

# COW'S MILK PROTEIN ALLERGY (CMPA): MISDIAGNOSIS AND MANAGEMENT



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**Milk allergy affects less than 2% of UK infants, but diagnosis can be challenging as most of the typical symptoms are common in well babies. In infants with significant and persistent multiple symptoms that are resistant to medical treatment, it is important to consider the diagnosis of CMPA.<sup>1</sup>**

CMPA is a condition that presents in infants before the age of six months, with a prevalence suggested to be between just 2% and 3% in developed countries.<sup>2</sup> Nevertheless, CMPA is the most common food allergy in infants<sup>3</sup> and is more common in infants from families where there is a history of asthma or eczema.<sup>4</sup> Due to the symptoms of milk allergy being common in well babies, overdiagnosis of CMPA can occur. Misdiagnosis can also be commonplace and CMPA can go untreated for long periods, affecting not only the infant, but also impacting parental anxiety. Most infants will be able to tolerate cow's milk and its contained products by the age of five.

There are two distinct types of CMPA: IgE-mediated and non-IgE-mediated. Both are an adverse reaction to milk protein contained in breast milk, formula milk, or in food containing cow's milk. It is felt that around 56% of CMPA in Europe is non-IgE-mediated. However, this figure may be even higher in the UK.<sup>5</sup>

Table 1 overleaf outlines the differences between IgE- and non-IgE-mediated CMPA. The most distinctive

difference, which will inform diagnosis, is the speed at which symptoms occur. NICE (2021) indicates that infants should display one or more of the symptoms in Table 1 and that symptoms have not responded to treatment, e.g. reflux or constipation.<sup>5</sup>

## REFERRAL TO DIETETICS

In clinical practice, referrals are generally completed to dietetic teams for infants aged from around four weeks up to 18 months and beyond. The reason for the variation in referral age may be due to differences in knowledge base amongst healthcare professionals. This can lead to under- and overdiagnosis. This is echoed in NHS data from 2018, showing that in the UK there has been a five- to six-fold increase in the prescription of formula for CMPA. However, this is not replicated in a rise in the number of infants who have a diagnosis.<sup>6</sup>

We know that in primary care settings, GP knowledge can vary greatly with regards to the aetiology, diagnosis and management of CMPA. This has been linked to repeated GP visits, over- and under-prescribing of infant formula

## ESSENTIAL RESOURCES

The Milk Allergy in Primary Care (MAP) Guideline 2019. The GP Infant Feeding Network.

<https://gpifn.org.uk/imap/>

NICE CKS. The Milk Allergy in Primary Care (MAP) Guideline 2019.

<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>

## REFERENCES

Please visit:  
[www.NHDMag.co.uk/article-references.html](http://www.NHDMag.co.uk/article-references.html)

Table 1: The differences between IgE- and non-IgE-mediated CMPA<sup>5</sup>

IgE-mediated	Non-IgE-mediated
An immediate reaction within minutes and up to two hours after consumption	A delayed reaction which occurs between two and 72 hours after consumption
Swelling to lips, face, or eyes	
<b>Skin reaction:</b> hives, urticaria, itchy, reddening	<b>Skin reaction:</b> itchy skin, reddening erythema, atopic eczema
<b>Gastrointestinal upset:</b> nausea, vomiting, diarrhoea, abdominal pain or discomfort	<b>Gastrointestinal upset:</b> reflux, vomiting, loose stools, blood and/or mucous in stools, constipation, abdominal pain or discomfort, irritability
<b>Lower respiratory:</b> cough, chest tightness, wheezing and shortness of breath	<b>Lower respiratory:</b> cough, chest tightness, wheezing and shortness of breath
<b>Upper respiratory:</b> nasal itching, sneezing, congestion, conjunctivitis	

and insufficient advice provided to parents. Some studies have also found that it may take 2.2 months between the initial GP visit and the initiation of prescribed infant formula for the management of CMPA.<sup>7</sup>

Local guidelines for CMPA can also vary greatly and may not be frequently reviewed to support correct diagnostic criteria. A study showed that within 191 CCGs, 71% had guidelines for CMPA that required review and 36% of guidelines had expired. The diagnostic criteria for IgE- and non-IgE-mediated CMPA also varied, with 32% showing a diagnosis tool that did not distinguish between non-IgE and IgE allergy.<sup>8</sup>

Concerns may arise with regards to inconsistencies in diagnosis and treatment for babies with suspected CMPA, including inappropriate advice provided by healthcare professionals, which may lead to the cessation of breastfeeding. Breastfeeding mothers have been found to have been correctly advised to continue breastfeeding within primary care if it is suspected that a baby has CMPA. However, without a referral to a dietitian to support the required maternal exclusion diet, the risk of nutritional deficiency for both mother and infant is greater.<sup>6</sup>

The dietitian plays a key role in education for parents, but also for healthcare professionals to support diagnosis and management of CMPA, and prevent nutritional deficiency. Education for general practice delivered by dietitians is also likely to support a more efficient diagnosis, as well as a reduced spend on infant formula and better patient outcomes for both parents and baby.

## THE DIAGNOSIS AND MANAGEMENT OF NON-IGE-MEDIATED CMPA

### Assessment

NICE has recently updated its guidelines for the assessment and diagnosis of food allergies in children under 19 years.<sup>5</sup> When an infant attends the GP with suspected CMPA, it is recommended that an allergy-focused history be completed.<sup>5</sup> Guidelines for diagnosis and management have also been shown by BSACI to support this.<sup>9</sup> On referral to a dietetic service, the allergy history provided by the GP can then support the dietetic assessment. The dietitian should also take a full allergy-focused history to ensure that the patient is referred for the correct diagnosis.

A dietetic assessment will include discussion around history of feeding and current feeding methods, anthropometry, symptoms including onset and speed at which they occur and also medical history. This information is essential to the diagnostic stage of non-IgE-mediated CMPA.

The majority of children with non-IgE-mediated allergy can be managed in primary care with the support of a dietitian. However, if it is suspected that an infant has an IgE allergy then a referral should be completed to secondary care for follow-up for allergy testing.<sup>5</sup>

### Diagnosis

Diagnosis of CMPA can be difficult and this may be why over- and under-diagnosis are commonplace, due to a large number of symptoms included in the diagnostic criteria also being commonplace in infants of this age, such as colic, reflux, fluctuation in stool consistency and skin rashes/redness.

The gold standard diagnosis of non-IgE-mediated CMPA 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.

Within the case of a formula-fed baby, if non-IgE-mediated CMPA is suspected and symptoms are mild to moderate, then an eHF (extensively hydrolysed formula) 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 CMPA.<sup>5</sup>

### Concerns with diagnosis

Parents may understandably be reluctant to complete a reintroduction challenge due to the time it has taken for symptoms to settle for their infant, and also the pathway they have been on from suspected diagnosis to support received. In some cases this may be 13 to 19 visits to a GP over a period of 12 months.<sup>10</sup> A dietitian's role during this phase is crucial, and draws not only on thorough clinical assessment, but also on the additional skills of behaviour change and motivational interviewing techniques with the parent/carer. The dietitian should outline that in order to correctly manage infant nutrition, a challenge should be completed to ensure that a food group is not incorrectly eliminated. Reassurance and education on the clinical rationale for completing a milk challenge with parents is essential. Asking parents to look forward and envisage their infant's diet in six or 12 months' time can also help during this assessment, as it can prompt parents on the importance of the challenge.<sup>5</sup>

### MANAGEMENT PHASE <6 MONTHS OLD

Once diagnosis is complete, management of CMPA is imperative to ensure that baby (or mother) does not experience nutritional deficiency or that diet impacts growth.

### Baby formula

eHF is recommended as the first-line formula for babies with mild to moderate CMPA. eHF can vary in composition, with some formulas whey- and others casein-based. More recently, companies have included pre- and probiotics within eHF. Guidance of which formula to prescribe as the first line will depend on local prescribing criteria.

For infants with severe symptoms, including faltering growth, AAF (amino-acid formula) should be the first-line choice. It may also be provided if symptom relief is not seen within two to four weeks of trialling eHF. Awareness and clinical judgement is required, as symptoms exhibited may not be CMPA-related. Reassurance should again 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.<sup>5</sup>

### Breastfeeding

Breastfeeding should continue for as long as the mother wishes and continuation of breastfeeding is particularly important for atopic children.<sup>1</sup> 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.<sup>4</sup> Mothers should never be advised to stop breastfeeding if a baby has a diagnosed milk allergy, unless they request to include formula in their baby's diet, or there are concerns with growth and formula top-ups may be required. If this is the case, then families should be supported on techniques required for the introduction of prescribed formula. Parents may also require signposting to local support services.

It must be noted that difficulty may arise due to the altered taste of eHF or AAF and again mothers should be supported by the dietitian on techniques to adjust infants to taste changes. Mothers' knowledge of nutrition during breastfeeding should be explored and the dietitian has an important role to play in this

area. Mothers should be educated on ensuring adequate energy and protein, with a discussion around calcium, iodine and omega-3, as well as advice on utilising supplementation if required. Vitamin D supplementation for both mum and baby should also be advised.

If mum is following a vegan/vegetarian diet then special attention to macro- and micronutrient intake should be considered and this should be monitored closely by the dietitian.

### MILK-FREE WEANING

Prior to baby reaching weaning age, advice should be given regarding how to follow a milk-free weaning diet to ensure nutritional balance. This can be completed as a group session as outlined in the BDA Toolkit,<sup>9</sup> but should include (but not exhaustive to) the following:

- Reading labels to ensure products are milk free, including medications. This should also include discussion around 'may contain' products.
- Utilising plant-based fortified alternatives (calcium, iodine, vitamin B12) products in the baby's diet, eg, soya, oat, or coconut-based products that contain adequate kcals for growth.
- The introduction of other common allergens and what to do if an additional reaction is observed.
- Multivitamin use and when it can be introduced to baby.

### REINTRODUCTION OF MILK INTO BABY'S DIET

If a baby is diagnosed with CMPA, it is recommended that the infant follows a milk-free diet for six months, which is typically until around 12 months of age. After this time, milk will be reintroduced into the baby's diet via the iMAP milk ladder.<sup>1,5</sup> 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.

Support with diagnosis of CMPA can be a challenging area of dietetics, as it draws upon clinical knowledge and also behaviour change skills, whilst offering reassurance to the parent/carer. However, if managed correctly and referral is completed at the appropriate time, then the experience for parents can be a positive one.

### FUTURE MANAGEMENT OF CMPA IN PRIMARY CARE

NHS service provider, Oviva, is a digital health company helping to improve outcomes in CMPA by remote support for parents and carers of infants with CMPA. This support is received from specialist paediatric dietitians via telephone and video consultations and utilising the Oviva smartphone app. The rapid access clinic, for infants with suspected mild to moderate non-IgE-mediated CMPA, receives referrals from GPs, health visitors and other healthcare professionals. The Oviva programme includes: an initial allergy-focused clinical assessment by a dietitian; parent/carer support by weekly coaching via the Oviva smartphone app or telephone calls; a one-to-one weaning call; and additional support for parents for the reintroduction of milk into their baby's diet.

Oviva also supports medicines optimisation by working with GP practices to audit prescription of specialist infant formula, supporting cost savings by facilitating appropriate management of infant formula. Education for practice staff with regards to the aetiology, diagnosis and management of CMPA is also delivered.

### CONCLUSION

Diagnosis of CMPA is particularly challenging as most of the typical symptoms are common in well babies and no further assessment will be needed. However, for babies with multiple symptoms, CMPA should be considered.<sup>1</sup> Diagnosis by dietetic assessment followed by milk exclusion is the gold standard. A cow's milk exclusion trial must, however, be followed by the reintroduction of cow's milk in order for the correct diagnosis to be confirmed and to avoid over-diagnosis.

It is also important to promote breastfeeding amongst the mothers of infants suspected of milk allergy. The 2019 MAP guidelines provide full resources for diagnosing and managing CMPA, including information on the importance of continued breastfeeding, the milk ladder for reintroduction of cow's milk, and the assessment, diagnosis and treatment pathways.<sup>1</sup>