

Cow's Milk Protein Allergy in Children (Cow's Milk Protein Intolerance, CMPA) — Types and Treatment

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Milk protein allergy or intolerance is characterized by an allergic reaction to the protein found in cow's milk. It manifests as a variety of symptoms and signs that develop during infancy and regress by age 5. However, the intolerance is responsible for significant anxiety and parental distress, leading to children being placed on milk-free diets that lead to significant nutritional deficiencies. It is therefore important to diagnose this condition promptly and counsel parents accordingly.



Epidemiology of Milk Protein Allergy in Children

Cow's milk protein allergy (CMPA) or cow's milk intolerance occurs in up to 4% of children. The highest prevalence rates are in infancy, with a resolution of symptoms in 50% of children by the age of 1 year, and in 90% by the age of 5 years.

Principal Allergens in Cow's Milk

The diagnosis of CMPA can be confusing to both physicians and parents. It is important to differentiate between lactose intolerance and CMPA, as the latter is characterized by a hypersensitivity reaction that is triggered by specific immunologic mechanisms.

Two main proteins in cow's milk can trigger an allergic reaction: casein and whey proteins. α 1, α 2, α 3, and κ -casein belong to the casein family of proteins and can trigger a reaction. α -lactalbumin and β -lactoglobulin belong to the whey protein family and can also cause allergic reactions.

Types of CMPA

Two types of CMPA have been reported:

1. **IgE-mediated** (immediate allergic reaction): Immunoglobulin E-associated CMPA is characterized by rhinorrhea, sneezing, hives, skin rash, and wheezing within 2 hours of a child drinking cow's milk
2. **Non-IgE mediated** (delayed allergic reaction) is characterized by allergic symptoms occurring approximately 2 to 7 days after a child drinks cow's milk. CM-induced enterocolitis syndrome, CM-induced enteropathy of the small bowel, and CM-induced proctitis and proctocolitis are non-IgE mediated.

Because both of these reactions can also occur in atopic eczema and *Eosinophilic gastroenteritis*, these conditions should be ruled out before consider a diagnosis of CMPA.

Presentation of Milk Protein Allergy in Children

The clinical manifestations of CMPA are varied but predominantly involve the skin and gastrointestinal tract (GI). Dermatological symptoms include itching, hives, and eczematous reaction, while GI manifestations include nausea, vomiting, diarrhea, abdominal pain, and hematochezia.

Other manifestations include irritability (especially in infants), poor feeding and growth retardation due to malabsorption of nutrients, facial edema, and wheezing.

Workup of Milk Protein Allergy in Children

No specific tests are used to detect CMPA. Diagnosis is based on a detailed history of symptoms and a thorough physical examination. It is important for the physician to obtain details and a timeline of symptoms from the parents and to confirm that symptoms occur following the consumption of cow's milk. In children with atopic dermatitis, if there is no direct relationship between cow's milk consumption and symptoms, then no further testing is required.

In the case of a positive correlation, other tests in the workup include:

- **Skin prick:** The negative predictive value of this test is more than 95%. However, a food challenge test is indicated to exclude atopic reactions.
- **Serum specific IgE test to cow's milk protein:** This test may help only in 60% of children who have CMPA and a positive IgE test.
- **Elimination of cow's milk:** If CMPA is suspected, then the infant should be fed a diet free of cow's milk for up to 1 month. A child without GI symptoms

can be fed extensively hydrolyzed formula (eHF) or soy formula (SF). Although amino acid formula (AAF) is non-allergenic, it is also expensive and bland, and is therefore not recommended.

In older children, EHF, SF, and AAF substitution are not required, as there are several foods available to replace cow's milk.

In infants with suspected IgE-mediated reactions, if there is an inadequate response with EHF or SF, then AAF substitution can be tried for 2 weeks.

An oral food challenge is indicated if symptoms improve following the elimination of cow's milk. This is the gold standard test for detecting CMPA. It must be performed in a specialized medical setting with facilities for resuscitation if required. In infants and children with immediate reactions to cow's milk, including GI symptoms, anemia, and hypoalbuminemia, oral food challenge is not indicated, however.

An Evaluation Algorithm of Infants Suspected to have CMPA

1. If the infant shows symptoms and signs suggestive of CMPA including anaphylaxis or a clear, immediate allergic reaction, a CMP elimination diet and testing for specific IgE are indicated. A positive specific IgE test will confirm a diagnosis of CMPA; a therapeutic elimination diet should be commenced thereafter. If specific IgE is negative, however, a standardized oral challenge with CMP is recommended.
2. If the infant's symptoms and signs do not include anaphylaxis or other immediate type of reaction, a diagnostic elimination diet can be used. If symptoms improve, a standardized oral challenge with CMP is recommended; a positive result confirms a diagnosis of CMPA. Specific IgE testing is not recommended for this group of patients.
3. If the infant's symptoms and signs do not improve after the commencement of a diagnostic elimination diet, the diagnosis of CMPA can be excluded and a CMP elimination diet is not needed.

Differential Diagnosis of Milk Protein Allergy in Children

Infectious gastroenteritis should be excluded before carrying out allergy testing.

CMPA is also not associated with an irritable, crying infant with infantile colic.

Treatment of Milk Protein Allergy in Children

Avoid SF in infants with allergy symptoms under the age of 6 months or in children with GI symptoms. Soy milk can also cause GI symptoms.

Children with mild atopic dermatitis and no history of cow's milk protein reactions should not be prescribed a CMP elimination diet.

Infants and children with CMPA should be prescribed a nutritionally balanced diet and calcium supplementation should be considered.

In breastfed infants with confirmed CMPA, the mother's diet should be free of cow's milk

protein, eggs, etc., for a month. If the infant improves, then the mother should begin consuming large amounts of cow's milk for 7 days, to see if symptoms recur in the infant. If symptoms reappear, then the mother should commence a cow's milk-free diet until the infant weans. If there are no symptoms after the reintroduction of cow's milk in the mother's diet, then all foods that were previously excluded can be reintroduced to the mother's diet one at a time.

Substituting cow's milk with goat's or sheep's milk will not help treat CMPA.

Several dairy foods such as yogurt, butter, and cheese contain milk protein. Parents should carefully read nutritional labels if their child has been prescribed a diet free of cow's milk protein.

Prognosis of Milk Protein Allergy in Children

CMPA usually resolves within the first year of life and by no later than the age of 5. Elimination of cow's milk from the diet may be required for up to a year after confirming the diagnosis. Later, the child can be given the cow's milk challenge, beginning with small amounts of milk products. If no reaction is seen, then milk products can be reintroduced to the child's diet.

References

[Cow's milk protein allergy in children: a practical guide](#) via ncbi.nlm.nih.gov

[Milk Allergy Diet for Children](#) via stanfordchildrens.org

[Cow's Milk Protein Intolerance](#) via gikids.org

[Cow's milk allergy: evidence-based diagnosis and management for the practitioner](#) via ncbi.nlm.nih.gov

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