

Human Milk for the Premature Infant

Mark A. Underwood, MD, MAS

KEYWORDS

• Human milk • Premature infant • Necrotizing enterocolitis • Donor milk • Lactation

KEY POINTS

- Fortified mother's own milk is the optimal diet for the premature infant to maximize growth, development, and protection against necrotizing enterocolitis and infection.
- Fortified pasteurized human donor milk is recommended by the American Academy of Pediatrics Section on Breastfeeding as the preferred alternative for premature infants whose mothers are unable to provide a sufficient volume of their own milk.
- Pasteurized donor human milk does not provide the same nutrient or biologically active molecules as unpasteurized own mother's milk.
- Careful attention to establishing and maintaining milk production in women delivering preterm has significant benefits.

Human milk provides the optimal nutrition for term infants. Human milk is also recommended for preterm infants, but does not alone provide optimal nutrition. The growth and neurodevelopmental needs of the evolutionarily new population of very premature infants are best met by appropriate fortification of human milk. To explore the role of human milk in the care of premature infants, it is appropriate to begin with a comparison of amniotic fluid (the optimal beverage of the fetus), milk from mothers delivering preterm, and milk from mothers delivering at term. We then consider the benefits and challenges of providing human milk to premature infants, approaches to human milk fortification, the advantages and challenges of donor human milk products, and finally some practical approaches to increasing human milk consumption in premature infants.

In the United States, approximately 12% of infants are born preterm (<37 weeks gestation).¹ This is a very heterogeneous population with widely diverse nutritional

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Department of Pediatrics, University of California Davis, 2516 Stockton Boulevard, Sacramento, CA 95817, USA

E-mail address: munderwood@ucdavis.edu

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requirements and highly different stages of immunocompetence. A 2.5-kg neonate born at 34 weeks gestation differs from a 500-g neonate born at 24 weeks gestation in essentially every physiologic aspect of the gastrointestinal system and the innate and adaptive immune systems. Consequently, the current body of knowledge about nutrition and host defense of premature infants has many gaps. Studies performed on larger, older premature infants may not be applicable to the extremely low birth weight infants (<1000 g) that now survive routinely.

AMNIOTIC FLUID, “PREMATURE” HUMAN MILK, AND “TERM” HUMAN MILK

Amniotic fluid contains amino acids, proteins, vitamins, minerals, hormones, and growth factors. Although the concentration of these nutrients is much lower than that found in human milk, the large volumes of amniotic fluid swallowed in utero (up to 1 liter a day late in gestation, considerably more than the newborn consumes after birth) have a significant impact on growth and maturation of both the fetus and the fetal intestine.² Animal studies and limited human observations suggest that swallowed amniotic fluid accounts for about 15% of fetal growth.^{3–5}

Milk from women who deliver prematurely differs from that of women who deliver at term. Preterm milk is initially higher in protein, fat, free amino acids, and sodium, but over the first few weeks following delivery these levels decrease (Fig. 1A). The mineral content (including trace minerals) of preterm milk is similar to that of term milk, with the following exceptions: Calcium is significantly lower in preterm milk than term milk and does not seem to increase over time, whereas copper and zinc content are both higher in preterm milk than term milk and decrease over the time of lactation.^{6,7}

Lactose is the major carbohydrate in human milk. This disaccharide is an important energy source, is relatively low in colostrum, and increases over time with more dramatic increases in preterm milk (see Fig. 1A). Complex oligosaccharides are the second most abundant carbohydrate in human milk. These human milk oligosaccharides (HMOs) are not digestible by host glycosidases and yet are produced in large amounts with highly variable structures by the mother.⁸ HMOs seem to have 3 important functions: Prebiotic (stimulation of commensal bacteria containing the bacterial glycosidases to deconstruct and consume the HMOs),^{9,10} decoy (structural similarity to the glycans on enterocytes allows HMOs to competitively bind to pathogens),¹¹ and provision of fucose and sialic acid, which seem to be important in host defense and neurodevelopment, respectively.¹² Preterm milk is highly variable in HMO content with differences between populations¹³ and significant variability over time in content of fucosylated HMOs in individual mothers delivering preterm.¹⁴ Glycosaminoglycans also seem to act as decoys, providing binding sites for pathogenic bacteria to prevent adherence to the enterocyte. Premature milk is richer in glycosaminoglycans than term milk.¹⁵

Bioactive molecules in human milk are important components of the innate immune system. Differences in cytokines, growth factors, and lactoferrin between preterm and term milk are most dramatic in colostrum and early milk and mostly resolve by 4 weeks after delivery (see Fig. 1B). Leptin is produced by mammary glands, secreted into human milk, and may be important in post-natal growth. Human milk leptin does not seem to differ between preterm and term milk.¹⁶ Bile salt-stimulated lipase activity is similar in term and preterm milk, whereas lipoprotein lipase activity is higher in term milk.¹⁷

BENEFITS OF HUMAN MILK FOR PREMATURE INFANTS

The most recent policy statement from the Section on Breastfeeding of the American Academy of Pediatrics represents a significant shift from previous statements in its

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