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Cow's Milk Allergy in a Preterm Infant

A Case Presentation

Patricia J. Becker, MS, RD, CNSC

Abstract: *For the infant born prematurely, it is the immaturity of organ systems, such as the pulmonary system, the immune system, and gastrointestinal tract, that is most problematic. Apnea of prematurity, respiratory distress syndrome, uncoordinated suck, swallow, breathe sequence, immature protection of the airway during feeding, and an immature gut are the sequelae that must be overcome to support extrauterine growth. In some infants, as is the case in the patient presented here, other issues influenced by familial trait can also occur, making supporting growth even more of a challenge. In this case, an infant born at 31 weeks gestational age, with a history of several first-degree relatives with cow's milk allergy (CMA), is presented. CMA, respiratory distress with oral feeds, and dysphagia diagnosed by modified barium swallow study are discussed here. Eliminating food allergens from the maternal diet, the use of an amino acid-based infant formula for fortification of human milk to support growth goals, and the modification of thin liquid consistency of human milk to prevent aspiration were required in the treatment of the patient.*

Keywords: growth and development; early life span nutrition; gastrointestinal disorders

Medical nutrition therapy (MNT) for the preterm newborn often involves a multifaceted plan of care. The primary goal of MNT is to promote the growth and development of the preterm newborn at a pace that mirrors intrauterine rates. It is the immaturity of all organ systems that can impede the progress of this goal. The immature gut and the respiratory and immune systems often pose the greatest obstacles. The presence of other familial traits can also affect the outcome.

Common problems associated with the preterm newborn often include osteopenia of prematurity, apnea of prematurity, immature swallow function, and feeding intolerance. The immature gut can contribute to the occurrence of adverse reactions to foods in preemies. Although rare, in those with a family history of food hypersensitivity, this can be exacerbated.

Adverse reactions to food, often referred to as *food allergies*, have been described in broad generalization for reactions that can present with a variety of symptoms.

The American Academy of Allergy and Immunology has recommended the standardization of terminology for describing these food-induced reactions.

1. Adverse reaction to food: a clinically abnormal response to an ingested food or food additive.

2. Food hypersensitivity (allergy): a clinically abnormal response to an ingested food/additive caused by an immunological reaction.
3. Food anaphylaxis: allergic hypersensitivity reaction in response to a food/additive involving IgE antibodies with rapid onset, which may be life threatening.
4. Food intolerance: general term describing an abnormal physiologic response to an ingested food/additive or an idiosyncratic response to an ingested food/additive.
5. Food idiosyncrasy: abnormal response that may mimic food hypersensitivity but does not involve an immune response.
6. Food toxicity: poisoning. An adverse response caused by a food/additive, not involving immune mechanism, and nonimmune release of chemical mediators may occur. Toxins may be from the food itself or from microbial contamination of the food.
7. Food aversion: may mimic adverse food reactions but are not reproduced under blinded testing.¹

The American Academy of Pediatrics (AAP) Committee on Nutrition: Section on Allergy and Immunology offers valuable information on the treatment of

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Table 1.**Twelve-Day Feeding Protocol**

Day	Caloric Density, cal/oz	mL/kg/d	Special Instructions
1-4	20	10 mL/kg	Provide mother's own milk or donor breast milk
5	20	20 mL/kg AM 30 mL/kg PM	
6		40 mL/kg AM 50 mL/kg PM	
7	22		Fortify with human milk fortifier
8		60 mL/kg AM 70 mL/kg PM	
9		80 mL/kg AM 90 mL/kg PM	Decrease intravenous (IV) lipids to 50%
10	24	100 mL/kg	Fortify with human milk fortifiers; discontinue IV lipids
11		110 mL/kg AM 120 mL/kg PM	Discontinue parenteral nutrition
12		140 mL/kg AM 150 mL/kg PM	

infants who exhibit symptoms of cow's milk allergy (CMA). Although the incidence of cow's milk allergy is very low in the breastfed infant, cases of anaphylaxis and cow's milk-induced proctocolitis do occur. The presence of immunologically recognizable proteins from the maternal diet can be found in breast milk.

This statement includes clinical practice treatment recommendations, including the following:

1. In the breastfed infant, elimination of cow's milk protein, eggs, fish, peanuts, and tree nuts from the maternal diet is recommended.
2. Formulas based on partially hydrolyzed cow's milk protein, which contain peptides and intact cow's milk protein, are noted to provoke significant reactions in a high percentage of infants with CMA.

3. Extensively hydrolyzed formulas may also provoke allergic reactions, but more than 90% of these infants tolerate extensively hydrolyzed formulas.
4. Infants who continue to exhibit symptoms have been shown to have fewer symptoms with free amino acid-based infant formulas.^{2,3}

The occurrence of true food hypersensitivity affects less than 10% of children under 2 years of age. If present, undiagnosed food hypersensitivity can result in failure to thrive.⁴

Distinguishing true food hypersensitivity from an adverse reaction to food in the preterm newborn can be difficult. Repeated challenges with the food as the infant matures can be key in determining the cause of food-induced reactions.

The medical nutrition therapy provided in this case was patient specific. As with all patients, MNT must be individualized to meet the needs of the patient.

History

Baby girl M was born at 31 weeks gestational age by obstetrical dates. Preterm labor progressed rapidly with increasing fetal distress. The patient's mother was prepared for emergent cesarean section delivery because of fetal bradycardia. Prior to the procedure, baby girl M was born by precipitous vaginal delivery. With stimulation, the infant breathed spontaneously and required no respiratory support.

Family history included 1 parent and 1 sibling with documented CMA. The patient's sibling had a history of positive IgE antibodies reaction to cow's milk with a history of failure to thrive resulting from gastrointestinal symptoms related to CMA. Baby girl M's (B/G M) brother was followed by the pediatric allergy clinic at a large tertiary care hospital.

At birth, B/G M weighed 1.37 kg, with a length of 41 cm and a head circumference of 28 cm, plotting on the Fenton growth chart (<http://members.shaw.ca/tanisfenton>) between the 25th and 50th percentile for gestational age.

The baby's mother stated her intent to breastfeed the infant and her desire to avoid the use of formula given the CMA history of her other child.

Nutrition support with parenteral nutrition was initiated on day 1 of life. On day 2 of life, B/G M was started on a 12-day feeding protocol of maternal breast milk at an initial rate of 10 mL/kg/d providing 2 mL every 3 hours (see Table 1).

Her mother eliminated all dairy products from her diet as a precaution to prevent potential food hypersensitivity. The mother also verbalized her desire to avoid fortification of maternal breast milk with human milk fortifier, a cow's milk base fortifier. Discussions with the pediatric allergy/immunology team determined that avoiding cow's milk protein was not indicated if no symptoms of CMA were present. Therefore, as indicated on the neonatal intensive care unit

Table 2.

Nutrient Content of Feeds

Item Name	Unit of Measure	Calories	Protein	Calcium	Phosphorus
Preterm human milk	1 oz	20	0.42 g	7.5 mg	3.9 mg
Preterm human milk	150 mL/kg	120 cal/kg	2 g/kg	37.5 mg/kg	19.5 mg/kg
Preterm human milk + similac human milk fortifier	1 oz	24	0.72 g	41.4 mg	23.4 mg
Preterm human milk + similac human milk fortifier	150 mL/kg	120 cal/kg	3.6 g/kg	207 mg/kg	117 mg/kg
Preterm milk + Neocate	1 oz	24	0.55 g	12.5 mg	7.62 mg
Preterm milk + Neocate	150 mL/kg	120 cal/kg	3 g/kg	63 mg/kg	38 mg/kg
Recommended intake for preterm newborn	150 mL/kg	120 cal/kg	3-4 g/kg	120-220 mg/kg	60-140 mg/kg

(NICU) feeding protocol, the patient's maternal breast milk was fortified with human milk fortifier on day 8 of the 12-day feeding protocol.

Presenting Complications

Respiratory distress/apnea of prematurity.

On day of life (DOL) 7, B/G M experienced episodes of apnea and bradycardia. Treatment included the initiation of caffeine. On DOL 9, B/G M had 11 events of apnea and bradycardia, requiring respiratory support with continuous positive airway pressure. On DOL 15, after failing a room air trial, B/G M received a low-flow nasal cannula with a one-quarter liter of oxygen with no recurring apnea and bradycardia.

Rule out sepsis. On DOL 7, blood cultures were found to be positive for gram-positive cocci that were sensitive to vancomycin. Urine and cerebral spinal fluid were both negative. B/G M received a 7-day course of antibiotics for presumed pneumonia. Also during this period, B/G M began to experience stridor with feedings, raising concerns for possible aspiration.

Because of the immaturity of the immune system in the preterm newborn, fever and

increased white blood cell production are generally not the first signs of infection. Preterm newborns most often present with respiratory distress and feeding difficulty. This fact makes discerning the cause of feeding difficulty and/or respiratory distress problematic.⁵⁻⁷

Gastrointestinal (GI) anaphylaxis: GI symptoms/bloody diarrhea. On DOL 21, B/G M had increased stool output with frank blood noted. With the occurrence of bloody stools, the pediatric allergy-immunologist recommended that the patient's mother eliminate all dairy products, egg, chickpeas, peanuts, and tree nuts from her diet. The product used to fortify the infant's maternal breast milk was also changed from a cow's milk-based human milk fortifier to a free amino acid-based infant formula. Food protein-induced proctocolitis is a non-IgE-mediated disorder. Newborns may present with overt or occult blood in stools, which is often the sole manifestation.^{8,9}

Poor growth/failure to thrive. In this patient, poor growth was treated with fortification of maternal breast milk to increase the caloric density above the 20 calories per ounce generally accepted

value for human milk. Because of the patient's GI dysfunction associated with intact cow's milk protein-based human milk fortifiers, a free amino acid-based infant formula (Neocate) was used to increase the caloric density.^{10,11} With the caloric density of 24 calories per ounce of the mother's own milk plus free amino acid-based infant formula, the protein, calcium, and phosphorus content was increased to within the recommended range for preterm newborns.

To ensure that the AAP recommendation for vitamin D was met, and as recommended by the feeding protocol, an infant multivitamin with iron was added once the infant was receiving full enteral feeds. The multivitamin with iron provided 400 IU vitamin D and 5 mg iron (see Table 2).

Recommended dietary intakes of nutrients, such as protein, calcium, and phosphorus for the preterm newborn, are greater than those recommended for the full-term newborn.¹² Supplementation with commercially manufactured human milk fortifiers (HMFs) is associated with short-term increases in weight gain and linear and head growth. With supplementation, nitrogen retention and blood urea levels appear to be increased,¹³ and

therefore supplementation is generally indicated.

In the preterm infant with CMA, as cow's milk-based HMF cannot be used, caloric density and protein content goals can be met with amino acid-based infant formula. It is not possible to meet the recommended range for calcium and phosphorous intake with amino acid-based infant formula. Additional calcium and phosphorus supplementation is an option for some infants, as the osmolality of these supplements is very high, causing concerns for tolerance. As this infant already had altered GI function related to CMA/protocolitis, this was not an option. Given the constraints of the nutrient composition of the free amino acid formula used for fortification, we were able to increase the calcium/phosphorus content of the mother's milk but were unable to increase intake into the recommended range.

Swallow difficulty/dysphagia. One of the diagnostic tools in the treatment of dysphagia is the use of the modified barium swallow study (MBSS), which allows for visualization of the pharyngeal phase of the swallow mechanism. In this patient, the results of the MBSS indicated aspiration of both thin and nectar-thick consistency liquids. No laryngeal penetration was noted with honey-thick consistency of liquids. The treatment recommended by the pediatric feeding specialist was to provide honey-thick maternal breast milk for oral feedings.

In general, pediatric feeding specialist recommendations for providing modified consistency of liquids for the treatment of dysphagia include thickening infant formula with infant cereal, as infant cereal is inexpensive and readily available. However, given the presence of amylase in breast milk, the use of infant cereal as a thickening agent is ineffective. In this situation, other thickening agents are required. For this patient, a commercially available thickener made from xanthan gum was added to the patient's human milk.

On DOL 40 after B/G M began to consume feeds thickened with xanthan gum, she again developed large, pale-colored stools. Concerns were raised regarding

the possible presence of cow's milk protein in the thickening agent. The product's manufacturer was contacted.

Per the manufacturer, the thickener xanthan gum is extracted from a bacterial by-product. Xanthan gum is produced from carbohydrate slime via alcohol extraction. Per the manufacturer, although the bacteria may consume whey protein, this product contains no protein. However, a side effect of this product may be pale, large-volume stools with an appearance similar to yellow chifon.

As xanthan gum thickeners are nonnutritive, increasing the caloric density of human milk to achieve the desired calories per ounce is required. To achieve honey-thick consistency, 30 g (1 oz) of thickener is added to 4 oz of human milk, producing a total volume of 5 oz. The goal for caloric density for B/G M was 24 calories per ounce maternal breast milk.

day. Her length and head circumference remained stable, continuing along her established growth curve (25th percentile for age). Diet instruction for the preparation of the thickened fortified human milk and contact information for the neonatal dietitian were provided. Discharge instruction included information on positioning the infant at feeding time to promote safe swallow, instruction on the use of the Avent variable flow nipple, and techniques for pacing the infant at feeding to allow for periods of rest during feeding to prevent tiring.

After discharge, follow-up appointments were scheduled with the pediatric feeding specialist and with the pediatric allergy-immunology clinic. It is appropriate to reevaluate swallow function, as dysphagia often improves and may resolve as the infant matures. Food hypersensitivity may also decrease in degree as the infant matures. Up to 80% of these

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A 30-calorie per ounce recipe for the 4 oz of human milk was required to provide a final caloric concentration of 24 calories per ounce of human milk.

The honey-thick feeds were delivered via the Avent variable flow nipple. The variable flow nipple is a soft silicone nipple. The manufacture's slot-cut opening in the nipple is designed to accommodate thicker liquids. The flow rate can be varied by turning the bottle to align the I, II, or III markings on the nipple with the infant's nose.

On DOL 56, B/G M was discharged home. At the time of discharge, B/G M was consuming 50 mL per feeding of honey-thick consistency maternal breast milk fortified to 30 calories per ounce with a free amino acid-based infant formula. She continued to use the Avent variable flow nipple for feeding.

Her discharge weight was 2.9 kg. She was gaining an average of 29 to 30 g per

children outgrow the reactivity and/or develop tolerance by 4 years of age.¹⁴

Treatment Implications

Supporting growth and ensuring adequate nutrient intake of macro- and micronutrients can be a challenge when caring for preterm newborns. This challenge is escalated when standard forms of human milk fortification are contraindicated, as well as when other nutrition diagnosis such as impaired swallow related to immaturity are present.

Support of the nursing mother in the neonatal critical care setting is also essential for the well-being of the preterm infant. This challenge escalates when dietary modification of the mother's diet is essential for the nutritional support of the infant. There is controversy regarding the efficacy of eliminating food proteins associated with

food hypersensitivity from the maternal diet. Several recent studies, including a randomized controlled trial of a low-allergen maternal diet in exclusively breastfed infants, suggest that in infants with CMA, restriction of the maternal diet reduced the incidence of adverse reactions to food.¹⁵⁻¹⁷

Ensuring safe swallow in the preterm breastfed infant with dysphagia related to immature swallow anatomy and physiology, poor growth, and GI dysfunction presents a host of challenges.

Fortification of Human Milk

The recommended nutrient intake for the preterm newborn is greater than those for the full-term newborn. The estimated resting metabolic rate in the enterally fed preterm newborn is approximately 50 kcal/kg/d. Each gram of weight gain requires between 3 and 4.5 kcal. To support weight gain at the recommended rate of 20 to 35 g per day, an intake of 110 to 150 kcal/kg/d may be required.¹ To provide human milk with this caloric content, fortification of maternal breast milk is often required.¹⁸ Most preemies tolerate commercial human milk fortifiers well. For some preemies, such as those with CMA, extensively hydrolyzed or free amino acid–based infant formula is indicated. Ensuring that the protein provided reaches 4 g per kilogram per day for infants born at less than 2 kilograms and that phosphorous and calcium are in the recommended range of 100 to 110 mg and 200 to 220 mg/kg/d,¹⁹ respectively, has been shown to support growth within the recommended goal range.¹²

Recommendations for Practice

Including standardized language as part of the nutrition care process model in the documentation of patient care allows the professional nutrition community to provide a consistent structure and framework to nutrition care. Selection of a nutrition diagnosis in this case could include choices from several domains. In the case of baby girl M, either NC 1.4

(altered gastrointestinal function) or NC 2.1 (impaired nutrient utilization) appears appropriate.^{20,21}

The nutrition-related interventions should address these nutrition-related problems. The nutrition diagnosis of altered GI function allows for the inclusion of the impaired swallow mechanism and aspiration of thin liquids and the GI symptoms of occult blood in stools. The intervention of feeds of maternal breast milk thickened with xanthan gum is associated with upper GI dysfunction and the change in human milk fortifier to an extensively hydrolyzed infant formula with intestinal malabsorption due to inflammation.

Accurate diagnosis and treatment of cow's milk allergy is essential to prevent the imposition of unnecessarily restrictive diets in young children. Eliminating potential allergens during pregnancy or lactation has not been shown to prevent food hypersensitivity.⁸ However, once documented food hypersensitivity reactions occur, elimination is often required to prevent symptoms.²² Some infants with failure to thrive and/or atopic eczema may require amino acid–based formulas made from crystalline amino acids versus extensively hydrolyzed formula made from cow's milk for remittance of symptoms.²³

Ensuring growth in the low birth weight preterm newborn with documented food hypersensitivity frequently requires increasing the caloric density of feedings. Fortifying human milk with extensively hydrolyzed infant formula may be necessary in this population.¹³ In the presence of impaired swallow mechanism, modified consistency of liquids may be needed to avoid aspiration.²⁴ Use of commercially available gums to thicken human milk is appropriate, as other thickening agents may be ineffective because of the presence of digestive enzymes in human milk.

Modification of the consistency and fortification of feeds contributed to successful oral feeding and growth in this preterm newborn, allowing for discharge on DOL 35 at a corrected gestational age of 36 weeks and weight of 2.8 kg. ■

References

1. *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2008.
2. Greer FR, Sicherer SH, Burks AW; Committee on Nutrition, Section on Allergy and Immunology. Effects of early nutrition interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008;121:698-702.
3. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106(pt 1):346-349.
4. Fortunato JE, Scheimann AO. Protein energy malnutrition and feeding refusal secondary to food allergies. *Clin Pediatr*. 2008;47:496-499.
5. Whitsett JA. Acute respiratory disorders. In: Avery GB, Fletcher MA, MacDonald, eds. *Neonatology: Pathophysiology and Management of the Newborn*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2007:485-508.
6. Hodson WA. Principles of management of respiratory problems. In: Avery GB, Fletcher MA, MacDonald, eds. *Neonatology: Pathophysiology and Management of the Newborn*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2007:533-556.
7. Vanderhooft JA. Gastrointestinal disorders. In: Avery GB, Fletcher MA, MacDonald, eds. *Neonatology: Pathophysiology and Management of the Newborn*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2007:739-764.
8. Chehade M. IgE and Non-IgE mediated food allergy: treatment in 2007. *Curr Opin Allergy Clin Immunol*. 2007;7:264-268.
9. Lake AM. Food induced eosinophilic proctocolitis. *J Pediatr Gastroenterol Nutr*. 2000;30(suppl):S58-S60.
10. Sicherer SH, Eigenmann PA, Sampson HA. Clinical features of food induced enterocolitis syndrome. *J Pediatr*. 1998;133:214-219.
11. Heine RG. Allergic gastrointestinal motility disorders in infancy and early childhood. *Pediatr Allergy Immunol*. 2008;19:383-391.
12. Tsang RC, Uauy R, Koletzko B, Zlotkin SH, eds. *Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines*. 2nd ed. Cincinnati, OH: Digital Educational Publishing; 2005.
13. Kuschel CA, Harding JE. Multicomponent fortified human milk for promoting growth in preterm infants. *Cochrane Database Syst Rev*. 2004;(1):CD000343.

14. Sampson HA. Update on food allergies. *J Allergy Clin Immunol.* 2004;113:805-819.
15. Hill DJ, Roy N, Heine RG. Effect of a low allergen maternal diet on colic among breastfed infants: a randomized controlled trial. *Pediatrics.* 2005;116:e709-e715.
16. Osborn DA, Sinn J. Formulas containing hydrolyzed protein for prevention of food allergy and food intolerance in infants [review]. *Cochrane Database Syst Rev.* 2007;(4):CD003664.
17. Halken S. Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention. *Pediatr Allergy Immunol.* 2004;15(suppl 16):s4-s32.
18. Arslanoglu S, Moro GE, Ziegler EE. Adjustable fortification of human milk fed to preterm infants: does it make a difference? *J Perinatol.* 2006;26:614-621.
19. Schanler RJ. *Approach to enteral nutrition in the premature infant. UpToDate.* 2008. <http://www.uptodate.com/patients/content/topic.do?topicKey=~U9EIUCJHoVmHsmg>
20. Nutrition care process part II: using the international dietetic and nutrition terminology to document the nutrition care process. *J Am Diet Assoc.* 2008;108:1287-1293.
21. *International Dietetics & Nutrition Terminology (IDNT) Reference Manual.* 2nd ed. Chicago: American Dietetic Association; 2009.
22. Chehade M, Mayer L. Oral tolerance and its relation to food hypersensitivity. *J Allergy Clin Immunol.* 2005;113:1-12.
23. Hill DJ, Murch SH, Rafferty K, Wallis P, Green CJ. The amino acid based formulas in relieving the symptoms of cow's milk allergy: a systemic review. *Clin Exp Allergy.* 2007;37:808-822.
24. Prasse JE, Kikano GE. An overview of pediatric dysphagia. *Clin Pediatr (Phila).* 2009;48:247-251.