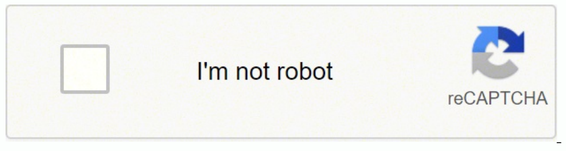

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Nice guidelines cow' s milk allergy infants

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REVIEW

Clinical practice. Diagnosis and treatment of cow's milk allergy

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Abstract
Introduction Cow's milk allergy (CMA) is thought to affect 2–3% of infants. The signs and symptoms are nonspecific and may be difficult to objectify, and as the diagnosis requires cow's milk elimination followed by challenge, often, children are considered cow's milk allergic without proven diagnosis. *Diagnosis* Because of the consequences, a correct diagnosis of CMA is pivotal. Open challenges tend to overestimate the number of children with CMA. The only reliable way to diagnose CMA is by double-blind, placebo-controlled challenge (DBPCFC).
Therapy At present, the only proven treatment consists of elimination of cow's milk protein from the child's diet and the introduction of formulas based on extensively hydrolysed whey protein or casein; amino acid-based formula is rarely indicated. The majority of children will regain tolerance to cow's milk within the first 5 years of life.
Conclusions Open challenges can be used to reject CMA, but for adequate diagnosis, DBPCFC is mandatory. In most children, CMA can be adequately treated with extensively hydrolysed whey protein or casein formulas.

Keywords Cow's milk allergy · Double-blind placebo-controlled food challenge · DBPCFC · Hypoallergenic formula

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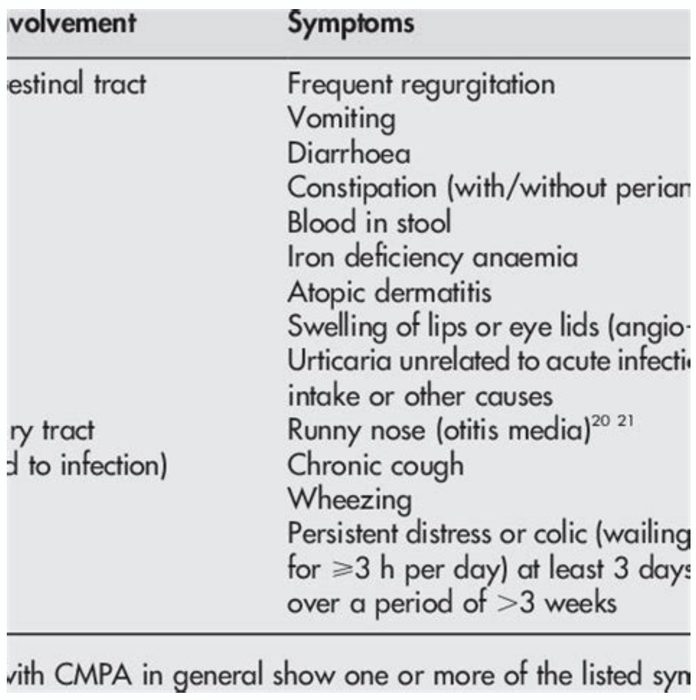
Introduction

The prevalence of cow's milk allergy (CMA) is estimated to be between 2% and 3% in infants and marginally lower in older children [1, 2]. The percentage of parents that believe their child has CMA (or any other food allergy), however, amounts to between 5% and 20% [2–4]. Signs and symptoms of CMA are nonspecific and often difficult to objectify. Due to diagnostic burdens, the number of children treated for CMA is probably two to three times higher than justified [5]. A wrong diagnosis of CMA may not only result in somatisation but also in insufficient topical treatment of eczema, fear for or problems with the introduction of solids, and dietary deficiencies. Moreover, the long-term elimination of cow's milk protein (CMP) in a sensitised child without CMA may elicit severe adverse reactions when cow's milk is reintroduced [6]. Careful diagnosis of CMA, therefore, is of utmost importance.

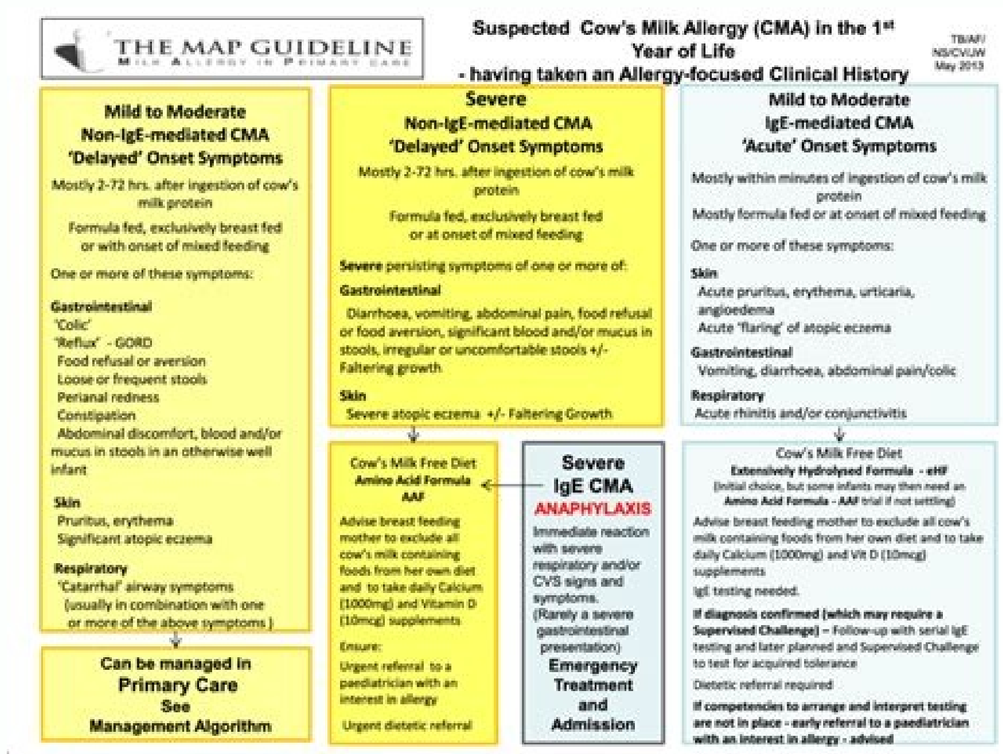
Definitions

Adverse reactions to CMP can be present from birth, even in exclusively breast-fed infants. Not all reactions are of allergic nature. In 2001, the EAACI published a report on the terminology of adverse reactions [7]. The umbrella phrase, food hypersensitivity, covers non-allergic food hypersensitivity (traditionally named 'food intolerance') and allergic food hypersensitivity (food allergy). The latter requires an underlying immune mechanism. Most children with CMA have immunoglobulin E (IgE)-mediated allergy as a manifestation of their atopic constitution, with or without atopic eczema, asthma, or allergic rhinitis. A small group have cell-mediated allergy with gastro-intestinal symptoms [8].



volvement	Symptoms
estinal tract	Frequent regurgitation
	Vomiting
	Diarrhoea
	Constipation (with/without perian
	Blood in stool
	Iron deficiency anaemia
	Atopic dermatitis
	Swelling of lips or eye lids (angio-
	Urticaria unrelated to acute infecti
	intake or other causes
ry tract	Runny nose (otitis media)[20 21]
d to infection)	Chronic cough
	Wheezing
	Persistent distress or colic (wailing
	for ⩾3 h per day) at least 3 days
	over a period of >3 weeks

vith CMPA in general show one or more of the listed sym



The pleasant site of clinical knowledge summaries (CKS) is only available for users in the United Kingdom, Crown dependencies and British Overseas Territories. The content of CKS is produced by Clarity Informatics Limited. It is available to users outside the UK through the subscription of the Prodigy website. If you think you're looking at this page in error, contact us. Important notice: our evidence search service will be closed on March 31, 2022. Please address the consultations to Nice@nice.org.uk. Skip to search results The United Kingdom has recently seen a significant increase in the number of children suspected of having a food allergy. This is defined as an adverse health effect that arises from a specific immune response that occurs reproducibly in exposure to a particular food.1 The immune response can be clinically subdivided into the following: Response mediated by the IgE antibody of immediate start, where adverse effects Generally, they appear in a matter of minutes (may be up to 2 hours) after the response mediated by the IngestionDelayed IgE antibody, where the effects usually develop more than 2 hours, or even days, after Ingestion.2Milk allergy in primary care: current guide to the UK2 , The UK birth cohort study has shown that up to 3 % of 1 cow's common allergy In a study (published in 2010) of 1000 babies with a diagnosis of milk allergy, randomly chosen from a UK health care database, 86% were first diagnosed in primary care. and most were administeredIn primary care.6 This study highlighted evidence of low recognition, incorrect diagnosis, significant delay in diagnosis, and subsequent suboptimal management of infants, especially when choosing the most appropriate initial hypoallergenic formula to prescribe a response, nice published the 2011 Clinical Guideline 116 (CG116) on the Diagnosis and Evaluation of Food Allergy in Children Children Children children in primary care and community settings.3 The Pleasant Clinical Knowledge Summary (CKS) on cow's milk protein allergy in children (aged 5 years and under) was published later in 2014, drawing largely in Nice CG116 with respect to the diagnosis Initial and Evaluation of any food allergy in primary care and indications for derivation; The CKS also refer to other guidelines, notably the UK Map Milk Allergy Guide published in 20 134,7 to address the continuous care of children with milk allergy who should be administered in primary care. Nice CG116 recommends that the initial recognition and assessment in primary care of a suspected allergy to any food in a child should always be carried out in a certain order (see Box 1, below).3The stated objectives of the CKs are to support health care professionals in the field of primary care. primary care to: 2Recognize the possible characteristics of MAC in NamesaSassess those children with suspected children appropriate for diagnosis and management of early specialists, the remaining children with suspected MAC in care 3n primary. The indiscussion around these four objectives forms the basis of the remaining article, which summarizes the key recommendations of the evidence relevant to primary care.) Recognize the possible characteristics of CMA in the primary care professional of CMA in the primary care health care professional of Childrenthe: 3Recognize that the three main organ systems most frequently affected by food allergy are the skin, intestine and a respiratory system that lends special attention to food allergy. persistent signs or symptoms involving more than one of these systems and / or where initial treatment of any of the signs or symptoms It has not been shown that the early clinical distinction between the suspicion of food allergy mediated by IgE and not by IgE has not been made useful, see Table 1, below, which lists the typical signs and symptoms mediated by IgE and not IgE related to C AM in childhood. (NB, some signs and symptoms appear in both groups; the list is not exhaustive) realize that any family of atypical disease (e.g., eczema, allergic rhinitis, asthma, or food allergy) in parents or siblings makes it more likely that IgE-mediated or non-IgE-mediated food allergy will be confirmed, although there will still be children presenting with CMA who will not have a family history of the disease. spikes. Table 1: IS-mediated Signs and Symptoms (adapted from NICE CG116 to relate to childhood MAC) 3 Signs and SymptomsBy IgENo-mediated IgE Response Rate Usually minutes after food intake (can be up to 2 hours) Usage usually more than 2 hours or even days after food intakeSkinPruritusErythema urticaria (localized or generalized) Acute angioedema (most commonly of the lips, face or around the eyes) Acute flar of atypical eczema. PruritusErythemaSignificant atopic eczema.GastrointestinalAngioedema of the lips, tongue and palate Cold abdominal painVomitingDiarrhoea. ColicChildren's Vomiting"Reflux'Gastro-oesophagic Reflux Disease (GORD) Refusal or aversion of food Stool or stools Frequent perianal Redemption Constipation, especially soft stools with excess tension abdominal discomfort, flatus painful Blood and/or mucus in the stool False growth with one or more previous gastrointestinal presentations (with or without significant atypical eczema). Respiratory (usually in combination with one or more of the above signs or symptoms) Upper breathing: sneezing, runny nose, nasal congestion (with or without conjunctivitis) More serious signs: Anaphylaxis, e.g. stridor, cough, wheezing, shortness of breath, with or without list, pallor. Upper breathing: sneezing, runny nose, nasal congestion (with or without conjunctivitis) Better respiratory â e.g., coughing, wheezing, or shortness of breath.2) Evaluate children with suspected CMACwhen a pattern of signs and symptoms is recognized that might cause due to CMA (and this suspicion may or may not be reinforced by a Positive family of an overload) overload) History is the cornerstone of the evolution of diagnosis. The required questions that the first contact doctor should ask, shown in box 2, below, have been adapted from the NICE CG116 to specifically refer to a baby suspected of CMA. Box 2: Allergy-centric clinical history —' Diagnostic Angular Stone (adapted from NICE CG116 to Relate to WMA in Childhood)3Question: family history of atopic disease (e.g., eczema, asthma, allergic rhinitis or food allergy) in parents or siblings: a positive story along with signs or symptoms of suspicion that the CMA makes the symptoms more likely; this applies to the first dose Presuming that there are no acute signs that need immediate attention, a physical examination should be performed: look for persistent signs such as the growth of falterization and malnutrition, and signs that indicate comorbidities related to allergy (e.g. atopic eczema). Other Research Offer Penis Tests or Blood Analysis for IgEspecific to cow's milk protein (CMP) and, if indicated, also to co-existing allergenic proteins (e.g. soya). State Competence Examinations should only be performed by a health professional with the appropriate competence to perform them; skin testing should only be performed in facilities equipped to deal with anaphylactic reaction3 Test results should be interpreted in the context of the clinical history (e.g. a positive test). shows sensitization, but does not necessarily confirm the clinical allergy; the size of the positive test is not related to the clinical severity of the allergy). 1 Do not perform a cow's milk challenge if it is necessary to confirm the diagnosis of suspected immediate onset IgE CMA in primary care or community settings. 3Initial investigation2 Try to remove all COP/MOP sources for a 2- to 6-week trial of the infant's diet or the mother's diet if the infant is exclusively breast-fed. Next, please resubmit to the COP/MOP at home to confirm or rule out the diagnosis of milk allergy. Dietary advice2 Infants exclusively breastfed: initiate the mother on a strict diet without CMP and prescribe for her daily supplements of 1000 mg of calcium and 10 Î1⁄4g of vitamin DFormula-fed or mixed infants (i.e., breast milk and top-up formula) âPrescribe an appropriate replacement hypoallergenic formula: a extensively hydrolyzed formula (eHF) or an amino acid diet Support for a dietitian2 Exclusively breast-fed, early dietary help to advise on a complete maternal elimination diet Formula fed, mixed fed and weaned, seeks dietitian support in early course in confirmation of the diagnosis.3) Referral of appropriate children for diagnosis and management of early specialists As soon as the presentation of the alleged food allergy, the NICE emphasizes the importance of differentiating between immediate and IgE-mediated and and Food allergy not mediated by IgE. 2.3 A CMA guideline throughout Europe8 also proposes to divide the CMA into 'mild to moderate' and 'severe'. In relation to this to milk allergy in infants and using the limited clinical writing used by the NICE, the reference recommendations are set out in table 2, below. If the remission is done or not at this stage, if a change in formula is indicated, it is important to know which category of hypoallergenic formula should be prescribed,2 and this is also highlighted in table 2. The different categories are: HFs - hydrolyzed formulas with high intensity: these formulas are tolerated by 90% of babies and children with milk allergy.2 While based on cow's milk protein (CMP; casein or serum fractions), they are widely divided into smaller peptides that are less recognized by the immune system. AAFs — amino acid-based formulas: based on amino acids, building blocks that make up proteins, these do not contain CMP as such and are indicated for more clinically serious cases. Examples of EHF and AAF are listed in CKS NICE on CMA in children. 2 Regarding the choice of a preferred individual formula of EHF or AAF over another, there are very few randomized controlled trials of "head to head" that compare different formulas within the categories of EHF or AAF, and the clinical profiles of patients who improved or did not improve are often very poorly described. 4Table 2: recommendations of reference and initial formula of the NICE (adapted of NICE CG116 and CKS CMA)2,3Clinical category of non-mediated CMANICE reference*Minimum to moderate presentation of milk allergy in childhood You can manage in primary care with the continuous entry of HFSevere dietist:faltering growth with one or more gutone suspected reactionPrompt specialist† referral of allAAFIgE-mediated CMA*Mild to moderate: Orientation aboutremission is less clear (see below)‡ HFSevere:9 one or more acute systemic reactions. Emergency response, if indicated, will then be derivedAAAFOtros scenariosClinics suspects multiple food allergies Prompt specialist† referralAAFPersisting parental suspicion of food alergy (especially in children where symptoms are difficult or perplexed) despite lack of history of support Another opinion at the level of specialists could be useful for both N/A4) The management of children who are still suspected of CMA in primary careNICE CG116 only addressed the initial assessment and recognition of food allergy in children in primary care and in community settings. Its mandated scope does not include the continued management of any child with confirmed food allergy. In 2013, a subgroup of NICE CG116 (name T Brown, C Venter, AT Fox and J Walsh) clinicians with the co-opted help of a pediatric gastroenterologist (N Shah), decided that another guideline is needed to focus specifically on recognizing, confirming and then managing babies suspected of not IgE CMA.4 The guideline would also provide guidance on referral for more specialized care for babies with more severe signs and symptoms.4 This guideline has been piloted and audited in a UK NHS Region (North Ireland). 10 It has evolved as a result, and now is called the MAP milk allergy guide for the use of primary and secondary care.4 Subsequently, the NICE CKS has been published, giving detailed advice on the management of these young children with milk allergy in primary care, and often refers to the MAP, which focuses on two key algorithms as discussed below. 4 MAP algorithms The NICE CKS describes three key aspects related to the management of the non-moderate non-medium CMA in thePrimary, namely: 2history Clulling of a Test of a Diet Free Diet of the CP / RP: With a challenge at home early to confirm or exclude diagnostic diagnosis CMA Once the CMA has been confirmed, a diet without CMP should be continued with subsequent natural-acquired tolerance tests.Clinical antecedentsâ"" the cornerstone of the diagnosisThe first MAP algorithm (see Figure 1 below) 4 describes all possible clinical presentations and the need for a clinical history focused on allergy, and advises on the category of first choice of hypoallergenic formula for each presentation. It also highlights when derivation should be considered to specialists.Starting a diet without CMP with early home challengeThe management of the CMA from mild to moderate not mediated by IgE is the focus of the second MAP algorithm (see Figure 2, below). After an initial trial of a strict diet without CMP, the signs and symptoms of the baby are usually solved comfortably in 2 to 4 weeks if they are due to a mild to moderate non-IgE CMA. A planned homework challenge should then be made to confirm the diagnosis. The MAP protocol for this challenge can be accessed at www.ctajournal.com/content/3/1/23 (see Additional Archive 1, Part 1).Continuation of the non-CMP diet with subsequent evidence of naturally acquired tolerance Once the CMA has been confirmed, all CMPs with dietary support should be strictly avoided up to at least 9"12 months of age and for at least 6 months in total. A tolerance test can then be performed using a dairy scale such as the MAP4 dairy scale for reintroduction in the home (see figure 2, below). Additional resources can be accessed at: www.ctajournal.com/content/3/1/23 (see additional file 1, part 2). Most infants with mild to moderate allergy to non-IgE milk show at this stage a degree of tolerance acquired naturally. Guideline NICE CKS2 confirms that parents or caregivers should be advised to initiatere-introduction with baked dairy products, as thermal warming reduces the allergenicity of some CMP.4In case of any delay in dietary support for reasons of service, the following websites may be useful for both thewww.allergyuk.org/milk-allergywww.cmpasupport.org.ukConclusionCow's Allergy to milk is the most common and clinically most complex form of food allergy among UK children.4 Early signs or symptoms usually appear in the first few weeks of life and are usually present in primary care.2.6 There is evidence of apparently failed, incorrect, late diagnosis and subsequent suboptimal management in a significant number of these infants6. We now have three United Kingdom guidelines related to early recognition, diagnosis and treatment of milk allergy in primary care with a very real potential of "directional overload". The recommendations for the primary care of these three guides have been collected in this article. Diagram 2: MAP milk allergy algorithms in p.48 and p.50, designed by a subgroup of the NICE CG116 food allergy guide's development group, have been tested in the Northern Ireland region of the NHS and have demonstrated a significant positive impact on patients' results and prescription, with a potential cost savings.Figure 1: CMA suspected in the first year of life4

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