

bsaci guideline for the diagnosis and management of cow's milk allergy

Definition and mechanism

CMPA is defined as a **reproducible adverse reaction** to one or more milk proteins **mediated by an immune mechanism**.

An underlying immunological mechanism distinguishes CMPA from other adverse reactions to milk, e.g. lactose intolerance.

CMPA is classified as:

- Immediate onset** (usually IgE mediated) typically with skin, respiratory, gastrointestinal and rarely cardiovascular symptoms.
- Delayed onset** (non-IgE or combined IgE / non-IgE) with gastrointestinal symptoms and / or eczema.

Prevalence, onset and evolution

CMPA affects **2-3%** of children, presenting typically at **3-6 months** (rarely after 12 months).

Presentation can be **delayed** for weeks to months.

CMPA has a favourable outcome, resolving in most children with **2/3 tolerant by school age**. Predictors of persistence are:

- Immediate onset symptoms vs delayed onset symptoms.
- Reactivity to baked milk on first challenge or exposure.
- Presence of other food allergies, especially egg allergy.
- Concomitant asthma and / or allergic rhinitis.
- Large SPT weal size or higher sIgE level at diagnosis.

Clinical presentation and diagnostic evaluation

Immediate onset (within minutes to two hours)

Presenting with symptoms affecting the:

- Skin:** urticaria, pruritis and angioedema.
- Gut:** abdominal pain, vomiting (repeated or profuse), diarrhoea.
- Respiratory tract:** red/itchy eyes, blocked/runny nose, sneezing, cough, wheeze, breathlessness.
- Cardiovascular system:** drowsiness, dizziness, pallor, collapse.

Wide range in severity from skin symptoms only, to life-threatening or fatal anaphylaxis. Presentation mild in the majority.

Delayed onset (frequently delayed - hours to days)

Presenting with:

- Gastrointestinal symptoms** (range of symptoms and severity).
 - Blood in stool** in otherwise well child.
 - Vomiting** in irritable child with back arching and screaming.
 - Feed refusal** and aversion to lumps.
 - Dysphagia** (possible oesophageal eosinophilia; warrants biopsy).
 - Diarrhoea:** often protracted with propensity to faltering growth.
 - Constipation:** straining with defecation, but producing soft stools.
 - Unwell child:** delayed onset protracted vomiting and diarrhoea.

Wide range in severity from well child with bloody stools to unwell shocked child after profuse vomiting and diarrhoea (FPIES).

Diagnostic evaluation (confirmation of suggestive history)

Immediate onset: **typical** symptoms confirmed by SPT >3mm. **atypical** or **absent** symptoms need SPT >5mm.
 Delayed onset: **GI symptoms:** milk exclusion and assess symptoms.
Eczema: milk exclusion 2-6wks, then reintroduction.

Treatment

Dietary avoidance (avoidance advice)

How to read a label for a milk-free diet

Look out on labels for any of the following ingredients*

- | | |
|---|---|
| <ul style="list-style-type: none"> Butter, butter fat, oil, acid, ester or milk Casein, casein hydrolysate, sodium or calcium caseinate Cow's milk (fresh, UHT, dried, powdered, condensed) Cheese, cottage cheese Cream, artificial cream Curds, ghee, custard | <ul style="list-style-type: none"> Lactalbumin, lactoglobulin, lactoferrin margarine Milk solids (non-fat milk solids milk sugar or protein) Animal milks (goat's milk) Sour cream or milk solids Whey, whey powder or syrup sweetener, hydrolysed whey Yogurt, fromage frais |
|---|---|

Milk is sometimes found hidden in the following:

- | | |
|--|---|
| <ul style="list-style-type: none"> Biscuits / baked goods Processed meat | <ul style="list-style-type: none"> Savoury snacks, soup, gravy Pastry, batter |
|--|---|

*In EU all pre-packaged must declare milk on allergy list if it is an ingredient

Choice of substitute milks (replacing cow's milk in diet)

Suitable milk substitutes

- Breast milk** (suitable for most with CMPA).
- Hypoallergenic formulas** (first choice; AAF for severe CMPA).

Extensively hydrolysed formulas <ul style="list-style-type: none"> Aptamil Pepti 1, Althéra Nutramigen lipil, Similac Alimentum Pepti Junior, Pregestimil Pepdite, MCT pepdite 	Amino-acid formulas <ul style="list-style-type: none"> Neocate LCP Nutramigen AA Neocate active (>12mo) Neocate advance (>12mo)
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- Soya based fortified drink** (not recommended in infants <6mo).

Unsuitable (U) or less desirable (L) milk substitutes

- U - Heated or processed fresh cow's milk.**
- U - Other mammalian milks** (e.g. goat's, donkey's, etc.).
- L - Alternative milk 'beverages'** (e.g. almond, coconut, rice, soya) to be used under dietetic guidance in older children.

Reintroduction (rate of resolution varies so timing and location (home or hospital) must be individually assessed)

Guidance for reintroduction of cow's milk

- Consider reintroduction from **12 months**.
- Review every **6-12 months** (repeat SPT if IgE mediated).
- Start with **baked** milk as less allergenic.
- Home reintroduction** may be attempted where:
 - Mild symptoms on noteworthy exposure.
 - No reaction in past 6 months.
 - Significant reduction in SPT (in IgE mediated).
- Hospital reintroduction** recommended in:
 - Any previous moderate to severe reaction (incl. FPIES).
 - Less severe reaction to trace exposure.
 - Regular asthma preventative treatment.
 - Multiple or complex allergies.
 - Parents unable to understand protocol

Once tolerance is established, encourage greater exposure of **less processed** milk as in 'Milk Ladder'

Milk Ladder

Factors considered:

- Volume or quantity
- Effect of heating – degree and duration
- Wheat matrix effect

*Less denatured / High protein dose
More allergenic*

*More denatured / Lower protein dose
Less allergenic*

Stage 1	Stage 2	Stage 3	Stage 4
Small crumb of biscuit with <1g of CMP per biscuit. Build up to whole biscuit over 5 weeks.	Other baked products containing CMP, e.g. biscuits, cakes, muffins, waffles, scotch pancakes. Butter, margarine Cheese powder flavoured	Products containing cooked cheese or whole cow's milk as heated ingredient e.g. custard, cheese sauce, pizza, rice pudding. Chocolate, chocolate coated items. Fermented desserts Yogurt	Fresh milk products.
			NOTES (all stages): <ul style="list-style-type: none"> Proceed with caution Classification not perfect, so step-up may be bigger than expected, esp. in Stage 3. If reacting, stop and go back to lower stage