FACT FILE

COW'S MILK ALLERGY

This Fact File has been compiled with the help of Paediatric and Maternal Health Dietitian, Hannah Whittaker, RD.

WHAT IS COW'S MILK ALLERGY (CMA)?

CMA, also known as cow's milk protein allergy (CMPA), is an immune-mediated allergic response to one or more proteins in cow's milk.

It can be triggered in an infant by drinking cow's milk or by drinking or eating products made from cow's milk.[1] This also includes the transition of milk protein from mum to baby when breastfeeding if mum has milk protein contained in her diet.[2,3] Cow's milk protein (CMP) can cause the immune system to be 'sensitised' so that when the protein is again consumed, the immune system remembers this protein and may react to it by producing allergic symptoms.[4,5]

CMA is one of the most common food allergies in babies and young children, affecting around 7% of formula and mixed-fed infants,[2] 0.5% of exclusively breastfed infants,[3] and 2-3% of one- to three-year-olds[4] in the UK. CMA is, however, still classified as rare.[6] The majority of infants will present with symptoms before the age of 12 months.[1] The 2015 EuroPrevall prospective birth cohort study showed that affected infants without detectable specific antibodies to cow's milk were very likely to tolerate cow's milk one year after diagnosis.[9]

ALLERGIC REACTIONS

Immunoglobulin E (IgE) are antibodies produced by the immune system. In IgE-mediated allergy (immediate), antibody production is present and a small amount of the food protein will bind to IgE allergy receptors in the body and release inflammatory chemicals. In non-IgE (delayed) allergy, the immune system will again 'overreact', but there is no interaction with IgE receptors. The body will again produce chemicals in order to protect from the allergy. This can then cause the symptoms that present in CMA (see Table 2 overleaf for symptoms).

Immediate allergy symptoms may include itchy rash, redness or hives (nettle rash), swelling, runny nose, itchy eyes, coughing, vomiting, swallowing, or even (rarely) breathing difficulties.

Delayed allergy symptoms may include diarrhoea, constipation, reflux, vomiting, mucus or blood in stools, nausea, abdominal pain, bloating, painful wind and eczema.[7]

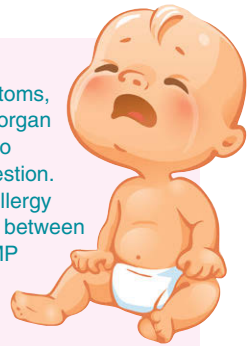
Is CMA a delayed or immediate reaction?

There are two distinct types of CMA classified according to the underlying immune mechanism: IgE-mediated (immediate) and non-IgE-mediated (delayed).[1] Both are an adverse reaction to milk protein contained in breast milk, formula milk, or in baby's food containing CMP. See Table 1 overleaf for the presentation of suspected CMA. It is felt that around 56% of CMA in Europe is non-IgE-mediated. However, this figure may be even higher in the UK.[1]

Table 1: Presentation of suspected CMA in the first year of life (adapted from reference 6)

Mild to moderate non-IgE-mediated CMA	Severe non-IgE-mediated CMA
Mostly two to 72 hours after ingestion of CMP.	Mostly two to 72 hours after ingestion of CMP.
Usually formula fed, at onset of formula feeding. Rarely in exclusively breastfed infants.	Usually formula fed, at onset of mixed feeding. Rarely in exclusively breastfed infants.
Mild to moderate IgE-mediated CMA	**Severe IgE-mediated CMA**
Mostly within minutes (maybe up to two hours) after ingestion of CMP.	Mostly within minutes to two hours after ingestion of CMP.
Mostly occurs in formula-fed infants or at onset of mixed feeding.	Very rare.

- **IgE-mediated** food allergy produces immediate symptoms, which may affect multiple organ systems, typically up to two hours after cow's milk ingestion.
- **Non-IgE-mediated** food allergy reactions usually manifest between two and 72 hours after CMP ingestion.
- **Mixed IgE and non-IgE** allergic reactions are typically delayed.[1]



WHAT ARE THE SYMPTOMS OF CMA?

The symptoms relating to mild to moderate non-IgE-mediated CMA are very common in otherwise well infants or in those with other diagnoses, so clinical judgement is required.[6]

Table 2: Symptoms of CMA (adapted from reference 6)

Mild to moderate non-IgE-mediated CMA	Severe non-IgE-mediated CMA	Mild to moderate IgE-mediated CMA	Severe IgE-mediated CMA
Usually several of these symptoms will be present: Persistent irritability – colic, vomiting Reflux – GORD Food refusal or aversion Diarrhoea Constipation Abdominal discomfort Blood and/or mucus in stools in an otherwise well infant Pruritus (itching) Erythema (flushing) Non-specific rashes Moderate persistent atopic dermatitis	One but usually more of these severe, persisting and treatment-resistant symptoms: Diarrhoea, vomiting, abdominal pain Food refusal or aversion Significant blood and/or mucus in stools Irregular or uncomfortable stools +/- faltering growth Severe atopic dermatitis +/- faltering growth	One or more of these symptoms: Skin (one or more usually present) incl. acute pruritus, erythema, urticaria, angioedema, acute 'flaring' of persisting atopic dermatitis Gastrointestinal incl. vomiting, diarrhoea, abdominal pain/colic Respiratory symptoms rarely in isolation of other symptoms Acute rhinitis and/or conjunctivitis	ANAPHYLAXIS Immediate reaction with severe respiratory and/or CVS signs and symptoms. (Rarely a severe gastrointestinal presentation) Emergency treatment and admission required

REFERENCES

Please visit: www.NHDmag.co.uk/article-references.html

ESSENTIAL RESOURCES

The Milk Allergy in Primary Care (MAP) Guideline 2019. The GP Infant Feeding Network. https://gpifn.org.uk/imap/ NICE CKS. NICE. CKS. Cow's milk allergy in children. https://cks.nice.org.uk/topics/cows-milk-allergy-in-children

BSACI guideline for the diagnosis and management of cow's milk allergy. https://www.bsaci.org/wp-content/uploads/2019/12/Milkallergyalgorithm.pdf

LACTOSE INTOLERANCE

Non-IgE-mediated allergy symptoms can be wrongly diagnosed as lactose or milk intolerance.[6] This is commonly due to some of the symptoms being similar, such as stomach discomfort, bloating, excessive wind and change in bowel movements (loose). Lactose intolerance is described as when the body cannot digest lactose (natural sugar) present in cow's milk.

Primary lactose intolerance is very rare in babies, however secondary lactose intolerance can be more prevalent. Secondary lactose intolerance is, however, temporary and is typically caused by an infant having a tummy bug or administration of antibiotics. Symptoms typically improve within two to four weeks and, during this time, the infant may require a lactose-free diet.[11]

HOW IS CMA DIAGNOSED?

Diagnosis should be completed following a full allergy-focused history, which can be taken by a GP and then referral to a dietitian if it is suspected that an infant has CMA. Depending on whether it is suspected that an infant has IgE or non-IgE will influence the referral process. If suspected IgE, the infant should follow a CMP-free diet and a referral complete to secondary care for allergy testing and follow-up. If suspected non-IgE allergy, then a milk-free diet should also be advised. However, referral should be to a dietitian to complete a milk challenge to diagnose.

Diagnosis of CMA can be challenging, as many of the clinical features are common and can overlap with other conditions, such as teething, colic, reflux and typical irritability for an infant under six months old. A large majority of babies will experience some of the symptoms of CMA from time to time, but the majority will not have CMA and, therefore, will not have to be assessed further. Clinical judgement and taking a thorough allergy-focused history is imperative when an infant presents with suspected CMA.[1,6]

In order to suspect a diagnosis of CMA, symptoms will be multiple, significant, persistent and resistant to medical treatment (commonly seen in infants with eczema). If there is a suspected severe IgE-mediated allergy, severe systemic reaction and/or anaphylaxis, emergency management is required.[1,6]

Trial exclusion diets must only be considered if history and examination strongly suggest CMA, especially in exclusively breastfed infants, where measures to support continued breastfeeding must be taken.[1] A referral to a dietitian should also be completed to ensure that nutritional balance is achieved.

As above, in non-IgE CMA, the gold standard is an elimination and reintroduction diet. In the case of breastfeeding mothers, a strict milk-free diet should be followed for two to four weeks, after which point encouragement should be given for the reintroduction of cow's milk-contained products into the mum's diet to identify if symptoms return in the baby.[10] In the case of a formula-fed baby, if non-IgE-mediated CMA is suspected and symptoms are mild to moderate, then an extensively hydrolysed formula (eHF) should be trialled for two to four weeks to identify if symptom relief occurs. Again, if after this period of elimination symptoms are resolved, parents should be encouraged to reintroduce standard infant formula to identify if symptoms return, which would confirm or deny diagnosis of non-IgE-mediated CMA.[7]

Breastfeeding is the best feeding option for babies and the diagnosis of CMA does not mean that breastfeeding should be stopped. Breast milk contains all the necessary nutrients that a baby needs in the first six months of life.

Breastfeeding provides the best source of nutrition for babies. Mums should be supported and encouraged to continue breastfeeding for as long as they wish. Guidelines from WHO (the World Health Organisation) advise preferably up to two years, alongside the introduction of solid foods from around six months.[10,12] Continuation of breastfeeding is particularly important for atopic children.[6] Mothers who are breastfeeding should be advised to follow a strict milk-free diet whilst continuing to do so. During breastfeeding, requirements for certain nutrients increase, including calcium and iodine. It is important that dietetic advice includes education around a milk-free diet for mums to ensure nutritional balance and appropriate growth for their babies, but also to maintain nutritional balance for mums.[9]

During exclusive breastfeeding, infants under six months old require vitamin D drops containing 8.5-10mcg per day. After six months, exclusively breastfed infants require a multivitamin containing vitamins A, C and D alongside a weaning diet. Mums who are breastfeeding require a daily vitamin D supplement of 10mcg, and may also require additional vitamin and mineral supplementation if they are unable to receive adequate amounts through their diet during breastfeeding. This will be assessed by a dietitian.

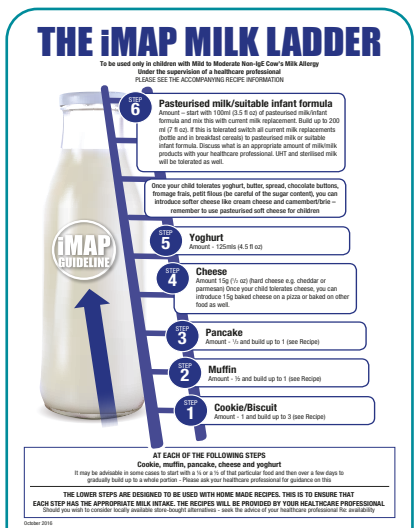
BABY FORMULA

Extensively hydrolysed formula (eHF) is recommended as the first-line formula for babies with mild to moderate CMA.[13] The composition of eHF can vary, with some formulas being whey-based and others casein-based. More recently, companies have included pre- and probiotics within eHF. Guidance of which formula to prescribe will depend on local prescribing criteria.[10]

For infants with severe symptoms (including faltering growth), amino-acid formula (AAF) should be the first-line choice.[10] AAF may also be provided if symptom relief is not seen within two to four weeks of trialling eHF. Clinical awareness and judgement are required, as symptoms exhibited may not be CMA-related. Reassurance should be provided to parents so that they persist with prescribed formula, as evidence suggests that it can take two to four weeks for symptoms to settle.[1]

If an infant is taking standard infant formula purchased from the supermarket or is combination feeding, then this formula will need to be changed to a hypoallergenic formula. These formulas are by prescription only. Partially hydrolysed formulas available online or over the counter are not suitable for the treatment of CMA. Soya formula is also not recommended for babies under six months of age unless closely monitored under the supervision of a dietitian. Soya-based formula can be provided for infants over six months old; however, it should be noted that around 50% of infants with non-IgE-mediated or delayed CMA also react to soya protein and, therefore, if this is the case, all soya should also be excluded from the diet alongside CMP.[15]

Since the publication of The World Allergy Organisation (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines in 2010 (Fiocchi et al),[13] a quality appraisal and systematic review has taken place on global CMA diagnosis and management guidelines published between 2010 and 2020. The full review can be viewed here: https://www.sciencedirect.com/science/article/pii/S1939455121001071.



If a baby is diagnosed with CMA, it is recommended that the infant follows a milk-free diet for six months, which is typically between 10 and 12 months of age. After this time, milk will be reintroduced into the baby's diet via the iMAP milk ladder.[6] This is a staged approach to milk reintroduction which begins with milk baked or cooked within a product leading up to cow's milk reintroduction.