Improving the Use of Human Milk During and After the NICU Stay

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- Milk dose and exposure period • Prematurity-specific morbidity

The feeding of human milk (milk from the infant's own mother; excluding donor milk) during the newborn intensive care unit (NICU) stay reduces the risk of short-and long-term morbidities in premature infants, including enteral feed intolerance, nosocomial infection, necrotizing enterocolitis (NEC), chronic lung disease (CLD), retinopathy of prematurity (ROP), developmental and neurocognitive delay, and rehospitalization after NICU discharge.[1–29] The mechanisms by which human milk provides this protection are varied and synergistic, and appear to change over the course of the NICU stay.[30,31] In brief, these mechanisms include specific human milk components that are not present in the milk of other mammals, such the type and amount of long-chain polyunsaturated fatty acids and digestible proteins, and the extraordinary number of oligosaccharides (approximately 130).[32] Human milk also contains multiple lines of undifferentiated stem cells, with the potential to impact a variety of health outcomes throughout the life span.[33] Other human milk mechanisms change over the course of lactation in a manner that complements the infant's nutritional and protective needs. These mechanisms include immunologic, anti-infective, anti-inflammatory, epigenetic, and mucosal membrane protecting properties.[34–41] Thus, human milk from

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the infant's mother cannot be replaced by commercial infant formula or donor human milk, and the feeding of human milk should be a NICU priority.

Recent evidence suggests that the impact of human milk on improving infant health outcomes and reducing the risk of prematurity-specific morbidities is linked to specific critical exposure periods in the post-birth period during which the exclusive use of human milk and the avoidance of formula may be most important.[29–31,42,43] Similarly, there are other periods when high doses, but not necessarily exclusive use of human milk, may be important. This article reviews the concept of ''dose and exposure period'' for human milk feeding in the NICU to precisely measure and benchmark the amount and timing of human milk use in the NICU. Similarly, the critical exposure periods when exclusive or high doses of human milk appear to have the greatest impact on specific morbidities are reviewed. Finally, the current best practices for the use of human milk during and after the NICU stay for premature infants are summarized.

DOSE AND EXPOSURE PERIOD: PRECISE MEASUREMENT OF HUMAN MILK USE IN THE NICU

Research, practice, and quality improvement initiatives focused on the use of human milk in the NICU have been limited by the lack of a precise, quantitative measure of ''human milk feeding'' for premature infants.[30] Whereas definitions for ''breastfeeding'' were standardized for term healthy infants in the early 1990s,[44] these six categorical definitions do not capture the critical components of human milk feeding patterns for NICU infants.[45] In addition, the existing definitions for ''human milk feeding'' used in studies of premature infants are limited and inconsistent. For example, human milk feeding might vary from receiving ''any'' human milk to having received a specific volume threshold, such as 50 mL/kg/d.[30] However, the measures usually do not specify *when* the infant received human milk and whether there were periods of exclusive or high doses of human milk feeding. Thus, quality improvement initiatives that focus only on increasing the percentage of NICU infants that are ''human milk fed'' will be inadequate if specific amounts and time periods of human milk feeding are not specified.

A second category of quality improvement indicators focuses on the use of human milk at the time of NICU discharge. Examples of these indicators include ''increasing the percentage of NICU infants that are exclusively breastfeeding or receiving exclusive human milk feedings'' at the time of NICU discharge. Although this outcome is precise and easily measured, it fails to capture the infant's human milk feeding history throughout the NICU stay. Similarly, it is dichotomous with respect to the individual infant and mother. For example, a mother who had no desire to breastfeed may have provided her milk for her infant for a significant portion of the NICU stay so that her infant was fed exclusive human milk for a substantial period (eg, 30 or 60 days). However, this mother-infant dyad would be classified as ''not breastfeeding'' at the time of discharge, even though the mother may have provided human milk throughout the most critical period of the infant's development. Indeed, current evidence suggests there are relatively short, critical exposure periods post birth when exclusive or high amounts of human milk are especially important in optimizing health outcomes for premature infants[30] and reducing the risk of enteral feed intolerance, nosocomial infection, and inflammation-based morbidities such as NEC.[7,27,28,46,47] From a cost outcomes perspective, these morbidities translate directly into higher costs of NICU care[15,48–50] and greater probability of long-term health problems.[10–21] Thus, the infant who receives exclusive human milk feeding in

the first month post birth may have a better health outcome than an infant who received low doses of human milk throughout the NICU stay.

Consistent with the emerging clinical and molecular evidence, quality improvement indicators should focus on measuring and benchmarking the "dose and exposure period" for human milk use in the NICU.[31] The *dose* of human milk should be quantitatively measured for each infant, both as a percentage of total enteral feedings and in mL/kg/d for each day of the NICU stay. These simple calculations require only the total amount in milliliters of human milk and nonhuman milk fed to the infant each day. The *exposure period* refers to the specific days during the NICU stay during which the infant received any human milk feeding. For example, 3 quality indicators using dose and exposure period might be: "Increase to 75% the percentage of very low birth weight infants (VLBW; <1500 g) who receive a dose of human milk of at least 80% over the first month post birth"; "Increase to 75% the percentage of extremely low birth weight infants (ELBW; <1000 g) who receive at least 50 mL/kg/d of human milk over the NICU stay"; and "Increase to 75% the percentage of ELBW infants who receive exclusive human milk feeding during the first 14 days post birth." These indicators are evidence-based, precise, objective, measurable, and, as continuous variables, are easily related to health outcomes and cost of care in statistical and economic analyses.

CRITICAL EXPOSURE PERIODS FOR THE USE OF HUMAN MILK

This section reviews the clinical evidence for use of critical exposure periods to conceptualize and measure the dose of human milk feeding for premature infants in the NICU. In addition, the underlying human milk mechanisms and their impact on the development of specific infant organs and systems during these critical exposure periods are detailed. These four critical periods include: colostrum as the transition from intrauterine to extrauterine nutrition; the transition from colostrum to mature milk feedings during the first month post birth; human milk feedings throughout the NICU stay; and human milk feedings after NICU discharge.

Colostrum: The Transition from Intrauterine to Extrauterine Nutrition in Mammals

The first critical exposure period for human milk feeding is the use of colostrum during the introduction and advancement of enteral feedings in the early post-birth period. Colostrum is secreted during the early days post birth when the paracellular pathways in the mammary epithelium are open and permit the transfer of high molecular weight antibodies, anti-inflammatories, growth factors, and other protective components into the milk product.[30,39,51,52] Colostrum, with a profile of growth factors, and anti-inflammatory and anti-infective components similar to amniotic fluid, facilitates the transition from intrauterine to extrauterine nutrition in mammals.[53–60] When colostrum is fed to the infant during the early post-birth period, the high molecular weight protective components of colostrum can pass through the open paracellular pathways in the infant gastrointestinal tract.[56,59] Colostrum feedings are especially important for extremely immature infants because, during the last trimester in utero, the infants would have swallowed approximately 750 mL of amniotic fluid daily.[56,59] An array of growth factors in the swallowed amniotic fluid more than doubles the weight of the intestinal mucosa during this time.[56]

For extremely premature infants, the early administration of colostrum may compensate for the shortened period of in utero amniotic fluid swallowing. Initial colostrum feedings stimulate rapid growth in the intestinal mucosal surface area, facilitate the endocytosis of protein, and induce many digestive enzymes.[53–60] In animal

models, the intestinal tract does not mature comparably if colostrum is not the first feeding.[53–60] This observation is true even when initial feedings consist of mature milk from the same mammalian species and are followed by colostrum.[53,55,59] Furthermore, artificial feedings appear to exert a separate detrimental effect when they replace colostrum as initial postnatal nutrition in piglets, including atrophy of the gastrointestinal tract, higher concentrations of inducible nitric oxide synthase in the intestinal tissue, and elevated serum cortisol.[53,55,56,60] These structural and biochemical outcomes have been linked to necrotizing enterocolitis in laboratory animals.[53,60]

Human colostrum is also different from mature milk, with higher concentrations of secretory IgA, growth factors, lactoferrin, anti-inflammatory cytokines, oligosaccharides, soluble CD14, antioxidants, and other protective components.[32,61–64] Recent studies suggest an inverse relationship between the duration of pregnancy and the concentration of these agents in maternal colostrum, meaning that mothers of the least mature infants produce the most protective colostrum.[65] Separate studies suggest that secretion of colostrum may be prolonged by several hours or days following extremely premature birth, and that the additional colostrum-type milk may be a specific protective mechanism for the compromised infant.[36,39] A recent study has also demonstrated the safety and feasibility of oropharyngeally administered colostrum before the introduction of trophic feedings in ELBW infants.[65,66] The mechanisms of protection with oropharyngeally administered colostrum, such as cytokine absorption via the oropharyngeal associated lymphoid tissues (OFALT) with subsequent systemic immunomodulation and the local interference with microbe attachment to the oral mucous membranes, may be additive to trophic feedings and may have a specific role in protection from ventilator-associated pneumonia.[65,66]

The evidence about the importance of colostrum as a first feeding has many implications in the NICU, especially for extremely premature infants who have not been exposed to the growth factors in amniotic fluid during the last trimester. **Box 1** summarizes clinical guidelines for colostrum feeding in the NICU, and **Fig. 1** shows patient information in the form of a handout that summarizes the importance of colostrum feeding for families of NICU infants.

Early Enteral Feedings: Transition from Colostrum to Mature Milk During the First Month Post Birth

A second critical period for high doses of human milk feedings is the first 14 to 28 days post birth, when several studies have demonstrated a dose-response relationship between the amount of human milk received by VLBW and ELBW infants and reduction in the risk for specific clinical morbidities including enteral feed intolerance,[28] nosocomial infection,[7,46] NEC,[24,27] CLD,[47,67] ROP,[47] and the total number of morbidities during the NICU stay.[47] The mechanism by which the feeding of high doses of human milk impacts morbidities during this critical period is linked to structural and functional changes in the gastrointestinal tract that occur as enteral feedings are advanced. Human milk appears to program or stimulate many of these healthy processes, whereas formula appears to exert an independent detrimental effect.[29,68] Unfortunately, no previous study has examined the effect of donor human milk during this transition to full enteral feedings, so the impact of donor milk during this period is unknown.

During the first days of life the gastrointestinal tract, sterile at birth, becomes colonized with an array of commensal and potentially pathogenic bacteria. Many factors surrounding the birth of a premature or NICU infant, such as Cesarean birth, antibiotic use, and delayed enteral feedings, predispose the intestine to a dysbiosis with respect to colonization and maturation.[68–70] However, several independent studies indicate

Box 1
Clinical application for colostrum feeding in the NICU

1. Colostrum should be the first feeding received by the infant.
2. Colostrum may be used for trophic feedings and can also be administered safely via the oropharyngeal route with and/or before trophic feedings.
3. Colostrum should be fed in the order that it is produced, even if it has been previously frozen.
4. After the first 3 to 4 days of exclusive colostrum feedings, colostrum can be alternated with fresh mature milk (to protect infant from microorganisms in the NICU via the enteromammary pathway).
5. Colostrum should be stored in small, sterile, food-grade containers that are easily identifiable in the refrigerator or freezer by the nurse.
6. Colostrum containers should be numbered in the order they were collected, in a manner easily identifiable by the nurse.
7. Small expressed drops of colostrum can be diluted with 1 to 2 mL of sterile water to remove the drops from the pump collection kit and/or to achieve a desired feed volume. Dilution is not necessary for any other reason.
8. Colostrum should not be mixed with fortifier or commercial formula.
9. Removal of colostrum from the breast may be most effective using a combination of a hospital grade electric breast pump and hand expression.
10. Formula should be avoided during the introduction and advancement of colostrum feedings, because formula may exert a separate detrimental effect on gastrointestinal integrity during this critical time.

that human milk, which has both probiotic and prebiotic activity,[32,61,62,71,72] results in a predominantly commensal gut microflora.[73–75] In contrast, even small amounts of formula fed during this time appear to interrupt the protective colonization conferred by human milk.[73–75] Related research indicates that soluble CD14, a pattern recognition molecule that functions as a coreceptor for Toll-like receptors II and IV, is highly concentrated in human milk, at a level up to 20 times higher in milk than in the serum of lactating women.[62,63] In combination, the pre- and probiotics, and soluble CD14 provide the substrates for healthy bacterial-enterocyte crosstalk in the developing intestine.[76]

A second protective mechanism that occurs during the transition from colostrum to mature milk feedings is the closure of paracellular pathways between the enterocytes in the infant's intestine. The closure of the paracellular pathways is positively associated with the volume of human milk feeding.[29] The resulting tight junctions inhibit the translocation of high molecular weight bacteria and their toxins from the lumen of the gut to the bowel wall where they can up-regulate inflammatory processes through activation of the cytokine, interleukin-8.[77–79] With little or no ability to mount a compensatory anti-inflammatory response, the extremely immature infant is susceptible to local inflammatory processes, such as NEC, as well as the spread of inflammation to distal organs such as the lungs, eyes, and brain.[78,80] The specific human milk components that protect from inflammation include pre- and probiotics, oligosaccharides, soluble CD14, transforming growth factor-β, epidermal growth factor, interleukin-10, and lactoferrin, all of which are concentrated most highly in the colostrum.[29,32,34–41,61–63,65,66,71–75,77,78,80] Furthermore, during this critical exposure period, which coincides with the introduction and advancement of enteral feeds,

Rush Mothers' Milk Club

Colostrum Milk Feedings in the Special Care Nursery

Colostrum is the early milk that your body makes during the first few days after giving birth. It is different from the milk that is made later in lactation. Colostrum contains high amounts of antibodies and other substances that help to protect babies in the Special Care Nursery (SCN) from infection, bowel diseases, and other complications. Colostrum is like a ***medication*** for your baby, and every drop that you remove should be collected and saved. Even if your plans do not include providing milk, we encourage you to remove the colostrum from your breasts so it can be fed to your baby.

Why is colostrum different from later milk?

At the time of birth, the breasts are still going through many changes as they begin to make milk. In the first few days after birth, the breasts move large amounts of protective substances from the mother's blood stream into the milk. One of these substances is ***Secretory Immunoglobulin A*** (sIgA), a special antibody that babies receive only through their mothers' milk. Over the first week of lactation, changes in the breast reduce the amount of protective substances that move from the mother's blood stream into the milk. This later milk is still very beneficial for babies, but the colostrum has the highest amount of protective substances.

How long does colostrum last?

Colostrum does not suddenly stop being made. The breasts change gradually, so the very first pumped milk is highest in protective substances, the second pumped milk is the next highest, and so on. For most mothers, small drops of colostrum during the first few days give way to larger amounts of yellowish-colored transitional milk that is still very protective for babies. After several more days, mature milk, which is bluish-white, replaces the transitional milk. Mothers who deliver very prematurely produce colostrum for a longer time, and their colostrum has higher amounts of protective substances than that of a mother with a full-term baby. This ***preterm colostrum*** is especially protective for premature babies.

Should I throw away my colostrum because I am receiving medications for pain or another birth-related condition?

Do not throw away your colostrum. Nearly all medications that mothers need in the early days after giving birth can be taken while they provide milk. Write the name of the medication on the label that you place on the milk storage container. Freeze or refrigerate your milk until it can be taken to the SCN. Your baby's doctors and nurses can decide about feeding this milk to your baby.

How can I help make sure that my baby receives the colostrum so that it is most protective?

Colostrum is very beneficial for your baby's first feedings. However, we depend on mothers to help us know which of their milk storage containers hold colostrum. In your ***Welcome to the Rush Mothers' Milk Club*** packet, you received 60 white circle stickers to identify colostrum. You should number these from 1 to 60, and place them on the lids of the first 60 milk storage containers that you fill after giving birth. Put **1** on the first milk collection, **2** on the second one, **3** on the third one, and so on (See photo). The nurse will prepare your baby's feedings in this same order, so that the very first colostrum is the very first feeding for your baby. Your baby will continue to receive colostrum until full feedings are tolerated.

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Special Care Nursery, Rush University Medical Center

Special Care Nursery
Rush University Medical Center

Fig. 1. Parent information handout about the importance of collecting and feeding colostrum in the NICU. (*Available in* English and Spanish, *Courtesy of* Rush Mother's Milk Club, Rush University Medical Center, Chicago, IL.)

formula appears to exert an independent, proinflammatory effect.[29,32,34–41,61–63,65,66,71–75,77,78,80]

Dose of Human Milk During the NICU Stay

Five well-controlled studies of four cohorts of extremely premature, VLBW, or ELBW infants have linked the dose of human milk feedings (mL/kg/d) received throughout the NICU stay with specific health outcomes during or after the NICU stay.[5,6,25,26,47]

However, only one of these studies examined the effect of specific exposure periods within the NICU stay, and found that high doses of human milk during the first 14 days post birth were most highly associated with the advantageous health outcomes that were noted throughout the NICU stay.[47] In 3 of the 4 cohorts, premature infants who received the highest doses or exclusive feedings of fortified human milk had shorter hospital stays than formula-fed infants, despite the fact that the human milk–fed infants grew either at a similar rate[47] or more slowly[5,6] than the formula-fed infants. Although the remaining studies[25,26] did not find a feeding related trend in hospital-based morbidities or length of the NICU stay, they established a dose-response relationship between the amount of human milk received during the NICU stay and better health outcomes during the first 18 and 30 months of age, corrected for prematurity.

In separate studies, Schanler and colleagues[5,6] compared health outcomes for extremely premature infants who received differing doses of human milk throughout the NICU stay. In the first study,[6] health outcomes were compared for 108 infants who received 50 mL/kg/d or more of fortified human milk (n = 62) and those who received exclusive formula feedings (n = 46). Infants who received human milk feedings had fewer days of total parenteral nutrition (TPN); fewer episodes of enteral feed intolerance; a lower incidence of NEC, CLD, and ROP; and a dose-response relationship between the amount of human milk and the number of episodes of late onset sepsis. Even though the human milk-fed infants gained weight more slowly, they were discharged nearly 500 g lighter and 2 weeks earlier than comparison formula-fed infants. The investigators speculated that the earlier discharge was a function of the lower incidence and severity of morbidities in the human milk-fed infants.

In a subsequent study, Schanler and colleagues[5] studied 243 extremely premature infants whose mothers initiated lactation with the intent of providing human milk throughout the infants' NICU stay. If the maternal milk supply was inadequate, the infants were assigned randomly to receive either donor human milk or formula as a supplement to the mother's own milk. Of the 243 infants, 29% received only their own mothers' milk throughout the NICU stay, and the other 71% were distributed equally between the 2 randomized groups. Only minor differences were noticed between the 2 groups randomized to either supplementation with donor human milk or formula, with the donor milk supplemented group demonstrating a slightly lower incidence of CLD and slower weight gain. In contrast, the infants who received only their own mothers' milk during the NICU stay had a lower incidence of all prematurity specific morbidities, and were discharged a week sooner than the infants who required supplementation with either donor human milk or formula.

In a retrospective study of 277 ELBW infants, Patel and colleagues[47] noted a similar trend toward earlier discharge in ELBW infants who received exclusive human milk feedings versus those who received exclusive formula feedings during the NICU stay. Although the human milk fed infants were 1 week less mature (25.2 vs 26.3 weeks) at birth, and demonstrated the same growth velocity from regaining birth weight until NICU discharge (14.5 vs 14.6 g/kg/d), their length of stay in the NICU was 11.7 days shorter (90.2 days vs 101.9 days), and their postmenstrual age at NICU discharge was 2.8 weeks less (38.0 vs 40.8) than the formula-fed infants. In this 5-year, retrospective cohort, Patel and colleagues also described a dose-response relationship between the dose of human milk (mL/kg/d) received during the first 14 days post birth and number of morbidities during the NICU stay.

In a secondary analysis of the National Institute of Child Health and Human Development funded glutamine trial of 1034 ELBW infants cared for in 19 NICUs in the United States,[81] Vohr and colleagues[26] found no differences in hospital-based

morbidities or length of NICU stay among formula-fed and human milk–fed infants. However, the investigators reported a dose-response relationship between the amount of human milk received during the NICU stay and developmental outcomes at 18 months[26] and 30 months of age[25] in this cohort. At the 18-month evaluation[26] there was no difference between formula-fed and human milk–fed groups in overall growth. However, the investigators reported that each 10 mL/kg/d of human milk received over the NICU stay was associated with a dose-response increase in scores on standardized neurocognitive and developmental tests, and with a reduced risk of rehospitalization during the first year of life. The most striking differences were observed between the exclusively formula-fed group and the highest quintile of human milk dose received (110 mL/kg/d), with a 5-point IQ advantage for the high human milk group. The investigators concluded that this difference, when considered from a population perspective, translated into significant health care, educational, and societal cost savings over the life span for ELBW infants.

Vohr and colleagues[25] followed this same cohort of infants, and reported outcomes at 30 months of age, corrected for prematurity, for 773 of the original 1034 infants. The relationship between dose of human milk received during the NICU stay and neurocognitive and developmental outcome persisted through this second developmental time point, with each 10 mL/kg/d of human milk ingestion in the NICU adding to infants' scores on standardized tests in a dose-response manner. The risk of rehospitalization remained lower as a function of human milk dose, especially for respiratory illnesses. Thus, it appears that human milk feedings during the NICU stay provide the foundation for better health outcomes during early childhood.

In summary, in 3 of the 4 cohorts of extremely premature or ELBW infants for whom dose of human milk during the NICU stay was measured, investigators reported a lower incidence and severity of morbidities, a shorter length of stay in the NICU, and hospital discharge at lower weights or postmenstrual age in infants who received exclusive or high doses of human milk.[5,6,25,26,47] These data are especially compelling because in the 3 studies, the human milk–fed infants grew either similarly[47] or more slowly[5,6] than comparable infants who received either low doses or no human milk.

In the single cohort for whom health outcomes were measured after the NICU stay, infants in all feeding groups grew similarly during the first 18 and 30 months of life, corrected for prematurity.[25,26] However, a dose-response relationship was described between the amount of human milk feedings received during the NICU stay and scores on tests of neurocognitive and developmental outcome and the risk of rehospitalization at both post-discharge time points. In all 4 cohorts, the most striking differences in outcome were between infants who had received high (or exclusive) doses of human milk and exclusive formula. The findings also suggest that proportionately higher doses of human milk (but not necessarily exclusive or extremely high doses) received over the longer exposure period of the entire course of the NICU stay impact the aforementioned outcomes. Thus, human milk feedings over the NICU stay do not have to be exclusive to confer benefit, but the greatest benefit appears to be linked to high doses or exclusive feedings of human milk.

The specific human milk mechanisms that impact these NICU and post-discharge outcomes are probably both protective and nutritive in nature. Several developmental outcome studies suggest that a lower incidence and severity of morbidities during the NICU stay translate into a shorter NICU stay, lower discharge weight and postmenstrual age, better neurocognitive and developmental outcome, and a lower risk of rehospitalization in premature infants.[10,11,14–16,18–21,49,82,83] By providing primary protection from these morbidities during the early NICU stay, human milk may indirectly impact the associated long-term outcomes.[30]

In addition, many protective components in human milk may be equally, or even more important beyond the first 14 to 28 days post birth, and probably affect these long-term outcomes. Examples of these components include antioxidant activity to counter the untoward effects of oxygen[41]; the ''customization'' of antibodies via the enteromammary pathway, providing protection from specific pathogens in the NICU environment[84]; oligosaccharides that inhibit the adhesion of pathogens to mucosal membranes in the mouth, throat, and gastrointestinal tract[85] the potential impact of oligosaccharides on neural development[32,86]; and other less studied factors that impact tissue growth and metabolism, such as vascular endothelial growth factor, transforming growth factors, and leptin.[35–37,87,88]

The Impact of Human Milk Feedings After the NICU Stay

Although it can be assumed that premature infants who continue to receive human milk after the NICU stay experience the same short- and long-term benefits as term infants,[89] no well-controlled studies linking these outcomes with either dose or exposure period of human milk have been reported for premature infants after NICU discharge. In contrast, most research in this area has focused on comparing short-term growth velocity and other anthropometric measures for cohorts of premature infants who are discharged in 1 of 3 feeding categories: receiving exclusive human milk, either from the breast, bottle, or a combination of the 2; receiving human milk feedings that are either supplemented with powdered formula or partially replaced with premature formulas; or receiving exclusive formula feedings. The findings from most of these studies suggest that premature infants grow more rapidly with exclusive formula feedings or when human milk feedings are either supplemented or partially replaced with formula. Although no studies have examined the impact of these practices on long-term health outcomes, they are common NICU discharge instructions for human milk–fed premature infants.[90–93]

However, a limitation in all of these post-discharge growth studies is the fact that human milk intake has seldom been measured precisely during breastfeeding, using accurate test-weighing procedures in the home.[91,94–97] even though a series of well-controlled studies indicate that premature infants are vulnerable to underconsumption of milk during exclusive breastfeeding until they achieve term, corrected age.[96,98–101] Similarly, no study has included actual compositional measures of the human milk consumed by the infant, despite the extensive evidence indicating that the caloric content of human milk varies markedly throughout the day and within the same mother.[102–106] Instead, the caloric content of human milk is assumed to be 20 calories per ounce for all feedings, a figure that is inconsistent with the research in this area.[101] Thus, at the present time it is unknown whether exclusively human milk–fed infants grow more slowly because they consume an inadequate volume of milk or because the milk that they consume is inadequate in calories or a specific nutrient such as protein. These are important distinctions, and are diagnosable and manageable for both research and practice, using human milk research technologies that enable an infant to continue receiving high doses of human milk.[42,99,101]

In summary, nothing is known about the long-term implications of feeding either exclusive human milk or human milk supplemented with commercial formula products. Although short-term growth is important, replacement of human milk with formula reduces the overall lifetime dose of human milk for premature infants. Studies with term, healthy infants suggest that many of the long-term health benefits associated with breastfeeding, such as higher scores on intelligence tests and protection from infections, eczema, and adult-onset morbidities, are conferred in a dose-response manner.[89] Thus, replacement of human milk feedings with formula may

accelerate short-term growth but has unknown implications for later-onset morbidities.

BEST NICU PRACTICES TO INCREASE DOSE AND EXPOSURE PERIOD OF HUMAN MILK FEEDINGS

This section addresses the best practices for optimizing the dose and exposure period of human milk feeding for premature infants in the NICU. These practices are conceptualized into four aspects of care: encouraging the mother to provide her milk for her infant; providing cost-effective, expert lactation and human milk feeding support for families and staff in the NICU; prioritizing the initiation, establishment, and maintenance of maternal milk volume; and using lactation technologies to manage human milk feeding problems.

Encouraging the Mother to Provide her Milk for her Infant

Exclusive human milk feeding is uniformly recommended as the first food and as the only food during the first months of life by all of the major health organizations with an interest in infant health, including the World Health Organization (WHO),[107] the United States Breastfeeding Committee (USBC),[108] and the American Academy of Pediatrics (AAP).[109] The WHO specifically addresses the importance of colostrum as the first feeding for infants in the immediate post-birth period,[107] and the AAP specifically addresses the importance of human milk feeding for premature infants.[109]

Although the benefits of human milk feeding for premature infants are well documented, many obstetricians, pediatricians, and nurses remain reluctant to encourage mothers to provide their milk and often simply accept the mother's decision to formula feed without further discussion. These professionals often mistakenly assume that they do not have any influence over a mother's feeding decision, or that they will increase the stress for a mother whose infant is in a critical care setting. Finally, some care providers think that it is unethical to encourage mothers to provide milk, and express concern that they are pressuring or coercing mothers at this sensitive time.

Recent research has dispelled many of these concerns and has demonstrated that provider encouragement of human milk feeding for premature infants is effective regardless of the social and ethnic background of families, and that families depend on health care providers to share this information with them.[110–115] A recent review of the ethical issues related to promoting breastfeeding concluded that fully informing mothers of the health benefits of human milk was an ethical responsibility for health care professionals.[111] In addition, concerns that promotion of human milk feeding may make women feel guilty, coerced, or forced into changing their decision were abated in a recent study of 21 mothers of VLBW infants who changed their feeding decision from formula to human milk.[110] The study participants indicated that they changed their decision almost immediately after learning from a health care provider that their milk was a critical component in the overall management of their infants' NICU plan of care.[110] Indeed, one mother was so disturbed that she had not been told of the importance of her milk by professionals in the hospital where she gave birth that she questioned the qualifications of the doctors and nurses who had cared for her and her baby in the referral hospital before her infant's transport to the hospital where this research was conducted.

Although the efficacy and ethics of promoting breastfeeding are documented, the language used to promote the provision of human milk is important when speaking with women and their families. For example, many women do not wish to feed at

the breast for several reasons, some of which are extremely sensitive, such as a history of sexual abuse. However, these women may be very amenable to using a breast pump to express their milk so it can be fed by bottle. Similarly, it is more appropriate to focus on providing milk for a limited period of time to ''get the baby off to the best start'' than to engage in discussions about long-term milk expression or feeding at breast. All decisions about feeding at breast or long-term milk expression can be postponed until the infant's condition is stable and the mother's stress about the premature birth has begun to lessen. These decisions can then be made calmly and thoughtfully with the support of professionals, family members, and friends.

Although this initial discussion with the mother and family should be conducted in a nondirective and noncoercive manner, the benefits of human milk feeding, particularly of the colostrum and early post-birth feedings, should be clearly and scientifically communicated.[30,34,42] Occasionally the terms ''noncoercive and nondirective'' are misinterpreted to mean that feeding options are presented as if they were two equally safe and efficacious choices. Although the care provider must be supportive and caring in this discussion with families, the scientific evidence about human milk feedings should be shared just like any other NICU therapeutic option that involves family decision making. Examples of talking points that accurately translate scientific terminology about human milk into understandable parent information were summarized in a recent review article.[34] The health care provider who wants to provide encouragement and accurate information about human milk feedings, but who is not a lactation expert, will find this article useful in guiding these discussions with families of NICU infants.

In the Rush Mothers' Milk Club lactation program, the perinatologists, neonatologists, nurses, and dietitians refer to human milk as a ''medicine'' that only the mother can provide. This explanation is accompanied by appropriate parent focused information packets and handouts that translate the scientific principles about human milk and lactation into understandable words and concepts (Welcome to the Rush Mothers' Milk Club).[116] An additional resource is a recently completed parent focused video about the importance of human milk feedings when an infant is born prematurely. This video, which features real families and infants from the Rush Mothers' Milk Club program, is culturally sensitive, available in Spanish, and can be used in a multitude of health care settings.[116]

Providing Cost-Effective, Expert Lactation and Human Milk Feeding Support for Families and Staff in the NICU

Whereas many maternal-infant health care providers recognize the importance of human milk for premature and NICU infants, individual institutions struggle with respect to implementing evidence-based models of lactation care for this population. Few neonatologists, NICU nurses, and dietitians are experts in the delivery of this care, and frequently turn to lactation consultants whose primary training and expertise is in the management of breastfeeding for term infants and their mothers. As a result, families are often ''caught in the middle'' with conflicting advice about the importance of human milk and the NICU-specific lactation problems they encounter, such as selecting and using an appropriate breast pump, collecting and storing their milk, and observing clinicians treat their infants' slow weight gain with formula, even when they have an abundance of available milk. The conflicting advice that families receive about providing human milk in the NICU is well documented, is a source of discouragement to mothers, and is a primary reason for lower doses and exposure periods of human milk feedings for recipient infants.[117,118]

The best practice approach to solving inconsistencies in the management of human milk feedings in the NICU is no different from any other care issue: policies and procedures must be based on available scientific evidence rather than individual opinions and attitudes of staff members. This approach includes evidence-based education of personnel, the completion of human milk and lactation competencies, and the development of standardized policies and procedures to guide practice. Similarly, the notion that some staff members are "pro" or "con" human milk should be addressed by NICU administrators in a manner that is consistent with all other NICU therapies. Most NICUs would not tolerate professional staff members providing information to families based on whether they are "pro" or "con" ventilator management or medication regimens, and human milk feedings should be no different. Simply said, the evidence supports the use of human milk in the NICU, and personal attitudes or experiences of individual staff members to the contrary ("I didn't breastfeed my babies and they turned out just fine…") should not be a part of evidence-based practice in the NICU.

Numerous studies have shown that health care professionals have very limited knowledge and skills related to assisting mothers with breastfeeding and providing milk for either healthy or NICU infants.[119–122] However, several recent studies have demonstrated that educational interventions can improve provider knowledge, skills, and attitudes.[123,124] The USBC has developed competencies for breastfeeding and lactation that are applicable to all care providers involved in the care of women and infants.[125] These competencies include skills such as "know how and when to use technology and equipment to support breastfeeding" and "the ability to preserve breastfeeding under adverse conditions."[125] Likewise, the AAP Policy Statement on Breastfeeding details the expectations of pediatricians in promoting, supporting, and protecting breastfeeding.[109] Competencies specific to professionals who provide support to breast pump–dependent mothers and NICU infants have also been developed.[116] Recent research demonstrates that a NICU-specific lactation education program was effective in changing NICU nurses' knowledge and attitudes,[123] and that overall staff breastfeeding education in the NICU resulted in increased human milk feeding rates.[124]

The provision of clinical and educational support for NICU families and professionals is a specialty area that requires education and expertise in complicated NICU situations as well as in the science of lactation and human milk. As such, NICU lactation programs should be under the direction of an advanced practice nurse, dietitian, or neonatologist. This professional needs expertise in the initiation, establishment, and maintenance of maternal milk volume in pump–dependent mothers who have numerous medical complications, and who may be taking multiple medications. Whereas lists of medications that are or are not compatible with breastfeeding are useful in decision making about term, healthy infants who will be breastfeeding exclusively,[126] these decisions must be approached from an individualized risk-benefit perspective for the NICU infant (**Fig. 2**). Similarly, the use of the highest possible dose and longest exposure period of human milk necessitates that this practitioner integrate technologies, such as the creamatocrit and test weights, on a daily basis to prevent, diagnose, and manage common NICU problems with human milk feedings.[42,101] The standardization of this model of practice requires interaction and education of NICU neonatologists, dietitians, nurses, subspecialists, and families.

The optimal lactation team in the NICU can minimize its costs and increase its efficacy by incorporating the use of breastfeeding peer counselors (BPCs). Although the role of the NICU-based BPC is new, research has demonstrated that BPCs in the NICU and in other settings improve human milk and lactation outcomes.[127,128]

Rush Mothers' Milk Club

Medications in Mothers' Milk for Babies in Special Care Nursery

Many mothers whose babies are admitted to the Special Care Nursery (SCN) at Rush University Medical Center have pregnancy and birth complications that require they take prescription medications after their babies are born. All families are concerned about whether these medications can be safely taken during breastfeeding or milk expression for their babies. This information sheet is to help you understand how the doctors and nurses in the Rush SCN make decisions about medications in mothers' milk. In addition, your baby's doctor or nurse will talk with you about your specific medications, and discuss them in relation to your baby's individual feeding plan.

What determines if a medication can be taken while I am breastfeeding or expressing milk for my SCN baby?

Most medications can be safely taken while mothers are breastfeeding or expressing milk for their babies. This is because the medication has to go through several steps before it reaches a baby's blood stream. First, the medication has to be in the mother's blood stream long enough and in high enough amounts that it reaches the milk-making tissue in the breast. Second, the medication has to pass through tiny barriers between the milk-making tissue and the ducts of the breast where milk is removed by the baby or the breast pump. Some medications pass through these barriers more easily than others, and some can't get through at all. Finally, some medications can make it into the milk, but are not easily absorbed into the baby's blood stream from the baby's stomach and intestines.

Are there lists about which medications can be taken during lactation and which ones cannot?

The doctors and nurses in the Rush SCN check mothers' medications with several sources, including recommendations by The American Academy of Pediatrics, and by researchers who specialize in studying medications in mothers' milk. For many medications, these resources compare the amount of medication in the mother's blood stream, her milk, and the baby's blood stream. These resources also alert us to any possible side effects to watch for. Your baby's care provider can share these publications and websites with you if you would like more information.

What other things will influence the doctors' and nurses' decisions about whether a medication can be taken while I provide milk for my baby?

Mothers' milk helps protect babies — especially those born prematurely — from infection and other complications, so the SCN care providers try to balance the risk of **NOT** feeding mothers' milk with possible effects from medications mothers need to take. This is especially true of colostrum, or the milk that is produced during the first days after giving birth. Colostrum is rich in protective substances, but babies receive very small amounts of it when feedings are started. In this way, babies receive maximum protection from the colostrum, and minimum amounts of any medications that may have been released into the milk. For some medications, the SCN care provider may recommend that mothers avoid milk expression during the time of day that the medication is highest in the blood stream. In rare instances, we may recommend that your baby receive partial feedings of mothers' milk and the remainder as formula in order to balance protection from your milk with minimum exposure to medications.

Why do I receive different information from other doctors and nurses about medications that can be taken during lactation?

Medications in mothers' milk is a subspecialty of lactation practice that is relatively new, and many health care providers who work outside of this area may not be aware of the new guidelines and resources listed above. Instead, they often rely on product inserts that accompany a medication, and these inserts almost always advise against combining the medication with lactation. Your baby's SCN care provider is best able to advise you about combining medications and lactation, because we understand both your baby's condition and the transfer of medications into mothers' milk. If you like, we would be happy to personally contact the doctor who prescribed your medications to discuss our recommendations and clarify your baby's feeding plan.

Regardless of conflicting advice, we recommend that you begin expressing and storing your colostrum until we can determine the suitability of the specific medication you are taking. Be sure to write the name and dosage of the medication on the ***My Mom Pumps for Me!*** milk label on the storage container. We will check the medication and discuss it with you prior to feeding the milk to your baby.

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RUSH UNIVERSITY MEDICAL CENTER

Special Care Nursery, Rush University Medical Center

Special Care Nursery
Rush University Medical Center

Fig. 2. Parent information handout explaining decision-making about medications in mothers' milk for infants in the NICU. (*Available in* English and Spanish, *Courtesy of* Rush Mother's Milk Club, Rush University Medical Center, Chicago, IL.)

The Rush Mothers' Milk Club has incorporated volunteer BPCs since 1997, and has employed BPCs as a part of the NICU lactation team since 2005, when this position was first funded with a foundation grant.[129] These women (and one male counselor) complete a 5-day BPC training program to function as volunteers. Employed BPCs complete an additional 3-month orientation program[116] so that they can acquire the necessary knowledge and skills to practice safely and effectively in the NICU environment. Two of the Rush Mothers' Milk Club BPCs have also met the demanding clinical

requirements for non–health care professionals without a college degree to become certified as International Board Certified Lactation Consultants (IBCLCs).

NICU-based BPCs can augment the work of the lactation specialists by performing many of the basic clinical services required in the NICU. For example, they can assume responsibility for teaching all mothers how to use the breast pump, how to clean the collection kit, and how to safely collect, label, store, and transport their milk. However, equally important is that the BPC is a peer of the mother, and can help solve many of the cultural and ethnic lactation and human milk feeding problems that arise. This aspect is particularly important for African American mothers who are significantly more likely to experience preterm birth[130] but less likely to breastfeed or provide their milk.[131,132] A recent study demonstrated that African American mothers experience issues with anxiety and trust when working with nurses and physicians.[133]

A recent study conducted with women in the Rush Mothers' Milk Club demonstrated that the mothers preferred the BPCs to a health care professional when they sought help to address their personal barriers to providing milk for their infants.[134] In addition, the data from this study revealed that the BPC's personal experience with a NICU infant and providing her milk had a profound impact on the new mother and influenced her decision to provide milk for her infant. The mothers who participated in this study also reported that the BPCs provided informational, instrumental, appraisal, and emotional support. The study also demonstrated that BPCs gave the mothers hope that their lives would ''eventually return to normal,'' and made them feel empowered with their decision to initiate and continue providing milk for their infants.

In addition to designated lactation personnel, mothers need basic physical resources in the NICU to provide milk for their infants. These resources include access to a hospital-grade dual electric breast pump and pump kit for adequate milk removal[42,135]; volume-based, rather than ration-based, allocation of containers for storing their expressed milk[42]; refrigerator and freezer space for on-site milk storage of all milk to be fed to the infant during the NICU stay[42]; and access to additional lactation equipment (eg, nipple shields or infant scales to perform test weights) as needed to ensure that infants receive the highest dose of human milk.[42,99] A recent study demonstrated that the cost per 100 mL of maternal human milk is less expensive than donor human milk and specialty formula for NICU infants.[135] These and other health outcome data suggest that the NICU would realize cost savings by promoting maternal human milk feeding over formula or donor human milk feedings.[135] Another large clinical trial is underway to quantify the cost impact to the NICU for providing containers, volume-based refrigerator and freezer space, and additional support equipment.[31]

Prioritizing the Initiation, Establishment, and Maintenance of Maternal Milk Volume

Prioritizing maternal milk volume is the single most important lactation-related responsibility for maternity and neonatal caregivers. An abundant milk volume ensures that the infant has access to exclusive human milk feedings and facilitates the transition to feeding at breast during and after the NICU stay, whereas maternal milk volume problems compromise these goals.[42] Initiating, establishing, and maintaining an adequate milk volume is, however, a demanding task for mothers of premature infants. These mothers are breast pump–dependent, meaning that they must rely on the breast pump to replace the sucking stimulation and milk removal functions of a healthy breastfeeding infant.[136] As such, their needs are very different from those of a mother who is an occasional breast pump user,

and can depend on her infant to provide the necessary autocrine stimulus required for milk production.[42]

Several studies have demonstrated that breast pump–dependent women experience problems with delayed lactogenesis and inadequate milk volume,[137–143] with one large study demonstrating that only 29% of mothers with extremely premature infants were able to provide exclusive human milk throughout the NICU stay.[5] However, a recent randomized control trial[136] comparing different breast pump suction patterns suggested that "running out of milk" is at least partially iatrogenic for mothers of VLBW infants, and that implementation of evidence-based best practices may reduce the number of women who do not produce an adequate volume of milk.[42]

The process of developing an adequate milk volume begins during pregnancy, when the breast undergoes several anatomic and physiologic changes in preparation for breastfeeding.[144] Lactogenesis I occurs during the second trimester of pregnancy and is the phase of lactation wherein the mammary glands are sufficiently developed and differentiated to secrete a small amount of colostrum.[52,145] However, the milk secretion is suppressed throughout the remainder of pregnancy by high circulating levels of progesterone.[146] After the delivery of the placenta in the early post-birth period, circulating progesterone levels decline rapidly and, in response, lactogenesis II, the onset of copious milk secretion, occurs and the mother senses the milk "coming in."[52,146–148] Two recent studies[136,149] suggest that specific stimulatory interventions during the transition from lactogenesis I to lactogenesis II may have a programming effect on subsequent maternal milk volume. Whether these interventions exert some effect on the secretory mechanisms in the breast tissue or the neuroendocrine responses is unknown.

Following the onset of lactogenesis II, milk synthesis and secretion are regulated by a combination of autocrine and endocrine processes that depend on regular and effective milk removal via the feedback inhibitor of lactation (FIL) mechanism.[150] For women who exclusively breastfeed a healthy infant, the transition from endocrine to autocrine mechanisms of control occurs seamlessly, because the infant removes available milk and the milk is replaced. Regular and effective milk removal by the infant serves to increase the mean maternal milk volume to approximately 600 to 625 mL/d by the end of the first week post birth.[146] The transition from lactogenesis II to a milk output that is sufficient for exclusive breastfeeding of the infant has been termed "coming to volume" by the authors' research team.[151] This short, but critical transition is the time that most breast pump–dependent mothers experience milk volume problems that require rapid identification and resolution.[42]

In contrast to a term infant who regulates milk synthesis and secretion during this critical transition, breast pump–dependent mothers must undertake frequent and complete breast emptying with a breast pump. Numerous factors that are unique to these women, such as an ineffective breast pump, improperly fitting breast shields, infrequent pump use, or ending a pumping session before all of the available milk is removed, can compromise this transition. Similarly, the intense stress, fatigue, and pain in these early days can down-regulate prolactin via the dopaminergic prolactin inhibiting factor.[52,146] Best practices to prevent, diagnose, and manage milk volume problems in breast pump-dependent women have been summarized in a recent review.[42] However, mothers need measurable milk volume targets and daily monitoring during the critical "coming to volume" transition. In the Rush Mothers' Milk Club program, a BPC contacts each new mother on a daily basis during this period, either in the NICU or by telephone, and reviews with her each item in the brief checklist shown in **Fig. 3**.

Another potential problem experienced by breast pump–dependent mothers during this critical transition is that the administration of hormonal contraceptives in the early

Name: _____ **Infant's DOB:** _____

Assessment completed by: _____, **BPC(c) Today's Date**_____

☐ in NLFC ☐ in NICU ☐ by telephone ☐ Other

Item 1. Evaluate Maternal Milk Volume

Pumped volume recorded for last 24 hours: _____ mLs

Number of pumpings last 24 hours: _____

Total number of minutes pumped last 24 hours _____

Longest interval between pumpings last 24 hours: _____

Daily volume is steadily:

☐ Increasing ☐ Staying the same ☐ Decreasing

Item 2. Evaluate Breast Changes

Breasts feel full between pumping	☐ Yes	☐ No
Milk drips or leaks between pumpings	☐ Yes	☐ No
All areas of both breasts empty thoroughly with pumping If no, detail specific areas and plan to see mother	☐ Yes	☐ No
All areas of both breasts are free of local areas of pain and redness If no, detail specific areas and plan to see mother	☐ Yes	☐ No

Item 3. Evaluate Nipple Changes

Both nipples are free of pain or discomfort If no, detail area(s) of nipple(s) affected	☐ Yes	☐ No
Both nipples are free of redness and local pain at juncture of nipple and areola If no, detail which nipple is affected and complete assessment for correctly-fitted breast shields	☐ Yes	☐ No
Both nipples are free of lacerations and bleeding If no, detail which nipple is affected and plan to see mother	☐ Yes	☐ No

Item 4: Evaluate Medications that Impact Milk Volume

All medications and doses are the same as previous day If no, detail changes and discuss with lactation specialist	☐ Yes	☐ No
Ask specifically about OTC cold remedies and hormonal birth control		

Item 5: Additional Notes and Follow Up Plans:

Fig. 3. "Coming to Volume" checklist to be completed daily for breast pump–dependent mothers of NICU infants until daily milk volume is 350 mL or more for 5 consecutive days.

post-birth period may affect the initiation of lactation and the ''coming to volume'' transition. Whereas estrogen-containing contraceptives should be avoided in the early post-birth period, the use of progestin contraceptives during this vulnerable period is controversial.[152–156] However, the endocrine mechanism for lactogenesis II is the rapid decline in progesterone in the first days post birth, and conditions that result

in elevated progesterone levels, such as retained placental fragments and theca lutein cysts, are known to compromise the initiation of lactation due to the continued progesterone secretion.[157] After lactation has been fully established and the regulation of milk volume occurs via autocrine mechanisms, progestin-containing contraceptives are less likely to have a negative effect.[126]

Although the postponement of a subsequent pregnancy is an important aspect of post-birth care for mothers of premature infants,[158] the selection of a contraceptive must consider the potential impact of the contraceptive on the initiation, establishment, and maintenance of maternal milk volume. At present, the administration of progestin contraceptives such as depot medroxyprogesterone acetate in the immediate post-birth period is inconsistent with the guidelines of the United States Food and Drug Administration,[159] and with recommendations of the WHO[160] and the American Congress of Obstetricians and Gynecologists.[161] Because the obligation of maternal-child health care providers is to protect breastfeeding, progestins should be avoided in the early post-birth period for breast pump–dependent mothers of premature infants until research to support their use in this vulnerable population is available. However, these mothers should receive thorough contraceptive counseling, and nonhormonal methods of contraception should be made available to them.

USING LACTATION TECHNOLOGIES TO MANAGE HUMAN MILK FEEDING PROBLEMS

The prevention, identification, and management of common human milk feeding problems in the NICU is a priority for NICU care providers and lactation specialists so that the infant can receive the highest possible dose of human milk, especially during critical exposure periods. Fortunately, many of the technologies that facilitate these processes have been thoroughly studied by human milk and lactation scientists, and have been adapted for use in the clinical setting. These methods include breast pump technology that is designed to meet the unique needs of breast pump–dependent women[42,136,162]; the creamatocrit technique to accurately and quickly measure the lipid and caloric content in expressed human milk[101,103,163–166]; the use of nipple shields to facilitate milk transfer during breastfeeding[167,168]; and test weights to accurately and precisely measure milk intake during breastfeeding.[94–99] Use of these technologies is easy to learn and should be the standard of care in evidence-based NICU best practices for managing lactation and human milk feeding in the NICU.

Although there is a plethora of scientific literature detailing the scientific foundations and appropriate use of these technologies, they have not been universally integrated into routine NICU care. One reason for this is that many NICU personnel believe that it is just "too much work" to manage human milk feedings and lactation processes so scientifically. For example, many staff members want a simple visual scoring system to estimate milk intake during breastfeeding, or would prefer a single the use of a "default value" (eg, 20 cal/ounce) for the caloric content of expressed human milk. The problem with these less objective mechanisms is that extensive research has demonstrated they are not accurate indicators of either milk intake during breastfeeding[95–97] or caloric density in individual containers of mothers' milk fed in the NICU.[42,101,103,164]

The other primary reason that these effective technologies have not been integrated into NICU best practices is that many lactation proponents believe they are not necessary, and that the focus on "numbers" undermines mothers' confidence. However, research with both test weights[95,96,98] and creamatocrits[163] has shown that NICU mothers can easily learn both techniques, and are reassured by knowing how much milk their infants consume and the caloric content of their milk. Another concern of

lactation proponents is that these lactation technologies have been adapted from the research arena to the clinical setting by for-profit industries, so the industry's profit motive versus the "need" for the products is questioned.[169] However, nearly all other NICU products have evolved from industry and have been studied in industry-funded trials because federal dollars are more appropriately directed toward achieving the broader national health objectives for breastfeeding.[170] Rather than focusing on the politics of infant feeding, lactation products should be selected based on the evidence that they are effective in ensuring that infants receive the highest dose of human milk, especially during critical exposure periods.

Use of Breast Pump Technology Designed for and Tested with Breast Pump–Dependent Mothers

Despite the fact that mothers of premature and NICU infants must remain breast pump–dependent for weeks or months, few studies have focused on the effectiveness, efficiency, comfort, and convenience of the hospital-grade electric breast pump that mothers use. In fact, many lactation proponents believe that it is unethical to recommend a specific type of breast pump, despite support from the literature showing that certain breast pumps and breast pump features appear to be superior or more acceptable to pump-dependent mothers than are other pumps.[136,143,149,171,172] In contrast, most of the research in this area has been focused on care practices that influence maternal milk volume such as skin-to-skin holding or pumping regimens (eg, single vs double pumping). However, a breast pump is fundamental to a mother's ability to produce milk, and it is critical that NICU mothers receive the most effective, efficient, comfortable, and convenient breast pump available. Thus, NICU caregivers should provide breast pump recommendations based on the scientific evidence available for the pump, which should include scientific, systematic evaluation of the pump characteristics by breast pump–dependent mothers. Mothers will need to use the pump until their infants consume all milk directly from the breast, which for most infants is when they achieve term, corrected age or slightly later.[98]

Use of the Creamatocrit Technology to Measure Lipid and Calories in Expressed Human Milk

The creamatocrit technique, which involves centrifuging a small specimen of human milk in a capillary tube and then calculating the percentage of total milk volume equal to cream, has been the standard in the research arena since its first description for use with human milk in 1978.[103,165] The creamatocrit provides a quick, inexpensive, easy-to-perform, and accurate method of measuring the lipid and caloric content in expressed human milk[101,103,163–166] Recently the laboratory equipment used in the research arena was adapted into a 2-pound, portable, user-friendly device (Creamatocrit Plus, Medela Inc, McHenry, IL) that is ideal for use in the clinical setting.[101,103] Since it is well established that the lipid and caloric content vary tremendously in individually collected milk samples[103,105,164,166,173–175] and that NICU storage and feeding procedures further reduce baseline lipid and caloric content,[101,176,177] this device should be an essential part of routine NICU care.

A complete review of best NICU practices for preventing, diagnosing, and managing slow weight gain in premature infants that are predominantly or exclusively human milk fed has been published.[101] This review article includes several NICU case studies that detail the use of the creamatocrit technique as part of an overall plan for managing slow weight gain in the NICU setting, without the use of routine supplementation or "rescue" with formula.

Use of Nipple Shields During the Transition to Feeding at Breast for Premature Infants

Few premature infants are able to consume 100% of their feedings from the breast at the time of NICU discharge. A recent study of VLBW infants revealed that while 30.5% of VLBW infants received exclusively human milk at the time of discharge, fewer than 10% were feeding exclusively at the breast.[100] Among the physiologic immaturities on the part of the premature infant is that suction pressures, essential for creating and sustaining the nipple shape during breastfeeding, are not mature until approximately term, corrected age.[99,178] Although positioning techniques that include the mother's hand supporting the infant's head and scapulae can help compensate for the relative weight of the head and the immature suction pressures, many premature infants demonstrate greater milk transfer when feeding with an ultrathin nipple shield.[118,167,179]

The modern nipple shield concentrates the infant's suction pressure in the tunnel of the shield, stimulates the milk flow, and allows the infant to remove milk even with immature suction pressures. Although many lactation proponents think that nipple shields are unnecessary and overused, shorten duration of breastfeeding, and compromise milk transfer to the premature infant, research clearly demonstrates that the nipple shield is advantageous in establishing and maintaining breastfeeding for many premature infants. The indications and correct usage of the nipple shield in preterm and late preterm infants have been summarized in a recent review article.[99]

Use of Test-Weighing Technology to Measure Milk Intake During Breastfeeding

Test-weighing methods, whereby the infant is weighed pre- and post-breastfeeding under identical conditions, have been the standard research technique for measuring milk intake during breastfeeding since the advent of electronic digital scales in the 1980s.[180] In the past decade a lightweight, portable infant scale for measuring test weights has been developed from the more cumbersome research scales of the 1980s.[95] The adapted scale (BabyWeigh, Medela Inc, McHenry, IL, USA), which features the ability to program in the "pre-feed" weight, and to calculate milk intake (1 mL = 1 g) automatically after the infant is weighed post-feed, is ideal for use in the clinical setting or in the infant's home.[98,99,118,179]

Numerous controlled, blinded clinical trials have demonstrated that test weighing is accurate[94,95,180] and acceptable to mothers,[95,96,98] and that breastfeeding effectiveness "tools" or scoring systems do not accurately estimate intake during breastfeeding.[95,96] A review article that summarizes the indications and use of test weights to manage the transition to exclusive feeding at the breast for preterm and late preterm infants has been published.[99] This review features photographs and detailed clinical examples for integrating test weights into an overall post-discharge management plan that includes nipple shield use and breast pump use for this population.

SUMMARY

The evidence about human milk feedings for premature infants in the NICU indicates that there are critical exposure periods post-birth when exclusive or high doses of human milk provide the greatest protection from costly and handicapping morbidities in premature infants. These data should form the basis for research, practice, and quality outcome indicators in the NICU. Best practices to increase the dose and exposure period of human milk feedings in the NICU include: encouraging the mother to provide milk for her infant, providing cost-effective, expert lactation and human milk feeding support for families and staff; prioritizing the initiation, establishment, and maintenance of maternal milk volume; and using lactation technologies to manage human milk feeding problems.

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