Hypoallergenic Formulas for Infants and Children: When to Use Extensively Hydrolyzed Formula (eHF) vs. Amino Acid-Based Formula (AAF)

The prevalence of allergy is steadily rising, with around 30-40% of the world's population now affected by one or more allergic conditions. ^{1,2} Cow's milk allergy (CMA) is one of the most common childhood allergies, affecting up to 3% of infants and children. The average time to diagnosis of CMA is 12 weeks, requiring more than 4 visits to a healthcare professional before a diagnosis is determined. During this time, the impact on infants and caregivers extends beyond symptoms alone, impacting physical, psychological, and financial aspects of their lives.

Common Symptoms of CMA

Allergic symptoms can happen immediately after feeding or be delayed by hours or days. Common CMA symptoms include, but are not limited to:

- Digestive symptoms: Vomiting, diarrhea, and gastroesophageal reflux
- Respiratory symptoms: Asthma-like symptoms, wheezing, and coughing
- Skin problems: Rashes, hives, or eczema, which may take 3-5 days to appear

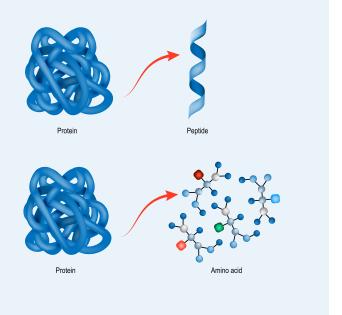
Breastfeeding is the best nutrition for all infants. If a breast-fed baby develops CMA, intervention such as a cow's milk elimination diet by the mother should be tried. When breastfeeding is not possible or becomes too difficult, there are hypoallergenic formulas specifically designed for infants and children with allergies. There are two types of hypoallergenic formulas: extensively hydrolyzed formulas (eHF) and amino acid-based formulas (AAFs) and each of these has some specific indications and benefits.

Extensively Hydrolyzed Formula (eHF)

These formulas contain short-chain peptides such as di- or tri-peptides, and some amino acids. They contain whey or casein protein from cow's milk that has been heat-treated for hydrolysis and/or enzymatically hydrolyzed.

Amino Acid-Based Formula (AAF)

These formulas are also called elemental formulas and contain 100% free amino acids. These products are 100% hypoallergenic and do not contain any cow's milk protein.⁷



References

- Fiocchi A, et al. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines. Pediatr Allergy Immunol. 2010;21 Suppl 21:1-125.
- Australasian Society of Clinical Immunology and Allergy (ASCIA). Cow's milk (dairy) allergy. 2019. https://www.allergy.org.au/patients/fast-facts/cows-milk-dairy-allergy Accessed June 6. 2023.
- 3. Høst A. Frequency of cow's milk allergy in childhood. *Ann Allergy Asthma Immunol.* 2002 Dec;89(6 Suppl 1):33-7.
- Edwards CW, Younus MA. Cow Milk Allergy. [Updated 2022 Jun 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. https://www.ncbi.nlm. nih.gov/books/NBK542243/
- Wilsey MJ, Florio J, Beacker J, et al. Extensively hydrolyzed formula improves allergic symptoms in the short term in infants with suspected cow's milk protein allergy. Nutrients. 2023 Mar 30;15(7):1677.
- Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's milk protein allergy in infants and children: ESPGHAN GI Committee Practical Guidelines. J Pediatr Gastroenterol Nutr. 2012;55(2):221-229.
- Malone A, Nieman Carney L, Long Carrera A, Mays A. ASPEN Enteral Nutrition Handbook, 2nd edition. Silver Spring, MD, 2019.
- American Academy of Pediatrics. Committee on Nutrition. Hypoallergenic infant formulas. Pediatrics. 2000:106(2):346-349.
- Meyer R, Groetch M, Venter C. When should infants with cow's milk protein allergy use an amino acid formula? A practical guide. J Allergy Clin Immunol Pract. 2018 Mar-Apr;6(2):383-399.
- American Academy of Pediatrics. Committee on Nutrition. Formula feeding of term infants. In: Pediatric Nutrition (8th Ed). Kleinman RE, Greer FR. (eds). 2020. Itasca, IL: American Academy of Pediatrics: 79-112.
- 11. Venter C, et al. Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy a UK primary care practical guide. Clin Transl Allergy. 2013;3:23.
- 12. Ludman S, et al. Managing cows' milk allergy in children. BMJ. 2013;347:f5424.
- 13. Vandenplas Y, et al. Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Arch Dis Child*. 2007;92:902-8.



Indications

eHF

- Mild-to-moderate CMA
- Impaired GI function and malabsorption syndromes
- Trouble tolerating polymeric formula
- Lactose intolerance, in some cases⁷
- Presence of CMA and soy protein allergies⁸

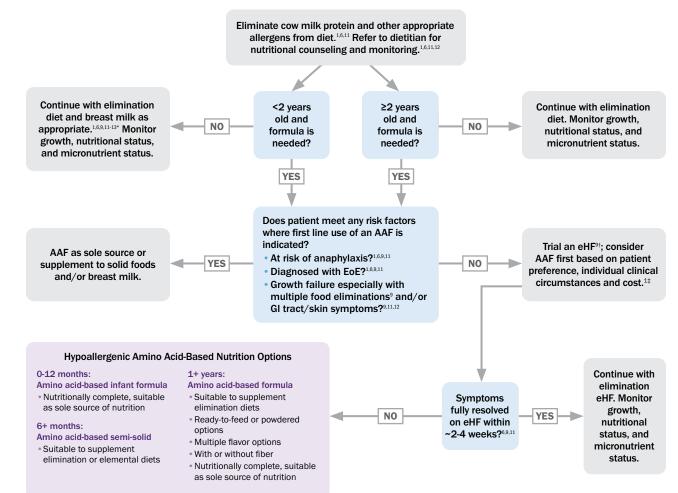
AAF

- Food allergies with faltering growth/failure to thrive⁹
- Severe allergies where an eHF formula has not resolved symptoms⁹
- Malabsorption disorders and GI impairment, short bowel syndrome or intestinal failure, food protein-induced enterocolitis syndrome (FPIES), eosinophilic esophagitis (EoE)^{7,10}
- Anaphylaxis, despite limited evidence, due to potential risk for a severe reaction⁹

Considerations for Reintroduction of Cow's Milk

- Children should be reevaluated every 6-12 months to assess if they have developed tolerance to cow's milk protein⁶
- This tolerance is generally achieved in greater than 75% of children by age 3 years and greater than 90% by age 6 years⁶

When to Use an eHF vs an AAF for the Dietary Management of CMA



Individual needs as directed by HCP. Monitor growth, nutritional status, and micronutrient status.

Breast milk is the preferred source of nutrition wherever possible.

- * May include maternal elimination diet if breastfeeding and patient continues to react. 6.11 Maternal elimination diet should always be conducted under medical supervision. Maternal vitamin and mineral supplementation should be considered 1.6.11 and diet should be monitored for nutritional adequacy. 6
- † In settings where the cost of an AAF is lower, the use of an AAF may be equally reasonable. 1
- [‡] Soy formula can be recommended as a third choice for patients without soy allergy and > 6 months of age.¹

AAF = amino acid-based formula; eHF = extensively hydrolyzed formula; EoE = eosinophilic esophagitis; HCP = healthcare professional

This flow chart is intended to be used as a reference for healthcare professionals when managing patient: with cow milk allergy/multiple food allergies as a **primary** diagnosis.

Note: This content has been developed for use by healthcare professionals to inform other clinicians and/or patients/caregivers. ASPEN is making this content available for informational purposes only. This content is not based on ASPEN Board Approved documents and should not be confused with ASPEN clinical guidelines as it was not developed according to ASPEN guideline processes. Recommendations provided here do not constitute medical or other professional advice and should not be taken as such. To the extent that the information presented here may be used to assist in the care of patients, the primary component of quality medical care is the result of the professional judgement of the healthcare professionals providing care. The information presented here is not a substitute for the exercise of professional judgement by healthcare professionals. Circumstances and patient specifics in clinical settings may require actions different from those recommended in this document; in those cases, the judgment of the treating professional should prevail. Use of this information does not in any way guarantee any specific benefit in outcome or survival. This tool is intended to supplement, but not replace, professional training and judgment.



Practice tool supported by Nutricia North America