 45:481–486.
8. Johannsen H, Prescott SL. Practical prebiotics, probiotics and synbiotics for allergists: how useful are they? *Clin Exp Allergy* 2009; 39:1801–1814.
9. Rona RJ, Keil T, Summers C, *et al.* The prevalence of food allergy: a meta-analysis. *J Allergy Clin Immunol* 2007; 120:638–646.
10. Fiocchi A, Assa'ad A, Bahna S. Food allergy and the introduction of solid foods to infants: a consensus document. Adverse Reactions to Foods Committee, American College of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 2006; 97:10–20.
11. Nowak-Węgrzyn A, Bloom KA, Sicherer SH, *et al.* Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol* 2008; 122:342–347; 347.