Cow's Milk Protein Allergy in Infants and Children

**Description/Etiology**

Cow’s milk protein allergy (CMPA; also called cow’s milk allergy [CMA] and cow’s milk protein intolerance [CMPI]) refers to an immunologic reaction to one or more of the proteins found in cow’s milk (commonly referred to as cow’s milk proteins [CMPs]), which results in adverse systemic manifestations (e.g., asthma, eczema, rhinitis) and gastrointestinal signs and symptoms (e.g., diarrhea, vomiting, colic). Most signs and symptoms of CMPA manifest in early infancy if the infant is fed formula and manifest after weaning in infants who are breastfed. Less frequently, breastfed infants react to CMPs consumed by the mother when they are delivered through breast milk.

There are 2 types of CMPA: the immunoglobulin E (IgE)-mediated type, in which histamine is released during exposure to an antigen, and the non-IgE-mediated type. IgE-mediated CMPA typically triggers vomiting, angioedema, and/or urticaria within an hour of ingestion of CMPs. Signs and symptoms of non-IgE-mediated CMPA develop within 1 hour to several days following exposure to CMPs and include diarrhea, atopic dermatitis, and/or general intestinal discomfort.

The most accurate method for diagnosing CMPA is to eliminate CMPs from the infant’s diet to assess if signs and symptoms improve and perform a challenge test with CMP to evaluate for the return of signs and symptoms. Treatment of CMPA requires eliminating all sources of dietary CMPs. In some cases, this can be accomplished by exclusive breastfeeding for the first 4–6 months of the infant’s life unless the infant develops signs and symptoms of reaction to the CMPs in breast milk. If the infant reacts to breast milk, the mother can attempt to eliminate all sources of CMPs from her diet. Alternatively, the infant can be fed an extensively hydrolyzed infant formula (e.g., Nutramigen or Alimentum, in which a process of enzymatic hydrolysis breaks down CMPs to amino acids), an extensively hydrolyzed rice protein-based infant formula (e.g., Novarice), or a milk-free amino acid-based formula (e.g., Neocate, EleCare). All of these formulas are expensive, leading many clinicians to recommend initially giving the infant a more economical soy-based formula (e.g., Isomil, Alsoy); however, approximately 50% of infants with CMPA also demonstrate sensitivity to soy protein. Goat’s milk should not be considered as an alternative to cow’s milk because it cross-reacts with CMPs and is deficient in folic acid. Rice milk is not recommended for children under 5 years of age due to its relatively high arsenic content.

**Facts and Figures**

CMPA is responsible for one-fifth of food allergies in children in the United States, affecting approximately 2.5% of infants under 12 months of age. Many affected infants develop a tolerance for CMP as they mature. In fact, study results suggest that 80–90% of children outgrow their allergy to CMPs by 3 years of age (Warren et al., 2013).

**Risk Factors**

Children are more likely to have CMPA if they have a family history of allergy-related conditions (e.g., asthma, eczema, hay fever, food allergies). White children have about twice the incidence of CMPA as compared with Asian and Black children (Warren et al., 2013).
Signs and Symptoms/Clinical Presentation
Infants and children with CMPA exhibit a wide range of signs and symptoms, including colic, diarrhea, vomiting, gastrointestinal bleeding, gastroesophageal reflux, chronic constipation, sleeplessness, wheezing, rhinitis, bronchitis, asthma, sneezing, coughing, eczema, excessive crying or fussiness, anaphylaxis, and failure to thrive.

Nutritional Assessment
› Patient Medical History
  • Ask about signs and symptoms (e.g., vomiting, diarrhea, constipation) that can indicate inadequate intake of nutrients or fluid and can negatively affect appetite
› Physical Findings of Particular Interest
  • Many children with CMPA also have eczema
  • Pallor may indicate anemia as a result of gastrointestinal bleeding
› Patient Dietary History
  • Ask the parents about the infant’s/child’s feeding history, including whether he/she was exclusively breastfed or received formula, the type of formula if appropriate, and the timing and description of signs and symptoms in relation to the time of feedings
› Anthropometric Data
  • Anthropometric tools are available for the measurement of adequate nutrition in children
    – The Centers for Disease Control and Prevention (CDC) established references for weight and growth patterns, which can be tracked on weight-for-age/height-for-age/weight-for-height age-based growth charts; as well as Body Mass Index (BMI) for age charts which assist in the calculation of BMI for ages 2 to 20 years
› Laboratory Tests and Diagnostic Tests of Particular Interest to the Nutritionist
  • Complete blood count (CBC), including hemoglobin and hematocrit, may identify anemia and/or malnutrition
  • Blood testing may show nutrient deficiencies (e.g., in iron, folate, calcium, essential fatty acid, vitamin D)

Treatment Goals
› Promote Resolution of Nutrient Deficiencies and Symptomatic Relief, and Increase Parental Knowledge Regarding CMPA
  • Monitor weight and results of laboratory tests and review feeding history; report abnormalities to the treating physician
  • Evaluate for signs and symptoms (nausea/vomiting/diarrhea/constipation) of CMPA and adjust dietary care plan if indicated
  • Review diet history information to assess dietary intake and patterns and provide detailed education to the parent (and child if age-appropriate) regarding a CMPA-appropriate diet/feeding plan
    – Provide breastfeeding mothers with encouragement and dietary recommendations for alleviating symptoms in breastfed infants with CMPA
    – Provide feedings with prescribed formula that replaces cow’s milk and educate parents on the risks, benefits, and details of the prescribed feeding regimen
  • Assess parental anxiety level and for knowledge deficits regarding CMPA; provide emotional support and educate about CMPA signs and symptoms, treatment risks and benefits, and individualized prognosis
  • Request referral, if appropriate, to a social worker for identification of local resources for inexpensive formula and/or for subsidy programs to offset cost of formula

Red Flags
› Parents commonly suspect food allergy when their infant/child develops signs and symptoms of CMPA and often attempt to restrict or make changes in the diet to prevent allergic reactions. Dietary changes often made by parents include switching to goat’s milk, soy milk, or rice milk; watering down formula; and/or giving juice instead of formula. These dietary changes can result in the development of nutrient deficiencies, gastrointestinal manifestations, and in some cases failure to thrive. It is important to educate parents regarding healthy alternatives for feeding infants and children with CMPA
› Researchers report that prepubertal children with persistent CMPA exhibit lower bone mineral density as compared with children with non-cow’s milk food allergies, likely due to lower intakes of calcium and vitamin D (Mailhot et al., 2016)
What Do I Need to Tell the Patient/Patient’s Family?

› While exclusive breastfeeding for the first 6 months of the infant’s life is the best choice for most infants with CMPA, partial breastfeeding for at least 6 months is also associated with reduced sensitization to cow’s milk
› Researchers report that exclusive breastfeeding for > 4 months is associated with a reduced risk for cow’s milk sensitization in early childhood (Liao et al., 2014)
› As reported with exclusive breastfeeding, study results indicate that partial breastfeeding for at least 6 months is associated with a lower risk of cow’s milk sensitization as well as the development of eczema in young children (Chih-Yung et al., 2016)
› If an exclusively breastfed infant continues to exhibit signs and symptoms of CMPA, it may be helpful for the mother to eliminate all CMPs and soy from her diet to prevent the transfer of CMPs and soy proteins through breast milk
› When exclusive breastfeeding is not possible, giving extensively hydrolyzed or milk-free amino acid-based formulas is recommended as the best feeding option
› Extensively hydrolyzed rice protein-based infant formula is also shown to be well-tolerated by infants with CMPA and can be used as an adequate alternative to cow’s milk-based extensively hydrolyzed formulas (Vandenplas et al., 2014)
› Introduction of solid food should be delayed until the infant with CMPA is at least 6 months of age. Foods should be offered one at a time for a period of several days in order to monitor for allergic reactions. All foods containing CMPs or soy should be avoided until the child is at least 12 months of age and should then be introduced in very small amounts in order to monitor tolerance
› It is important to read product labels when introducing solid foods. Terms that indicate the presence of cow’s milk include casein, caseinates, curd, lactoglobulin, lactose, milk solids, whey, buttermilk, milk sugar, whey sugar, and whey syrup sweetener
› Some children may tolerate CMP in baked goods while still reacting to unbaked CMP sources; approximately 75% of persons with CMPA exhibit a tolerance for baked milk (Savage & Johns, 2015)
› It is important to ensure adequate intake of calcium and vitamin D in children with persistent CMPA
› Symptoms associated with CMPA (e.g., excessive crying, sleeplessness) should improve with the removal of CMPs (and soy proteins when necessary) from the infant’s diet
› In most affected children, CMPA resolves by 3 years of age

Discharge Planning

› Provide dietary and feeding recommendations to the parent (and child if age-appropriate) according to the specific needs of the individual patient. Plan should include recommendations as outlined in What Do I Need to Tell the Patient/Patient’s Family, above

References

1. Chih-Yung, C., Sui-Ling, L., Kuan-Wen, S., Ming-Han, T., Man-Chin, H., Shen-Hao, L., ... Huang, J. (2016). Exclusive or partial breastfeeding for 6 months is associated with reduced milk sensitization and risk of eczema in early childhood: The PATCH Birth Cohort Study. *Medicine*, 95(15), 1-6. doi:10.1097/MD.0000000000003391