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'One day, it could be my child who needs it': Exploring Reasons for Breast Milk Donation in Rio de Janeiro, Brazil

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Publication Date
2013-04-01

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‘One day, it could be my child who needs it’: Exploring Reasons for Breast Milk Donation in Rio de Janeiro, Brazil

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A thesis submitted in partial satisfaction of the requirements for the degree of Master of Science in Health and Medical Sciences in the Graduate Division of the University of California, Berkeley

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Dedication

To my incredible parents, David Tait and Laura Hubbs-Tait, for always keeping me healthy and happy, from day one onward. Any achievements I may have in life are due to the excellent foundation I was given and the examples I was fortunate to witness on a daily basis as I was growing up.
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PART ONE: REVIEW OF THE LITERATURE

I. Background: The Importance of Breastfeeding

The World Health Organization and the American Academy of Pediatrics recommend six months of exclusive breastfeeding, followed by a combination of breastfeeding and complementary foods until a child is one to two years old. Breast milk is considered the optimal food for neonates and young infants, offering both nutritive and immunologic benefits that protect against childhood disease and facilitate growth and development. The research on breastfeeding leaves few ambiguities: in young infants, breast milk is protective against diarrhea, respiratory diseases, ear infections, and necrotizing enterocolitis. In addition, breastfeeding has been linked to long-term health benefits, including reduced risk of hyperlipidemia, hypertension, diabetes mellitus type 2, obesity, and asthma.

While breastfeeding is critical to the health of all children, it is particularly vital in developing countries. Approximately 10 million children under the age of five die each year, including 3.9 million neonates. Most of those deaths occur in poor or developing countries, with 42 countries accounting for 90% of global child deaths in 2003. Suboptimal breastfeeding is a significant cause of under-five child mortality in the developing world: it is estimated that approximately 1.4 million children under five die each year as a result of insufficient breastfeeding. Indeed, Black et al. report that, globally, infants 0-5 months old who are not breastfed have 14 times the risk of dying (all-cause mortality) than do children who are breastfed exclusively; non-breastfed infants also have 15 times the risk of dying from pneumonia. A case-control study in Brazil found that infants 1-12 months of age not receiving breast milk were 17 times more likely to be hospitalized for pneumonia than were children who breastfed exclusively. Children who are not breastfed have 19 times the risk of hospitalization for diarrhea relative to their exclusively breastfed counterparts. Pneumonia and diarrheal infections are, respectively, the two leading causes of child death in the developing world. Furthermore, Jones et al. estimated that a breastfeeding support and education program that reached 90% of the global population could reduce under-five mortality by as much as 13%. Moreover, an analysis of interventions for child health showed that counseling about breastfeeding and supplementation of Vitamin A and zinc were the two interventions with the biggest potential impact on child morbidity and mortality.

Illnesses and deaths due to suboptimal breastfeeding also have considerable economic consequences, leading to increased health care costs from hospitalizations and treatment. A 2010 cost analysis from the United States showed that if 90% of mothers in the US breastfed exclusively for six months, it would save 13 billion dollars each year. The analysis takes into account the costs of hospitalization, including medical treatment, the time lost from the workday for a medical appointment, and the projected earnings losses due to morbidity and premature mortality. The extensive
mortality and economic data on suboptimal breastfeeding lead to recommendations to improve breastfeeding initiation and duration, which is considered a critical and cost-effective way to reduce illness and death in children under five in both developed and developing countries.

Exclusive Breastfeeding to Reduce Neonatal Mortality

While the historical literature on duration of exclusive breastfeeding is extensive, less has been written about the importance of early initiation of breastfeeding in the attempt to reduce neonatal mortality. Huffman et al. note that in countries with lower infant (<12 months of age) mortality rates, neonatal (<1 month of age) mortality rates are proportionally higher. In Zambia, for example, the infant mortality rate in 1996 was 108/1000 live births, with neonatal deaths representing 33% of all infant deaths. In Bolivia, by contrast, the infant mortality rate was 67/1000 live births, and neonatal deaths comprised 51% of all deaths during infancy.11

In fact, in countries with the highest child mortality rates, neonatal deaths constitute 20 percent of all child deaths. By contrast, neonatal deaths constitute more than 50 percent of all child deaths in countries with lower under-five mortality rates (defined as less than 35 deaths/1000 births). Huffman et al. argue that, in the developing world, breastfeeding interventions are aimed at reducing infant morbidity and mortality during the first year of life, with less attention paid to the risk of neonatal death due to delayed initiation of breastfeeding.11 A 2000 review by the WHO showed that neonates who were not breastfed were 2.5 to 7 times more likely to die during the neonatal period than were neonates who were breastfed.12 A systematic review of interventions to reduce neonatal mortality showed that emphasis on initiation of breastfeeding during the early neonatal period could reduce global neonatal morbidity and mortality by 55-87%.13

The protective effects of breast milk differ according to the time of the neonatal period at which breastfeeding occurs. In the first week of life, neonates are at elevated risk of mortality due to hypothermia – risk that is reduced with early initiation of breastfeeding (optimally within the first hour of life), as well as early skin-to-skin contact between the mother and the child.11,14 A 2005 study of breastfeeding initiation in almost 11,000 Ghanaian neonates showed that delayed initiation – more than 24 hours after birth – was associated with a 2.4-fold risk of neonatal mortality.15 Furthermore, the authors estimated that 22% of all observed neonatal deaths would have been avoided if breastfeeding were initiated within the first hour of life – the standard practice recommended by the WHO.15

Early introduction of breast milk is critical to neonatal health, particularly in underresourced settings and where risk of perinatal infection is high. A particular subset of neonates, however – those born premature and/or of low birthweight – are at especially high risk of perinatal morbidity and mortality, in the developing and developed
world. Much of the literature on in-hospital management of preterm infants, including feeding recommendations, originates from studies conducted in developed countries. This research is presented in the remainder of the paper, although a robust discussion can be had about the applicability of developed world neonatal intensive care unit (NICU) feeding and management protocols to hospital and community settings in low-income countries. But because preterm birth carries with it a mortality risk in all countries, it is important to focus on all effective interventions, with a particular eye on what interventions and adaptations may be best for low-resource countries with high neonatal mortality rates.

II. Under-5 Mortality and Prevalence and Risks of Preterm Birth and Low Birth Weight (LBW)

The United Nations Millennium Development Goal #4 aims to reduce global under-five child mortality by two-thirds between 1990 and 2015, a target that will likely remain out of reach. Murray et al. reported in 2007 that under-five mortality is estimated to decline 27% by 2015, with efforts to curtail child mortality slowed primarily by high birth rates and elevated infant and child mortality rates in Sub-Saharan Africa. Yet under-five child mortality has fallen drastically since the 1970s, dropping from 16 million deaths per year in 1970, to 11.9 million in 1990, and finally to 7.7 million deaths in 2010. Neonatal mortality, however, is decreasing less rapidly, constituting 38% of under-five mortality in 2000 and 40% in 2010. Deaths among children aged two months to five years fell by roughly a third between 1980 and 2000; neonatal deaths dropped by only 25% over the same period. That is, efforts to reduce child mortality have been most successful outside of the neonatal period, and neonatal deaths in the developing world continue to be difficult to prevent. While gains in reducing child mortality should be celebrated and maintained, it is imperative to intensify efforts at lowering infant mortality, particularly neonatal mortality. A particular challenge to preventing neonatal mortality is the high prevalence of preterm birth and low birth weight, both of which are risk factors for neonatal death and morbidity during infancy and childhood.

Definitions and Prevalence of Preterm Birth and Low Birth Weight

Preterm birth is the leading cause of neonatal mortality, responsible for 28% of the four million neonatal deaths reported in 2005. It is defined as birth occurring prior to 37 weeks’ gestation, with severity determined by weeks’ gestation. Children born earlier – at fewer weeks’ gestation – are more likely to die during the neonatal period. Goldenberg et al. define extreme prematurity as birth at less than 28 weeks’ gestation, with severe prematurity used to classify births between 28-31 weeks. Moderate prematurity occurs with birth between 32-33 weeks’ gestation, and near-term prematurity is defined as birth at 34-36 weeks. Low birth weight (LBW) is characteristic of many preterm infants, although not all. By definition, LBW is classified as an infant weighing less than 2500 grams (5.5 pounds) at birth; very low birth weight (VLBW) is
used for infants weighing less than 1500 grams (3.3 pounds). Moreover, not all LBW infants are born preterm. There are two primary causes of LBW: (1) preterm birth and (2) intrauterine growth restriction, or IUGR. IUGR is most often defined as a fetus with a weight below the 10th percentile of what is appropriate for its gestational age, as well as an abdominal circumference below the 2.5th percentile. It is important to distinguish constitutionally smaller fetuses whose growth is normal, termed small for gestational age (SGA), from those whose reduced size is due to a pathologic process like IUGR. Multiple conditions can give rise to IUGR, including hypertension, infection, and poor maternal nutrition.

Most LBW infants with IUGR are born at term, and thus the term IUGR-LBW is applied to categorize a LBW infant born after 37 weeks’ gestation. Black et al. estimate that two-thirds of LBW is due to IUGR, while one-third is an outcome of preterm birth. A 2011 systematic review, however, examined prevalence of LBW in lower- and middle-income countries (LMIC), determining that approximately 50 percent of all LBW infants are born preterm. Statistical discrepancies are common in the LBW and preterm literature; about 40% of infants worldwide are born in homes with no traditional birth attendants (TBAs) present. Most of these infants are not weighed, and statistical data on gestational age is also difficult to obtain. In addition, gestational age is determined by different means in community clinics and hospitals around the world. Some facilities use the date of the last menstrual period to evaluate gestational age, while others rely on ultrasound and physical exam findings, or the physical exam alone. Use of ultrasonography to determine gestational age in a birth cohort in Pelotas, Brazil overestimated gestational age by two weeks, which may have influenced scheduled deliveries and led to more preterm births.

The lack of comprehensive data on gestational age and birth weight makes accurate assessment of LBW and preterm birth difficult. Robust global estimates, however, do exist: Beck et al. calculated that about 10% of all live births between 1997 and 2007 were preterm; approximately 15% of all live births – around 20 million infants each year – are LBW, which encompasses both preterm LBW and term LBW-IUGR. More than 95% of LBW infants are born in developing countries. Preterm birth, by contrast, is rising in developed countries due to increased use of reproductive technologies and multiple pregnancies achieved by artificial means. Morbidity and mortality resulting from LBW and preterm birth, however, remain concentrated in LMIC, with approximately 99% of neonatal mortality occurring in the developing world.

Mortality and Morbidity Associated with Preterm Birth and LBW

Almost 75% of global neonatal deaths occur in the first week of life, and a third of those – 25% of total neonatal mortality – happen in the first 24 hours after birth. Preterm birth is the leading cause of perinatal morbidity and mortality (28% of all deaths), followed by sepsis/pneumonia (26%) and birth asphyxia (23%). Kramer et al. examined neonatal mortality risk among birth cohorts in the United States, finding that
singletons of moderate (32-33 weeks) and mild (34-36 weeks) prematurity born in 1995 had 13.6 and 4.5 times the risk of dying in the first week of life, respectively, when compared to their counterparts of normal weight.  

Lawn et al. refer to LBW as an “important indirect cause” of neonatal death, often precipitating fatal infections in the early days of life as a result of immature immune defenses. LBW-IUGR infants born between 2000 and 2499 grams were 2.8 times as likely to die during the neonatal period from any cause than were infants whose birth weight exceeded 2500 grams; infants weighing between 1599 and 1999 grams had 8.1 times the risk of neonatal death than did their normal birth weight counterparts. A longitudinal birth cohort study in Brazil showed that the relative risk of neonatal death among LBW infants born in 2004 was 31 times higher than that of term infants of normal birth weight. Risk of death increased with decreasing gestational age, with the highest risk of neonatal death among infants of extreme prematurity (<28 weeks). Furthermore, the combination of preterm birth and LBW is the most detrimental; the same Brazilian cohort study showed that LBW infants of mild prematurity had 2.1 times the risk of neonatal death than did LBW-IUGR infants. A cohort study of LBW infants – preterm and LBW-IUGR – in Bangladesh determined that 75% of all neonatal deaths reported were of preterm LBW infants, even though only one-third of the LBW sample (363 of 931) was preterm. The neonatal mortality rate (NMR) of LBW mildly premature infants (34-36 weeks) was 3.9 times higher than was the NMR of term LBW infants.

Thus, the combination of LBW and preterm birth greatly increases the risk of neonatal death, particularly in the first week of life. A retrospective cohort study in Nepal identified infant respiratory distress syndrome (IRDS), sepsis, and necrotizing enterocolitis as the most common causes of death among preterm infants. In the Bangladesh cohort, birth asphyxia (34%) and infection (sepsis/pneumonia) (9%) were frequent causes of neonatal death; most commonly, however, autopsies found no etiology outside of preterm birth and/or LBW (45%). These findings coincide with Lawn et al.’s conclusion that preterm birth, neonatal sepsis/pneumonia, and birth asphyxia are the most common causes of neonatal death.

**Health Care and Non-Health Care Costs Associated with Preterm Birth and LBW**

Infants who are born preterm and LBW have longer post-delivery hospital stays, due to infections, as well as central nervous system abnormalities and lung immaturity that requires long-term ventilation support and oxygen supplementation. Future sections will show that morbidity and lengthy hospital stays due to preterm birth can be reduced with proper in-hospital management and nutritional support of preterm infants. Thus, feeding strategies are important to reducing costs associated with preterm birth.

Ventilation of preterm infants may lead to a chronic lung disease called bronchopulmonary dysplasia (BPD), which predisposes infants to future respiratory infections. A retrospective cohort study by Smith et al. found that 49% of preterm
infants with BPD (118 of 238) were rehospitalized during the first year of life, which was more than twice the rate of rehospitalization (23%, or 309 of 1359) among infants without BPD (p<0.0001). Indeed, preterm infants have an increased risk of rehospitalization relative to term infants, often for respiratory infections like respiratory syncytial virus (RSV). A cohort study in England found that, during the first five years of life, the total duration of hospital admissions among infants born before 28 weeks was 85 times that for term infants and 16 times longer for infants born between 28 and 37 weeks. In addition, preterm infants have increased risk of costly longitudinal problems, like learning difficulties and motor and sensory impairment.

A 2007 report from the Institute of Medicine (IOM) estimated that, in the United States, costs associated with preterm birth reached at least 26.2 billion dollars in 2005. Medical care services comprised 16.9 billion dollars of the total, with other long-term expenditures including special education services, early intervention services, and lost household and workplace productivity also factored into overall costs. The IOM report estimated that each infant born preterm resulted in additional hospital costs of $33,200. Included in the IOM report is Zupancic’s systematic review of costs associated with preterm birth and LBW, evaluating the direct medical costs of initial hospitalization, as well as medical and non-medical costs following discharge. For infants born at 500 to 999 grams, cost estimates varied from $67,027 to $221,450 per infant; these infants had initial hospital stays ranging from 64 to 106 days.

Gilbert et al. evaluated costs associated with preterm birth among singletons born in California in 1996. Infants born at 25 weeks’ gestation – the most premature infants included in the study – had an average hospital length-of-stay (LOS) of 92 days and a mean neonatal hospitalization cost of $202,700. Infants born at 30 weeks had an LOS average of 29 days and a mean neonatal hospitalization cost of $46,400. Infants born at 38 weeks, by contrast, had a mean LOS of 1.8 days and a neonatal hospitalization cost of $1,100. It is important to note that maternal hospital costs – that is, for labor and delivery – were highest for mothers of preterm infants ($9,500 for 28 week-old preterm infants, versus $2,500 for 38 week-old term infants). The authors investigated costs associated with moderate and mild prematurity, finding that hospitalization costs could have been reduced by almost 50 million dollars if births between 34-37 weeks’ gestation had been avoided. Another American study from 2001 estimating costs of infant hospitalizations found that complications from preterm birth and LBW were responsible for 47% of all infant hospitalization costs and 27% of all pediatric hospital costs – even though preterm birth and LBW were the underlying reason for just 8% infant hospitalizations as a whole.

Post-initial discharge hospitalizations, as well as the cost of long-term interventions like special education services, and limited parental wages and loss of productivity, are also important, albeit difficult to measure, costs stemming from preterm birth. The IOM estimated that early intervention services cost 611 million dollars ($1,200 per infant), while special education services were 1.1 billion dollars, or $2,200 per infant.
Finally, lost labor productivity was estimated at 5.7 billion dollars – $11,200 per preterm infant. Zupancic notes that most studies omit the costs associated with preterm infants who die during the infant period (e.g., lost earnings over time), as well as the lost earnings for parents and for preterm infants who survive into the adult period. Furthermore, estimations of educational costs, Zupancic contends, are not detailed enough to encompass the various disabilities preterm infants must contend with in later life, as well as their spectrum of ages at the time they are receiving interventions in school. Thus, he concludes that almost all published cost estimates are likely to underreport the economic costs of preterm birth, due to partial omissions of cost variables not pertaining to the initial hospitalization.

It is also worth noting that the preterm birth cost analysis is derived from studies in developed countries, like the US, the UK, and Australia. The economic burden of preterm birth in developing countries – where hospitals may be less equipped to accommodate prolonged hospital stays, neonatal mortality rates may be higher, and long-term resources like early interventions and special education services may not be widely available – is more difficult to decipher using the parameters established in developed countries, as well as the more expensive cost of health care in nations like the United States. A group in São Paulo, for example, found that the cost of neonatal care was 50 times higher in the US than in their study that examined cost of NICU stays and insurance reimbursement in one of São Paulo’s public hospitals.

The costs associated with preterm birth are concentrated most heavily in the first months of life, as long hospitalizations are required to reduce risk of respiratory complications and to prevent and treat life-threatening infections. Proper in-hospital management, in particular appropriate feeding practices, is critical to reducing morbidity and costs associated with lengthy hospital stays. As subsequent sections will show, maternal milk feedings are associated with significantly shorter hospital stays and significant cost reductions. In particular, human milk feedings reduce risks that arise most often in the late neonatal period.

III. Risks Associated with Preterm Birth and LBW in the Late Neonatal Period and Early Infancy

Neonates who survive the early neonatal period are at risk of specific late neonatal infections with high morbidity and mortality, particularly necrotizing enterocolitis, as well as pulmonary infections, sepsis, and neurologic complications. Moreover, improvements in neonatal care for preterm, LBW, and VLBW infants have improved survival rates for such babies, increasing the population at risk for later neonatal infections, in particular necrotizing enterocolitis and sepsis. Aggressive in-hospital management of preterm infants, many of whom are born with birth asphyxia or signs of respiratory distress, includes oxygen supplementation that can expose vulnerable infants to elevated concentrations of damaging reactive oxygen species (ROS). Therefore, the risks preterm infants face in the late neonatal period differ from those of
the first days of life, and proper in-hospital management is necessary to prevent mortality or significant morbidity due to infection, inflammation, and extensive organ damage.

*Necrotizing Enterocolitis: Epidemiology, Pathophysiology, Prevention, and Treatment*

The growing risk of necrotizing enterocolitis, which is almost exclusively a disease of the preterm and/or LBW infant, makes both prevention and successful intervention a critical aspect of neonatal care for at-risk infants. More than 90% of cases of necrotizing enterocolitis develop in preterm infants. Thompson and Bizzarro estimate that the disease occurs in 5-10% of VLBW neonates and is present in 1-5% of all babies admitted to the NICU. It is the most common gastrointestinal emergency among neonates, and it is the second most common cause of morbidity in infants born preterm. Moreover, risk of necrotizing enterocolitis is proportional to the degree of prematurity, with infants of younger gestational age most likely to suffer from the disease. Risk of necrotizing enterocolitis increases with decreasing birth weight; the 1999-2001 NICHD neonatal cohort study determined that 10 percent of VLBW infants weighing 501 grams or less acquired necrotizing enterocolitis, compared to just 4 percent of infants weighing 1001-1500 grams. Therefore, the combination of LBW and preterm birth discussed previously factors into risk of necrotizing enterocolitis in the late neonatal period.

Despite great clinical effort to reduce mortality due to the disease, its pathogenesis is not well understood, and the number of deaths from necrotizing enterocolitis has remained fairly constant over the past 30 years. Its mortality rate is estimated at 15-30%. Researchers have proposed multiple mechanisms that can give rise to necrotizing enterocolitis, notably hypoxic-ischemic injury to the gastrointestinal tract, abnormal bacterial colonization of the gastrointestinal (GI) epithelium, and early enteral feedings in preterm infants with immature GI motility and impaired peristalsis, which can promote stasis and resultant bacterial proliferation by providing a carbohydrate source for bacterial growth.

Recent research has called into question the established hypoxic-ischemic injury hypothesis, wherein early asphyxia results in what is known as the “diving reflex.” That is, hypoxia triggers shunting of gastrointestinal blood supply to the brain, the heart, and the kidneys at the expense of the GI tract. Insufficient perfusion of the GI tract can lead to inflammation and bacterial colonization. It has been shown, however, that most hypoxic-ischemic injury at birth – primarily birth asphyxia – does not result in necrotizing enterocolitis in the late neonatal period. Instead, the focus has shifted to gut maturity and motility in the preterm infant; Panigrahi proposes a model in which preterm birth results in impaired immunologic function, reduced GI motility, and increased GI permeability – all risk factors for abnormal bacterial colonization and subsequent inflammatory response leading to local necrosis and, in the worst cases, perforation of the intestinal wall. The immature intestinal epithelium of preterm infants,
moreover, mounts a potent inflammatory response to both endogenous and exogenous bacterial stimuli; the overreactive inflammatory response may be partially responsible for the increased risk of necrotizing enterocolitis in preterm infants.\textsuperscript{49} Morgan et al. refer to the pathogenesis of necrotizing enterocolitis as a combination of “immaturity, ischemia, and infection”\textsuperscript{46} (pg. 184). The result of the injury is irreparable damage to the mucosal barrier of the gastrointestinal wall; impaired mucosal function leads to what Patole calls “a self-perpetuating vicious cycle”\textsuperscript{44} (pg. 636) of progressively worsening necrotizing enterocolitis, leading to sepsis and, in extreme cases, death.

Preterm neonates typically present with necrotizing enterocolitis within the first two weeks of life.\textsuperscript{43} They often display feed intolerance and impaired gastric emptying, marked by abdominal distention and pneumatosis intestinalis – the presence of gas in the intestinal wall – on radiographic imaging.\textsuperscript{40} Infants with presumed necrotizing enterocolitis are treated medically first; they are removed from any enteral feeds, provided broad-spectrum antibiotics for both aerobic and anaerobic organisms, and they often receive pharmacologic cardiovascular and pulmonary support. Patients with severe, rapid progression of disease, including intestinal perforation, often require surgical intervention, which carries with it a greater mortality risk.\textsuperscript{40} A review of multiple cohort studies in the United States, Canada, and Australia found that infants who underwent surgery for necrotizing enterocolitis had mortality rates ranging from 23 to 36\%, whereas those who were treated medically had a mortality rate of 5 to 10\%.\textsuperscript{40,42} Infants who survive necrotizing enterocolitis are at increased risk of short-bowel syndrome, wherein the remaining intestine is unable to absorb nutrients commensurate to the body’s needs. They are also subject to intestinal strictures that can give rise to feed intolerance and bowel obstruction.\textsuperscript{42}

Infants with severe necrotizing enterocolitis are at increased risk of neurodevelopmental impairment, particularly of damage to the cerebral white matter.\textsuperscript{50} Stevenson et al.’s pivotal 1980 study evaluated 40 survivors of neonatal necrotizing enterocolitis over a three-year period, finding that 21 children (52.5\%) presented with long-term impairment.\textsuperscript{51} In particular, six children had moderate-to-severe neurologic impairment, ranging from spasticity to seizures to encephalopathy. The other 15 affected children presented with a range of abnormalities, such as abnormal electroencephalograms (EEGs), impaired hearing, retinopathy of prematurity (ROP), and lingering gastrointestinal dysfunction.\textsuperscript{51} Importantly, 17 of the 21 affected children had long-term impairment not involving the gastrointestinal tract; that is, while the short-term management of necrotizing enterocolitis requires aggressive intervention to preserve the GI wall, there are serious long-term neurologic consequences for some survivors of the disease. Indeed, nine children in the cohort had IQs that were significantly lower than those of their siblings (94.8 vs. 112, p<0.05), while five survivors were considered to have an “intellectual handicap,” defined as an IQ below 80.\textsuperscript{51}

A systematic review comparing infants with necrotizing enterocolitis to controls of similar age and gestation who are disease-free found that those with necrotizing
enterocolitis were significantly more likely to develop visual impairment (OR = 2.31), psychomotor impairment (1.72), cerebral palsy (1.55), and cognitive impairment (1.44). Both the case and control group had high incidence of neurologic impairment; 45% of infants with necrotizing enterocolitis were determined to be neurologically impaired, compared to 35% of the controls (p = 0.0003). That is, preterm, LBW infants are at risk of adverse neurological outcomes, but necrotizing enterocolitis increases the risk further. The long-term effects of undernutrition, due to impaired intestinal absorption during critical phases of early development, thus result in both restricted growth and neurological damage. Moreover, the risk of neurodevelopmental impairment is greatest among infants who underwent surgery for advanced disease.46,52

The devastating sequelae of necrotizing enterocolitis – both short- and long-term – make effective prevention integral to reducing morbidity and mortality. The focus of the remainder of this essay is the role of human milk feedings in reducing the incidence of the disease and of neonatal and infant mortality in general; other newer preventive strategies utilize immunologic components of human breast milk to encourage proliferation of non-pathologic, protective gut bacteria. Lin and Stoll note that the three cardinal preventive strategies include human milk feedings, conservative feeding practices, and trophic feedings.40 Human milk feedings focus on providing preterm infants breast milk, as opposed to infant formula. Conservative feeding practices are implemented because premature infants given enteral feeds are at increased risk of necrotizing enterocolitis. More than 90% of all infants who acquire the disease are fed enterally prior to onset.53 Trophic feedings provide small quantities of nutrients to the immature gut, priming it to develop and equip for future, more substantive feedings.54 Thus, management of enteral feeding is the chief modifiable risk factor for necrotizing enterocolitis.

Trophic and conservative feedings are similar in approach, in that both provide limited enteral feedings to preterm infants. Trophic feedings are also called “priming feeds,” because they are undertaken to promote peristalsis and facilitate proliferation of digestive enzymes.43 Conservative feeding practices are an extension of trophic feeds; they involve gradually increasing the amount of enteral intake over time, as rapid increases in enteral intake have been associated with development of necrotizing enterocolitis.46 Importantly, recent Cochrane reviews have suggested that trophic and conservative feeding practices are not associated with a reduced risk of necrotizing enterocolitis; however, both reviews emphasize the need for more extensive research and on ideal enteral feeding practices and prevention of necrotizing enterocolitis.46,56 In particular, Bombell and McGuire call for randomized control trials on the role of early trophic feedings and conservative enteral feedings in reducing the risk of necrotizing enterocolitis.56

At-risk infants who receive human milk feedings are less likely to acquire necrotizing enterocolitis when compared to infants whose enteral feeds contain infant formula.46 Lucas and Cole’s fundamental prospective cohort study of 926 preterm, LBW
infants determined that the risk of necrotizing enterocolitis was 6 to 10 times higher in infants fed formula alone when compared to those who received breast milk exclusively. In infants born at greater than 30 weeks’ gestation, those receiving only infant formula had 23.6 times the odds of developing necrotizing enterocolitis than did infants fed breast milk, either exclusively or in combination with formula. It is worth noting that breast milk feedings were most protective in premature infants of greater gestational age. In addition, the authors found that both maternal milk and pasteurized donor milk reduced the risk of necrotizing enterocolitis. Lucas and Cole’s findings, as well as those of other studies on human and donor milk, will be explored in detail in the following sections dedicated to the physiologic importance of breast milk and the utility of donor milk in the management of the preterm infant.

Human milk offers protective immunologic benefits to preterm infants, strengthening the gastrointestinal mucosal barrier and supplying non-pathologic bacteria that help protect against invasion by disease-causing organisms. In particular, secretory immunoglobulin A (sIgA) transmitted to the infant via breast milk prevents pathogens from crossing mucosal barriers like that of the gastrointestinal tract. Other components of human milk, including the milk protein lactoferrin and probiotic bacteria like Lactobacillus and Bifidobacterium, have been shown to reduce gastrointestinal inflammation and colonization by pathogenic bacteria. Indeed, newer strategies in the prevention of necrotizing enterocolitis include supplying at-risk infants with probiotic supplements that enhance immunologic response in the GI tract. Many of the new preventive strategies currently under study, including IgA supplementation and lactoferrin administration, rest on extensive research demonstrating that the immunologic components of breast milk help protect against neonatal and infant infections like necrotizing enterocolitis.

Oxidative Stress in the Preterm Infant

Preterm infants’ exposure to reactive oxygen species (ROS) – oxygen-containing metabolic intermediates that can damage tissues – during and after birth is thought to contribute to the pathophysiology of necrotizing enterocolitis, retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), and periventricular leukomalacia (PVL). BPD leads to alveolar and bronchiole injury and arises in infants requiring oxygen supplementation during the neonatal period; PVL is a neurologic disease of preterm infants in which segments of white matter closest to the lateral ventricles become necrotic. Reactive oxygen species, which arise from ATP production during mitochondrial oxidative phosphorylation, interact with lipids in cell membranes and catalyze lipid peroxidation. A “radical chain reaction” results, whereby membranous lipids are made radicals themselves, and they damage many nearby lipid molecules in a process called propagation. Reactive oxygen species can also cause damage to proteins and DNA, leading to the accumulation of DNA mutations. Extensive oxidative damage to proteins and membranes, in particular, is thought to contribute to
the development of disease in the neonatal period, while oxidative DNA damage has been linked to the pathogenesis of certain cancers in adulthood.\textsuperscript{63,64}

Preterm infants are at higher risk of oxidative stress and subsequent damage. The body’s antioxidant defense system, composed of antioxidant enzymes (AOEs) and non-enzymatic antioxidants like vitamins A, C, and E, matures during gestation.\textsuperscript{61,65,66} Endogenous production of antioxidants increases in late gestation, as does transplacental transfer of maternal antioxidant enzymes, so as to prepare the growing fetus for the extrauterine environment.\textsuperscript{61} There is a rapid increase in environmental oxygen pressure that occurs at birth, when infants are first exposed to air outside of the uterine cavity.\textsuperscript{67} Furthermore, preterm infants often receive oxygen supplementation in the neonatal period to improve oxygen delivery and spur lung development and function.\textsuperscript{65,66} As such, the combination of reduced antioxidative capacity and increased oxygen exposure contributes to elevated concentrations of reactive oxygen species.

Antioxidant enzymes, like superoxide dismutase (SOD), catalase, and glutathione peroxidase, are critical to neutralizing reactive oxygen species (ROS) that emerge after birth. SOD neutralizes the superoxide radical (O\textsubscript{2}\textsuperscript{-}), converting it to hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}). Hydrogen peroxide is itself an ROS; catalase converts H\textsubscript{2}O\textsubscript{2} to molecular oxygen (O\textsubscript{2}) and water (H\textsubscript{2}O).\textsuperscript{68} The enzyme xanthine oxidase generates free radical species; it oxidizes hypoxanthine to xanthine before producing uric acid. Xanthine oxidase can also produce ROS as a by-product in the uric acid reaction, including the superoxide anion, under certain circumstances.\textsuperscript{53,68} This system is referred to as the hypoxanthine-xanthine oxidase system and is implicated in the proliferation of ROS after birth. In particular, hypoxanthine concentrations increase substantially in the 10-20 minutes following a normal delivery. Moreover, hypoxanthine is a metabolite of ATP, the primary energy source of human cells, and it thus proliferates in a hypoxic state when ATP production slows.\textsuperscript{68}

As mentioned above, birth asphyxia is a common cause of perinatal morbidity and mortality in preterm infants. Alveolar development begins at 36 weeks’ gestation, and surfactant, which reduces alveolar surface tension and allows for lung expansion, is synthesized by alveolar epithelial cells in the late second and third trimesters.\textsuperscript{69} Thus, preterm infants have immature lungs, marked by little surface area for effective gas exchange and limited surfactant production to facilitate independent breathing. They are at much higher risk of hypoxic injury following birth, and insufficient surfactant production can lead to infant respiratory distress syndrome (IRDS). This early hypoxic injury leads to proliferation of hypoxanthine. Management of IRDS at birth includes oxygen supplementation; in the presence of oxygen, xanthine oxidase converts hypoxanthine to xanthine and then uric acid, releasing superoxide anions and hydroxyl radicals (OH\textsuperscript{-}) as by-products. It is thought that this transition from hypoxia to “hyperoxia” induces post-hypoxic reoxygenation injury, wherein oxygen therapy results in the proliferation of tissue-damaging reactive oxygen species at the same time that it resolves respiratory distress.\textsuperscript{68} Importantly, multiple studies stress the importance of antenatal corticosteroid administration to mothers about to deliver a preterm infant;
Antenatal steroids have been shown to spur fetal development, reducing risk of both respiratory distress and necrotizing enterocolitis.\textsuperscript{40,44,70}

Because preterm infants have both reduced antioxidant enzyme capacity and increased exposure to ROS, an “oxygen radical disease in neonatology” was proposed by Saugstad in the 1990s.\textsuperscript{68} That is, ROS damage could result in multiple pathologies, depending upon which organs were affected by protein damage and membrane destruction due to lipid peroxidation. Intestinal, pulmonary, ocular, and neurologic diseases of the preterm infant are thought to be exacerbated by circulation of damaging ROS. Indeed, Saugstad and Aune went on to call oxidative stress and inflammation in preterm infants “two sides of the same coin”\textsuperscript{71} and called for more restrictive oxygen supplementation for preterm infants requiring incubation.

The preterm infant’s source of nutrition, moreover, has been studied to determine whether certain food sources are protective against ROS. Some studies have found no difference in antioxidant protection between breast milk and infant formula.\textsuperscript{66} Yet another study demonstrated increased risk of lipid peroxidation and ROS generation in healthy term infants fed breast milk exclusively; the authors suggest polyunsaturated fatty acids (PUFA), which are more prevalent in breast milk, are prone to peroxidation and contribute to significant oxidative injury.\textsuperscript{62} The authors found that total antioxidant capacity did not differ among formula- and breast-fed infants, but the amount of urinary malondialdehyde (MDA), an ROS that serves as a marker for oxidative stress, was more than twice as high in the urine of breastfed infants than the urine of formula-fed infants.\textsuperscript{72}

Other studies, however, have demonstrated that breast milk has superior antioxidant protection than infant formula.\textsuperscript{65,73} Human milk contains many antioxidants, including the enzymes superoxide dismutase, catalase, and glutathione peroxidase, as well as non-enzymatic antioxidants like vitamins A, C, and E. In addition, human milk contains transition metals zinc and copper, which work in conjunction with antioxidant enzymes because they can receive or donate electrons.\textsuperscript{62,74} The human milk coenzyme Q10 (CoQ10) is linked to increased total antioxidant capacity (TAC); notably, a study on CoQ10 and tocopherols (vitamin E-like compounds) in the breast milk of mothers of preterm and term infants showed that CoQ10 and tocopherol concentrations were highest in the breast milk of term mothers, with the highest concentrations found in colostrum.\textsuperscript{75} The milk with the highest CoQ10 and tocopherol concentrations also had the highest TAC.

Friel et al. examined the antioxidant capacity of both breast milk and preterm formula and found that the rate of oxygen consumption and depletion was always higher in preterm formula, suggestive of more extensive proliferation of ROS.\textsuperscript{73} Importantly, Friel et al. also evaluated iron concentration in preterm formula and associated oxygen consumption. They showed that formulas with higher iron levels displayed an almost two-fold increase in oxygen consumption when compared with the same formulas that
had lower levels of iron. They propose that iron serves as a “free radical generator” in milk, because iron exists in both its ferrous (Fe^{2+}) and ferric (Fe^{3+}) forms and is able to both donate to and receive electrons from ROS in free radical reactions. Aycicek et al. came to a similar conclusion; they found a significant positive correlation between the amount of iron in infant formula and the presence of total peroxide in the blood of formula-fed infants (p<.05). The same study also showed that plasma total antioxidant capacity (TAC) and vitamin C levels were significantly higher among breastfed infants, while the oxidative stress index (OSI) and total peroxide levels were significantly higher among formula-fed infants (both p<0.05).

Exposure to significant oxidative stress during and after birth, particularly with oxygen supplementation, has been linked to multiple diseases that contribute to neonatal morbidity and mortality and that disproportionately affect preterm infants. The use of breast milk to clear ROS and prevent oxidative damage is encouraged by multiple studies, although others have not shown a link between breast milk feedings and reduced ROS. It is important to note that not all antioxidant components of breast milk are known, and that antioxidant supplementation, as with Vitamin E, has been studied as a means of reducing perinatal morbidity and mortality in preterm infants.

IV. Physiologic Effects of Human Milk on Preterm and LBW Infants

Breast milk is the recommended nutrition for all infants, including preterm infants. In particular, the immunologic content of breast milk is protective against necrotizing enterocolitis, described above as an infection most common among preterm infants. Breast milk, when compared to infant formula, facilitates faster GI emptying and may stimulate GI maturation. The content of preterm breast milk differs considerably from that of term breast milk; preterm breast milk is higher in total protein, as well as in immunologic proteins, lipids, and calories than mature breast milk. Still, Heiman and Schanler note that the composition of breast milk destined for preterm infants can differ greatly with respect to fat and protein content, with fat percentage highly variable from mother to mother, changing depending upon the time of day during which milk is expressed, and even varying during lactation. Early milk, called “foremilk,” is notably lower in fat content than is the milk that comes from the breast late during a single lactation, called “hindmilk.” Furthermore, the nutritional needs of the preterm infant often exceed the supply of nutrients in preterm breast milk, and thus breast milk destined for preterm infants typically is fortified.

This section will explore the many immunologic components of breast milk, focusing on its utility in the management of preterm infants. In particular, it will investigate the current recommendations for use of mother’s milk (MM), donor milk (DM), and preterm formula (PF) for hospitalized preterm infants. It will focus especially on the literature around DM, the process of milk pasteurization, and short- and long-term outcomes of MM and DM supplementation for preterm infants.
Immunologic Content of Breast Milk

The immunologic contents of breast milk are responsible for stimulating intestinal maturation, enhancing production of specific antibodies, controlling and preventing inflammation, encouraging proliferation of commensal bacteria, and facilitating the survival of substances that protect the infant. The composition of breast milk changes in accordance with the infant’s needs. Colostrum, for example, is the milk produced in the first few days following birth, and it provokes greater proliferation of intestinal epithelial cells (enterocytes) than does mature human milk, due to its increased concentration of growth factors like epidermal growth factor. Amniotic fluid also contains valuable trophic factors that stimulate intestinal maturation; preterm infants do not take in this amniotic fluid late in gestation, and thus epidermal growth factor is present in higher concentration in preterm breast milk. As preterm infants have less developed immune systems than do term infants, preterm breast milk contains high concentrations of sIgA, phagocytes that neutralize invading organisms, and immunomodulators.

Secretory IgA (sIgA) constitutes 80 to 90% of all immunoglobulins found in breast milk. sIgA inhibits invading pathogens from binding to mucosal membranes, and it is especially protective against gastrointestinal and respiratory pathogens. Very little sIgA is produced in the neonatal period, and levels of sIgA become sufficient to protect the infant at about 30 days of life. Thus, breast milk is the neonate’s predominant source of the immunoglobulin, and concentrations of sIgA in breast milk are at their highest during the neonatal period. Secretory IgA in breast milk protects the infant by way of enteromammary circulation. That is, when a foreign pathogen reaches the maternal GI tract, sIgA production is upregulated by way of antigen-presenting cells (APCs) in the gut epithelium. These IgA molecules enter the mammary cells and are expressed in breast milk, providing the infant with antibody protection against the same pathogen present first in the mother. Secretory IgA is considerably resistant to the proteolytic enzymes of the gastrointestinal tract, improving its ability to neutralize enteric pathogens like E.Coli and Campylobacter. S IgA from human breast milk is thus integral in providing immunologic defenses for newborn infants – which is yet more important in preterm infants whose immune systems and gastrointestinal tracts are even less mature. It is notable that sIgA concentrations are higher in the breast milk of mothers with preterm infants. sIgA can also prevent activation of other immunoglobulins (IgM, IgG), which trigger the complement system and phagocytic recruitment, resulting in inflammation. Thus, sIgA from breast milk can also protect against inflammation – a significant contributor to gastrointestinal morbidity in the neonatal period.

Secretory IgA is passed from the mother to the infant via the breast milk, but gastrointestinal plasma cells that synthesize sIgA are activated only after initial colonization by commensal bacteria, particularly Lactobacillus and Bifidobacterium. Partially digested milk proteins contain peptides that stimulate proliferation of non-

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pathogenic bacteria; *Lactobacillus* and other commensal bacteria have been shown to promote slgA synthesis and to induce oral tolerance of foods.\(^3\,\text{,}^{49}\) In addition, certain prebiotic oligosaccharides in human milk, called “bifidogenic” oligosaccharides, also promote propagation of these commensal gut bacteria.\(^83\,\text{,}^{85}\,\text{,}^{90}\) *Bifidobacterium* decreases intestinal pH by producing lactic acid – thus making the GI tract more able to neutralize pathogenic bacteria – and utilizes nutrients for its own growth, effectively “stealing” nutrients from foreign microbes.\(^91\) In infants who are exclusively breastfed, bifidobacteria comprise 95% of all fecal bacteria but less than 70 percent in infants receiving infant formula.\(^91\) Furthermore, breastfed infants have lower fecal concentrations of pathogenic bacteria like clostridia, enterobacteria, and enterococci species when compared to formula-fed infants.\(^89\)

Milk oligosaccharides also function as receptor analogues for pathogenic bacteria.\(^46\,\text{,}^{49}\) Because they are non-digestible, milk oligosaccharides remain intact in the intestine and bind to proteins on invading organisms, preventing them from attaching to the GI epithelium.\(^91\) There are more than 130 different oligosaccharides in human breast milk; different oligosaccharides competitively inhibit binding of pathogens or their toxins to the respiratory, gastrointestinal, and urinary tracts.\(^83\) Specific oligosaccharides prevent binding of *Streptococcus pneumoniae* to the respiratory epithelium, while others inhibit *E. coli* and *Vibrio cholerae*.\(^83\,\text{,}^{91}\) Breast milk also contains lysozyme, an enzyme that attacks the peptidoglycan layer in the cell wall of certain pathogenic bacteria.

While slgA and milk oligosaccharides prevent pathogenic bacteria from binding to mucosal surfaces, other immunologic components of breast milk inhibit the inflammatory response. The immature intestinal epithelium of the neonate has been shown to mount an excessive inflammatory response to both endogenous and exogenous bacteria; the inflammatory response of preterm infants is yet more potent and responds as powerfully to both pathologic and commensal gut bacteria.\(^49\) This propensity to generate an overreactive inflammatory response leaves the neonate, and particularly the preterm infant, at risk of chronic inflammation. The anti-inflammatory contents of breast milk help mitigate the risk of an overactive inflammatory response, which may be responsible for the pathogenesis of inflammatory bowel diseases in the preterm infant.\(^85\) Goldman enumerates nine of the many different classes of anti-inflammatory agents found in human breast milk, including enzymes that degrade inflammatory mediators, epithelial growth factors, antioxidants, and substances that bind to toxins.\(^86\)

Lactoferrin is a protein in human milk that functions both to prevent proliferation of pathogenic bacteria and to inhibit an excessive inflammatory response.\(^48\,\text{,}^{83}\,\text{,}^{86}\) Lactoferrin is a glycoprotein that binds iron, and it inhibits bacterial growth by competing with foreign bacteria for ferric iron (Fe\(^{3+}\)).\(^83\) With respect to its anti-inflammatory properties, lactoferrin prevents leukocytes from releasing pro-inflammatory cytokines like interleukin-1\(\beta\) (IL-1\(\beta\)), tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)), and IL-8.\(^48\,\text{,}^{49}\) Other anti-inflammatory cytokines in human milk, including IL-10, platelet activating factor (PAF), and transforming growth factor-\(\beta\) (TGF-\(\beta\)), have been shown to reduce expression of IL-
8 and other proinflammatory cytokines. These anti-inflammatory mediators are critical to the preterm infant, which has yet to begin producing endogenous anti-inflammatory cytokines and lacks the mature immune signaling that allows for local, as opposed to systemic, inflammatory response. Indeed, Newburg and Walker refer to human milk supplementation for preterm infants as the principal source of protection and immunomodulation against an inappropriate systemic and chronic inflammatory response.

Despite the importance of anti-inflammatory agents in human milk, it remains critical that the neonate be able to mount an inflammatory response when appropriate. The anti-inflammatory mediators prevent excessive or unnecessary inflammation, but the inflammatory cascade serves a pivotal role in localizing and neutralizing harmful infectious agents. Therefore, human milk also contains inflammatory cytokines, as well as substances that promote synthesis and activation of endogenous inflammatory and immune mediators like neutrophils. Walker notes that the intestinal secretions of newborns lack CD-14, an essential cytokine in the innate immune system’s inflammatory response. Breast milk, however, contains CD-14, and its levels are highest in colostrum and early milk. Therefore, breast-fed infants are more able to mount a defense against intestinal pathogens. In addition, breast milk has been shown to activate components of the endogenous immune system, including macrophages, T cells, and neutrophils. Leukocytes in breast milk, moreover, are present in their active form when they are transmitted to the infant.

The myriad immunologic mediators found in human breast milk are critical to the maturation of the infant and to the protection of immature epithelial surfaces in the respiratory, gastrointestinal, and urinary tracts. These factors play a yet more important role for the preterm infant, which is not exposed to amniotic fluid and placental nutrients available in late gestation. In particular, IgG, the only immunoglobulin that crosses the placenta in significant quantities, does so primarily in the third trimester. The fetus absorbs the majority of maternal IgG during the last four weeks of pregnancy. Placental IgG provides critical support and protection to infants while their humoral immune responses develop during early life. As such, preterm infants are at greater immunologic deficit at birth, due to reduced absorption of immunologic factors in the placenta and the amniotic fluid, as well as the uterus. The content of preterm breast milk, and of colostrum, primes the preterm infant for immunologic maturation, as well as for growth of the immature epithelium in the respiratory and gastrointestinal tracts, where infections like pneumonia and necrotizing enterocolitis occur.

*Human Milk Supplementation for Preterm Infants: Clinical Practice, Shortcomings, and Evidence of Benefit*

The American Academy of Pediatrics indicates that breast milk is the optimal form of nutrition for term babies as well as preterm infants. Preterm infants who receive breast milk have reduced risk of necrotizing enterocolitis, sepsis, retinopathy of
prematurity, and diarrhea when compared to preterm infants who receive preterm formula. Due to intestinal immaturity, many preterm infants cannot receive enteral feeds during the first days of life, and they are administered parenteral nutrition to ensure adequate delivery of nutrients. Appropriate feeding, including early parenteral and later enteral feedings, is essential to prevent postnatal growth restriction in preterm infants, which can have deleterious neurocognitive outcomes. An accepted, albeit imperfect, guideline is that preterm infants should achieve growth rates similar to those of a fetus of the same gestational age that is still in-utero. Parenteral feeding should begin soon after the umbilical cord is clamped to prevent nutrient deprivation, catabolism, and early growth restriction.

Parenteral feedings are curtailed when intestinal maturation, spurred by early trophic feedings, allows for oral food intake. Ziegler notes that the mother’s own milk is the ideal enteral food for preterm infants, as it reduces risk of infection and necrotizing enterocolitis in particular. Mothers of preterm babies, however, often have difficulty expressing significant quantities of milk— which remains a particular challenge, due to the increased nutritional demands of the preterm neonate. Indeed, in a randomized trial of donor milk and preterm formula supplementation for preterm infants, Schanler et al. found that just 27% of the mothers in the study were able to provide sufficient breast milk to satisfy the nutritional needs of their preterm infants. NICUs often must rely on other forms of nutrition, primarily donor breast milk and preterm formula, to ensure proper nutrition of preterm infants. Infants born preterm have increased caloric and protein demand, and they require more vitamins and minerals. Preterm human milk has been shown to lack sufficient protein, calcium, sodium, and phosphate for the nutritional needs of preterm infants.

As such, human milk provided to preterm infants is commonly fortified to guarantee increased nutrient delivery. Furthermore, supplementary preterm formula is often given to ensure adequate growth throughout hospitalization. Supplementary preterm formula provision has resulted in differences in methodology and in conclusions drawn from studies on the role of human milk in the management of hospitalized preterm infants. That is, researchers differ as to their definition of what “breastfed” means; exclusive, predominant, and partial breastfeeding have been classified as “breastfed,” and preterm infants classified as “breastfed” also take in differing volumes of preterm formula to supplement human milk feedings. DeSilva et al. conducted a systematic review on human milk supplementation and risk of infection in VLBW infants; the authors found no relationship between human milk use and reduced incidence of infection in studied VLBW infants. The authors postulate that the methodological inconsistencies of the studies contribute to the lack of findings: “Despite the current practice in most hospitals of providing any available HM [human milk] to infants, the imprecise categorization of feeding— that is, grouping infants with differing degrees of HM intake together, reduces the scientific validity of studies. Further, the true effect of HM may be grossly underestimated because of the varied definitions of HM feeding used in these studies (pg. F509). The authors note that just
11.1% of all infants in the cohort studies under analysis received exclusive HM feeds, as did 31.2% of preterm infants in the RCTs included in the systematic review. Studies in which infants are fed a combination of breast milk and preterm formula may distort findings on the relationship between human milk feeding and the incidence of necrotizing enterocolitis and other infections.

Some research on human milk feeding and outcomes in preterm infants has focused on a “dose-response” relationship between milk intake and risk of infection and other adverse outcomes. A prospective cohort study on human milk intake among VLBW infants during the first four weeks of life evaluated infants based upon the volume of human milk consumed. Furman et al. found that infants who received higher volumes of maternal milk had the lowest risk of sepsis. In particular, infants who received more than 50 mL/kg bodyweight of breast milk each day had the lowest risk of sepsis at week 2 (p=0.047) and week 4 (p=0.043). The authors thus conclude that a threshold daily amount of 50 mL/kg of breast milk (~50% of total intake) is required to reduce the incidence of sepsis among VLBW infants during the first four weeks of life. Schanler et al. conducted a similar study, evaluating outcomes in preterm infants fed fortified human milk (FHM) or preterm formula (PF). Infants fed FHM received at least 50 mL/kg/day. Those in the FHM group advanced to full enteral feedings significantly faster (28 vs. 36 days, p≤0.001), were significantly less likely to acquire necrotizing enterocolitis or late-onset sepsis (p≤0.01), and were discharged from the hospital approximately two weeks before members of the PF group (p=0.03). Of the 62 infants in the FHM group, 22 (35%) received exclusive FHM during their hospitalizations; on average, FHM babies received 84% of all energy intake from human milk. By contrast, all VLBW infants studied by Furman et al. received at least some PF supplementation. Schanler et al. and deSilva et al. suggest that an ideal study would examine exclusive provision of maternal breast milk and/or donor breast milk to determine the effects of human milk on preterm infants.

It is important to note that preterm infants fed human milk exhibit significantly less growth during the hospitalization period when compared to those receiving preterm formula. A retrospective cohort study involving infants from Chile, the UK, and the US found that infants fed predominantly with preterm formula weighed approximately 500 grams more when they reached the age of a term infant. Infants in the PF group also exhibited greater longitudinal growth and had larger head circumferences. Significant differences in weight between the predominant PF formula and predominant HM groups disappeared by 6 months of corrected age (i.e., 6 months after preterm infants reached term age). Similarly, Schanler et al. found a weight difference at discharge of 500 grams between the FHM and PF groups, and infants fed fortified human milk experienced slower weight gain over time than did their formula-fed counterparts.

The significant differences in growth between FHM- and PF-fed infants have raised questions about long-term delays in growth and cognitive development among
preterm and LBW/VLBW infants. Lucas et al. compared hospitalized preterm infants fed either unfortified donor milk (DM) or preterm formula to supplement maternal breast milk during the first weeks of life. While those fed PF demonstrated increased growth and weight gain in the short term, there was no observed difference in the Bayley psychomotor and mental development indices between both groups at 18 months.\textsuperscript{106} This study followed one in which Lucas et al. found that preterm infants fed nutrient- and calorie-rich formula designed for preterm infants showed significantly higher Bayley scores (both psychomotor and mental) at 18 months than did those preterm infants who received term formula.\textsuperscript{106} The follow-up study, comparing human milk to preterm formula, is notable because, despite unfortified human milk having fewer nutrients than preterm formula, those who received donor milk exhibited similar developmental outcomes at 18 months to those who received formula. The authors postulate that breast milk may provide benefits for later development despite lower nutrient content.\textsuperscript{106} A meta-analysis of 11 studies exploring the relationship between breastfeeding and cognitive development in infancy and childhood found that breastfeeding was associated with a cognitive development score 3.2 points higher than that of infants fed formula. The difference was more marked for LBW infants; LBW infants who were breastfed showed a 5.18 point score increase when compared to formula-fed infants.\textsuperscript{107}

Schanler et al. note that despite significant differences in weight between FHM and PF-fed infants, FHM infants were discharged from the hospital significantly earlier. The authors attribute it to reduced risk of infection among FHM-fed infants.\textsuperscript{94} Indeed, they conclude that the health benefits attained through FHM, namely significantly reduced risk of necrotizing enterocolitis and neonatal sepsis, offset slower weight gain in the short-term. A study of VLBW infants found that human milk decreased the odds of infection by 57\% and the odds of sepsis/meningitis by 53\%.\textsuperscript{96} Another found significantly reduced risk of necrotizing enterocolitis among human milk-fed preterm infants born at less than 32 weeks’ gestation.\textsuperscript{108} The reduced risk of infection results in shorter hospital stays, which can also have important economic benefits. Wight estimated in 2001 that neonatal infections stemming from formula use rather than human milk cost $9,669 per infant in the United States.\textsuperscript{79} With respect to short-term, neonatal outcomes, it is the reduced risk of systemic infection – and thus reduced morbidity and mortality in the neonatal period – that makes maternal breast milk the superior form of nutrition for preterm infants.

\textit{The Use of Donor Milk (DM) for Preterm Infants}

When maternal breast milk is insufficient to meet the demands of preterm infants, donor milk (DM) is frequently used to provide a source of breast milk. Lactation may not begin for the first few days following preterm birth, and preterm infants may not receive enteral human milk feeds during the first days of life.\textsuperscript{109} Even if mothers are able to produce breast milk, many do not have sufficient quantities to provide for the metabolic demands of their infants.\textsuperscript{98} Preterm infants thus receive supplemental nutrition in the form of either DM or preterm formula (PF).
Donor milk is most often collected at human milk banks, which exist with varying frequency in countries throughout the world. The first human milk bank opened in Vienna, Austria in 1909. The advent of HIV in the 1980s led to closure of multiple human milk banks in the UK, US, and Australia due to fear of vertical transmission through breast milk of donors not tested for HIV. Lucas advocated in favor of the milk banks, stressing that donor milk was subject to strict pasteurization processes that inactivated the virus and prevented transmission.

Donor milk is pasteurized to prevent transmission of viral infections, like HIV and cytomegalovirus, as well as potentially pathologic bacteria like *Staphylococcus*, *E. coli*, and *Klebsiella*. The most widespread method of pasteurization is the Holder technique, wherein breast milk is heated to 62.5°C for 30 minutes. The Holder technique kills all bacteria, inactivates HIV and human T-lymphotrophic virus (HTLV), but it also destroys some of the immunologic contents of human milk. In particular, pasteurization destroys all leukocytes and between 0-50% of sIgA, as well as 0-65% of lactoferrin. Holder pasteurization does affect the cytokines present in breast milk, with one study suggesting that anti-inflammatory cytokines are destroyed more readily than are proinflammatory cytokines. Breast milk oligosaccharides are not affected by Holder pasteurization.

The pasteurization of donor milk reduces the immunologic content of breast milk, raising questions about its viability in the nutritional management of the hospitalized preterm infant. Furthermore, preterm infants fed donor milk during hospitalization gain weight more slowly than their preterm-formula fed counterparts. In a study comparing preterm infants fed maternal breast milk (MM), donor milk (DM), and preterm formula (PF), 17 infants (21%) in the DM group were reassigned to the PF group due to poor weight gain. Infants in the DM group also required greater volume of milk intake and more nutritional supplements than did PF-fed infants. Both the MM and DM used in the study was fortified with a human milk fortifier to improve nutrient delivery. DM was obtained from preterm mothers only and was subject to Holder pasteurization and then frozen until used.

Because the composition of breast milk differs from woman to woman and throughout the lactation period, the contents of donor milk vary by donor. Most breast milk donors are mothers of term infants; their breast milk may not provide ideal nutrition for preterm infants. Aprile et al. highlight the importance of verifying the protein and caloric contents of DM prior to administering it to preterm and VLBW infants; in addition, they note that donors often provide DM when they need “relief milk-drawing,” or emptying overly-full breasts after feeding their own child, so as to prevent engorgement or excessive milk intake. As a result, relief milk-drawing results in calorically rich DM, as it is primarily extracted as hindmilk. By contrast, using foremilk, or “drip milk” that emerges from the breast at the beginning of lactation, gives a milk of lower caloric
value. As such, milk banks can pursue strategies that provide a more highly caloric DM to preterm infants.

Aprile et al. carried out such a strategy, conducting a prospective cohort study on MM and DM feedings for VLBW infants in São Paulo. DM was selected for its high calorie and protein content (>700 cal/L, 2g/dL of protein) and was either transitional in nature (moving from preterm to term milk in composition) or mature breast milk. The authors found that infants fed MM progressed to a full enteral diet within 6.3 days, while those in the DM group took 10.8 days to mature to full enteral feedings; the difference between the groups was not significant. Moreover, there was no significant difference in the incidence of necrotizing enterocolitis and sepsis between the two groups. The authors indicate that many studies utilizing donated human milk acquire DM from pooled sources, wherein multiple donors’ milk is combined and there are limited studies to assess the caloric and protein content of the milk. As a result, pooled DM is unlikely to meet the nutritional needs of a VLBW infant. They recommend more stringent analyses of milk content and delivery of highly caloric, protein-rich DM to VLBW infants.

It is important to note that Aprile et al. compared DM to MM, and there was no evaluation of preterm formula as an alternative to human milk. Schanler et al. compared MM, DM, and PF feedings among extremely premature infants (<30 weeks’ gestation); MM and DM were fortified when infants matured to feedings of 100 mL/kg/day. DM was obtained from three different milk banks in the United States and pasteurized via the Holder protocol. Infants in the PF and DM groups received approximately 50% of their enteral intake from MM. The authors found no significant difference in “infection-related events” among PF- and DM-fed infants; rates of late-onset sepsis and necrotizing enterocolitis were similar between the two groups. Infants fed DM gained weight significantly slower than did those in the PF group (p=0.001), a finding has been elucidated elsewhere in this paper as well. Importantly, infants who received MM had significantly fewer episodes of late-onset sepsis (OR = 0.47) and repeat episodes of sepsis and/or necrotizing enterocolitis (OR = 0.18; p = 0.023) than did infants fed DM or PF. MM-fed infants also spent significantly less time in the hospital (75 days vs. 87 days among DM-fed infants and 90 days for PF-fed infants). Schanler et al. advocate for greater MM use among hospitalized preterm infants, calling for strategies to improve MM production and delivery. They also suggest that, among DM- and PF-fed infants, a greater quantity of MM is required to protect against infection during the neonatal period. Moreover, they conclude that there were no short-term benefits – infection prevention, early growth – to DM supplementation when compared to PF. It is relevant, however, that infants fed MM or DM displayed significantly lower prevalence of chronic lung disease than did PF-fed infants, which the authors attributed to antioxidant protection that is not compromised by pasteurization.

Other studies have identified reduced infection rates among infants fed DM compared to those fed PF. Lucas and Cole evaluated outcomes among preterm infants fed exclusive pasteurized DM or exclusive PF; those fed only PF were 2.4 times as likely to acquire necrotizing enterocolitis compared to infants fed only DM. A
systematic review of the utility of formula and DM feedings for preterm infants compared fortified and unfortified DM to term and preterm formula, as well as DM and PF as supplements to MM feeds. The review assessed growth and neurodevelopmental outcomes, cognitive and educational deficits and outcomes during childhood, neonatal mortality, incidence of necrotizing enterocolitis and invasive infection, and feeding tolerance. Formula, whether term or preterm or taken exclusively or in conjunction with MM, was associated with significantly faster weight gain during the neonatal period, as well as a significantly greater head circumference. Infants fed DM exclusively were less likely to acquire necrotizing enterocolitis than were infants who received only PF; the meta-analysis revealed results of “borderline significance" (RR = 4.0 of necrotizing enterocolitis for PF, 95% CI 1.0-16.2). Infants fed with term formula were significantly more likely to have necrotizing enterocolitis than those fed with DM (RR=2.5, 95% CI 1.2-5.1), as were infants receiving a combination of MM and PF when compared to those consuming DM and MM (RR = 2.26, 95% CI 1.04-4.90). Infants fed PF only were significantly more likely to suffer feed intolerance than were their counterparts on DM-only diet (RR = 4.9, 95% CI 1.2-20.7). Feed intolerance can be a sign of developing necrotizing enterocolitis or of structural immaturity of the GI tract.

Another systematic review examined the incidence of necrotizing enterocolitis among infants fed PF or DM exclusively, as opposed to as a supplement to MM. McGuire and Anthony analyzed the results of four RCTs or pseudo-RCTs, all of which were conducted more than 20 years ago. They compared enteral feedings of PF and DM in preterm infants. None of the four trials found a statistically significant difference in the incidence of necrotizing enterocolitis among DM-fed infants compared to those fed PF. The meta-analysis, however, found a “borderline” statistically significant difference in the risk of necrotizing enterocolitis; infants fed DM had 0.34 times the risk of necrotizing enterocolitis when compared with those fed PF (95% CI 0.12-0.99). They calculate that one case of necrotizing enterocolitis would be avoided if 20 infants were fed DM rather than PF.

It is important to note, however, that the authors call into question the current clinical relevance of the results of the meta-analysis, given that all studies were completed more than 20 years ago. They argue that advancements in infant formula – particularly in formulas designed especially for preterm infants – and improvements in management of high-risk preterm infants may have affected the effect of DM in reducing the incidence of necrotizing enterocolitis. They conclude that “it may be that the findings of this review are not wholly applicable to the modern population of preterm and low birthweight infants” (pg. F13). Indeed, the development of preterm formulas, coupled with advancements in oral immunoglobulin and lactoferrin administration, has led some researchers to conclude that there are no “short-term” benefits to DM use among hospitalized preterm infants.

Therefore, there remains some debate as to the efficacy of DM feedings for preterm infants in the absence of adequate MM. The literature concludes without
reservation that MM is superior to all alternatives, but there are inconsistent findings across studies with respect to DM and PF supplementation and the risk of necrotizing enterocolitis and sepsis. A recent prospective cohort study in Norway, for example, found that extremely low birth weight infants (<1000g or 28 weeks’ gestation) had significantly reduced risk of late-onset sepsis (LOS) when they received enteral feedings of either MM or DM in the early days of life (<3 days). In this study, however, almost all infants received MM or DM, with only 2% receiving PF. Its findings underscore some of the methodological complications that contribute to the inconclusive literature on the efficacy of DM and PF. First, it is ethically fraught to randomize high-risk preterm infants into groups that receive MM, DM, or PF; indeed, studies that are “randomized” are randomized only for the DM and PF arm, with DM/PF randomization occurring after mothers who are willing and able to breastfeed have opted to provide their infants with MM. Furthermore, very few studies have examined the effect of exclusive PF or DM supplementation on risk of neonatal sepsis and necrotizing enterocolitis. Wight notes that the Schanler et al. study, in which DM- and PF-fed infants received approximately 50 percent of their intake as MM, may have underestimated the impact of DM supplementation. That is, early MM feedings “may have washed out some of the differences in outcome” (pg. 1610); the protective benefits of MM may have obscured a greater difference in incidence of neonatal infection than if the PF and DM groups had not received supplementary MM. Wight advocates for a multi-center trial examining a large number of infants who receive only DM feedings – something that has yet to be undertaken.

In addition, the Holder pasteurization process remains the standard protocol for preparing DM, but other methods are being researched and developed. While Holder kills viral and bacterial cells in breast milk, it also damages or destroys some of the immunologic components of human milk. Another technique, called high-temperature short-time pasteurization (HTST), has been proposed as an alternative to Holder pasteurization but has not been researched extensively. It is used widely for pasteurization of cow’s milk in the commercial dairy industry. It involves heating milk to 72°C for 15 seconds; Terpstra et al. evaluated HTST-pasteurized milk for remnants of HIV, hepatitis A virus (HAV), as well as three bacteria (E. coli, S. aureus, and S. agalactiae). The authors observed that HTST successfully killed HIV, HAV, and the three bacteria studied. HTST is not used widely for human milk pasteurization, however, because it is much more expensive than the Holder method.

As such, the literature on donor milk in the management of preterm infants offers no definitive conclusions as to its efficacy in reducing infection risk among preterm infants. Some studies and meta-analyses have shown reduced risk of necrotizing enterocolitis and sepsis, while others have not. There is more consensus that MM- and DM-fed preterm infants spend significantly less time in the hospital when compared with their PF-fed counterparts. All studies agree, moreover, that maternal milk reduces infection risk and hospital stay for preterm infants. But the same studies agree that it is difficult to provide sufficient quantities of maternal breast milk to provide for the needs of
preterm infants. More research must be conducted on the benefits and risks of DM and PF supplementation, with larger-scale trials offering the best chance to rigorously evaluate the outcomes of DM and PF use in preterm infants. Furthermore, innovations in the way donor milk is pasteurized may offer heat-treated milk that is richer in immunologic and nutritious content.

V. Conclusions and Future Directions

Maternal breast milk remains the best source of nutrition for all infants, according to both the WHO and the American Academy of Pediatrics. Maternal breast milk feedings reduce the risk of life-threatening neonatal gastrointestinal disease and sepsis, as well as overall risk of infection, and they can significantly shorten hospital stay. Providing sufficient maternal breast milk to hospitalized preterm infants is an efficacious, important, and life- and cost-effective strategy in the management of preterm and LBW infants.

The dilemma faced by NICUs and neonatal specialists is what to feed high-risk preterm infants when maternal breast milk “runs out” or is insufficient to meet the metabolic demands of infants born preterm and/or LBW. This paper has detailed the extensive research on the use of preterm formula and donor milk to supplement – or replace, in the case of mothers who do not or cannot breastfeed – enteral feedings of maternal breast milk. Indeed, multiple studies question the efficacy of donor milk when compared to maternal breast milk and preterm formula. While some studies and meta-analyses point to reduced infection risk in infants fed donor milk when compared to infants fed preterm formula, there has been no resounding conclusion as to the superiority of donor milk or preterm formula in the management of preterm infants.

It is important to emphasize that most studies comparing MM, DM, and PF have been carried out in the context of the world’s most developed countries – ones in which NICUs are state-of-the-art, in which infants born as many as 12-15 weeks preterm can survive with aggressive hospital management, and in which doctors rarely have to contend with very real and pervasive risk factors like severe maternal undernutrition. In most of the world, childbirth, neonatal care, and optimal infant nutrition looks nothing like the NICU-centered management protocols in countries like the United States. Therefore, we must carefully assess the results presented in papers on nutritional management of preterm and LBW infants, not only for their methodology, but more importantly for their applicability to the realities of low-income and middle-income developing countries.

It is imperative that we establish affordable, logical, and safe models for management of preterm infants in low-resource countries. Donor milk may yet be part of the solution, but it must be analyzed in future large-scale studies, in both developed and developing countries. Indeed, because the developing world carries most of the burden of neonatal and infant mortality, it, too, should be at the center of innovative research to determine how we might improve nutritional strategies for the management of high-risk
preterm infants. Thus, rigorous studies must be conducted on the utility and feasibility of PF and DM as supplements to maternal breast milk in the management of high-risk preterm neonates in the developing world.

PART TWO: ORIGINAL RESEARCH

Brazil provides a unique context in which to study breast milk donation and breastfeeding promotion at large. In Brazil, breastfeeding rates declined during the 1960s and 1970s as infant formulas grew more popular and as women entered the work force in greater numbers.\textsuperscript{124,125} A mid-1970s survey of randomly selected children in São Paulo, Brazil's largest city, found that the average duration of exclusive breastfeeding was one month, which children from higher-income families breastfed for just 24 days.\textsuperscript{126} A national survey conducted in 1975 found that Brazilian women breastfed (not necessarily exclusively) for just 2.5 months on average.\textsuperscript{127} In response, the Brazilian government founded the National Program to Incentivize Breastfeeding (PNIAM-\textit{Programa Nacional de Incentivo ao Aleitamento Materno}) in 1981, combining a policy and advertising campaign with a later program to enforce more stringent regulations on infant formula marketing and distribution.\textsuperscript{128-130} In addition, PNIAM designed education programs aimed at health care professionals, sought to protect the rights of working mothers who were breastfeeding, and disseminated information about the dangers of early weaning.\textsuperscript{131} Studies have attempted to examine the effects of PNIAM’s outreach programs on breastfeeding prevalence and duration of exclusive breastfeeding.\textsuperscript{131,132} Other studies have focused on targeted national efforts to restrict infant formula marketing\textsuperscript{129,133}, though it is difficult to isolate the effects of PNIAM and infant formula marketing restrictions from other interventions, such as the introduction of the Baby-Friendly Hospital Initiative (BFHI) in Brazil in 1992.\textsuperscript{134}

A São Paulo study of 380 mothers with children under eight months of age found an increase in breastfeeding from 1981 to 1987: prevalence of breastfeeding increased from 41\% to 63\% of all included mothers, and average duration of breastfeeding grew from 89 to 127 days. Duration of exclusive breastfeeding increased from 43 days in 1981 to 67 days in 1987.\textsuperscript{131} A Rio de Janeiro study of 19,044 children found that the number of children under six months of age receiving only breast milk grew from 19\% to 42\% between 1996 and 2008.\textsuperscript{132} Rea reported in 2003 that 50\% of Brazilian women breastfed for up to 10 months in 1975, compared to just three months in 1975.\textsuperscript{127} A 2007 WHO survey found that 40\% of Brazilian children younger than six months were breastfed exclusively.\textsuperscript{135}

An integral aspect of Brazil’s national breastfeeding promotion program is the incorporation of the Human Milk Banks (BLH – \textit{Bancos de Leite Humano}), introduced in Brazil in 1943. The BLHs have assumed central importance in the last two decades, as they have garnered support from both PNIAM and UNICEF. Brazil’s combined 325 milk banks and milk collection units service a population of almost 200 million people.\textsuperscript{136} The country’s first milk bank opened in Rio de Janeiro in 1943 to allow for exchange of
breast milk among women with young children. Early on, the banks gave rise to a post-colonial continuation of the “ama de leite” tradition, whereby poor women served as wet nurses to rich women in Brazil. From the 1940s to 1970s, the banks’ donors were most often poor women who donated breast milk in return for money, health care, and social services. In the past 25 years, the milk banks and collection units have been incorporated into Brazil’s national health care system. They are now non-profit institutions promoting breastfeeding with help of on-site medical and nutritional professionals. The banks prioritize donations for premature and low-weight newborns unable to feed directly from the breast, as well as infants whose mothers have HIV and who could acquire the infection from breast milk. In 2011, Brazil’s banks collected 167,483 liters of breast milk from 168,273 donors; this milk was then distributed to 170,751 recipients – the majority of whom were premature or low birth weight infants.

There is only a small body of literature on breast milk donation and its role in breastfeeding promotion, particularly in low- or middle-income countries. We found only three published studies that investigated reasons for donation and personal and professional characteristics of human milk donors in Brazil. There were two qualitative studies in Brazil: one based on interviews with 11 milk donors at a public hospital in the state of Ceará, the other also an interview study with 36 breast milk donors at two milk banks associated with public hospitals in Brasilia. Both studies found that women donated milk primarily because of (1) excess milk production; (2) a desire to help others (altruism); and/or (3) recommendation of a health care professional. However, both studies interviewed only donors who donated milk to other children; non-donors and women who donated milk primarily to their own child were not included. Twenty-five percent of participants in the Brasilia study were college graduates; the 2010 Brazilian census showed that just 7.9% of Brazilians had college degrees. This sample thus overrepresented college graduates in a country in which a college education is still fairly rare.

A quantitative, questionnaire-based study of 737 milk donors at all human milk banks in a northeastern state of Brazil evaluated the milk donors’ educational attainment and determined that donors who were younger, illiterate, and unemployed were more likely to have donated at the recommendation of a health professional. Conversely, women of higher educational level were more likely to donate because they reported being aware of the needs of the infants serviced by the milk bank. However, the study based its questionnaire on the blood donation literature, and their may be limitations to applying similar questions to a donation process that occurs for different reasons and attracts a different demographic (e.g., only women post-partum). Another quantitative study in France examined 103 donors at eight national milk bank and also found that women reported donating milk because of excess production and to help others, although almost 50% of participants were not working outside the home, which authors proposed might contribute to their ability to breastfeed and donate milk.
Though many other studies focus on clinical utility of donor milk for preterm and low birth weight (LBW) infants, few studies have investigated who the breast milk donors and users are, and why they donate and use human milk. Since milk banks can suffer from supply shortages, impairing efforts to provide donor milk to at-risk infants, it is important to study milk donors and factors driving donation, to maintain and increase donor milk supply. The purpose of this study was to acquire a more complete understanding of breast milk donation, including women of lower educational backgrounds, representative of the national demographics and potential donor pool; to study both donors and non-donors to better understand the motivations and barriers to breast milk donation; and to study the breast milk banking system within a maternity hospital to better understand the overall context of breast milk donation, banking and usage.

**Methods**

**Population and Setting.**

The study took place at Hospital Maternidade Herculano Pinheiro (HMHP), a public maternity hospital in a low-income region of Rio de Janeiro, Brazil. It is a designated Baby-Friendly Hospital (BFH) and has an on-site human milk bank where mothers of young infants are encouraged by health care professionals to donate breast milk after delivery. Women also receive education about appropriate breastfeeding technique and optimal duration of breastfeeding. HMHP serves a diverse population of women, including women from the many slums (favelas) that surround the hospital, as well as women who come to HMHP from peripheral parts of Rio de Janeiro that are a one-to-two-hour bus ride away. The ethnic makeup of HMHP’s patient base is as diverse as Brazil’s, although the majority of patients in this study self-identified as black or “brown-skinned” (parda, best translated as “mixed race” in English).

**Recruitment and Data Collection.**

The study consisted of 27 semi-structured qualitative interviews, 17 with milk donors and 10 with non-donors. Eligible participants were women 18 years or older who had donated or not donated breast milk to HMHP’s milk bank. The donor population included those who were donating to the HMHP milk bank, either as in-patients following the birth of their infants, or as “outside donors” who visited the hospital to donate milk. All participants had to have given birth within the past year.

Women who were “non-donors” had received information about breast milk donation, but they had not been screened for donation or donated milk at the time of interview. Donors have to be medically cleared to donate breast milk; that is, they cannot have diseases like HIV or hepatitis, which can be transmitted through breast milk, and they could not smoke or use illicit drugs. Milk bank staff obtains such health information through a questionnaire prior to donation. All women were recruited in-person in the hospital by determining, with the help of the milk bank and hospital staff, which eligible women were donating milk and which were not.
Those who agreed to the study participated in a 30-45 minute interview. Interviews were carried out in July and August 2011. All interviews were conducted in Portuguese by a fluent, non-native Brazilian Portuguese speaker from the United States who has spent significant time in Rio de Janeiro but is still an outsider to the environment in which the study took place. Interviews were recorded and later transcribed and translated into English.

Written informed consent was obtained from all 27 participants. The study was approved by the Committee for the Protection of Human Subjects of the University of California, Berkeley (CPHS#2011-02-2845), and the Comitê de Ética em Pesquisa da Secretaria Municipal de Saúde e Defesa Civil in Rio de Janeiro, Brazil.

**Interview Details**

Interviews were semi-structured, and participants were asked about their knowledge and opinions of breastfeeding and child health, if and/or how they acquired knowledge about the milk bank and milk donation, previous experience with milk donation (if any), opinions on the role of the milk bank in the hospital, and thoughts on the benefits of milk donation. Donors were asked why they elected to donate milk to the hospital, as well as their opinions on the donation process as they experienced it. Non-donors were asked about their perceptions of milk donation, as well as if they had any personal reasons for not donating milk. The interview also contained questions about pregnancy history, health status, socioeconomic status, and educational attainment.

All interviews were conducted in Portuguese by a fluent, non-native Brazilian Portuguese speaker and female graduate student in her mid-20s. She has spent significant time in Rio de Janeiro but is still an outsider to the environment in which the study took place.

**Data Analysis.**

This paper utilizes Strauss and Corbin’s grounded theory approach. Data collection and analysis occurred simultaneously, leading to the development of preliminary analytic codes and themes derived from interview transcripts. Themes were marked as important when they emerged across multiple interviews. Early codes and categories were used to update interview guides and generate preliminary hypotheses. These hypotheses were further tested in subsequent interviews, with coding, theme identification, and hypothesis generation occurring throughout data collection. Interview transcripts were re-read iteratively and preliminary codes were refined to best fit the content of all 27 interviews. These preliminary codes were used to formulate “focused codes,” as articulated by Charmaz. Focused coding involves the use of the most illuminating preliminary codes to synthesize large quantities of data (in this case, interview transcript) and analyze them to generate a theory that explains the content of the interviews. Analysis also included summary memos that attempted to synthesize and explain emerging themes that appeared in multiple interviews. Focused coding gave rise to a preliminary model of the “milk donation experience,” based on the multiple
experiences and perspectives of the participants. The model of donation experience was used to organize codes relating to opinions about breast milk donation, the process by which women decide whether or not to donate milk, and participants’ thoughts about how and to whom donor milk is distributed.

Results

Twenty-seven women between the ages of 18 and 38 were interviewed and their characteristics are presented in Table 1. Their history of donation is presented in Figure 1.

Table 1: Participant characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Categories</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Range (mean)</td>
<td>18-38 (24.5)</td>
</tr>
<tr>
<td>Self-reported race/skin color</td>
<td>Black</td>
<td>15 (55%)</td>
</tr>
<tr>
<td></td>
<td>Brown-skinned (“parda”)</td>
<td>8 (30%)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>3 (11%)</td>
</tr>
<tr>
<td></td>
<td>Did not identify</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Employment status prior to pregnancy</td>
<td>Employed</td>
<td>12 (44%)</td>
</tr>
<tr>
<td></td>
<td>Unemployed</td>
<td>15 (56%)</td>
</tr>
<tr>
<td>Bolsa Familia** enrollees</td>
<td>Enrolled</td>
<td>3 (11%)</td>
</tr>
<tr>
<td></td>
<td>Not enrolled</td>
<td>24 (89%)</td>
</tr>
<tr>
<td>Educational attainment</td>
<td>Completed high school</td>
<td>10 (37%)</td>
</tr>
<tr>
<td></td>
<td>Some high school</td>
<td>10 (37%)</td>
</tr>
<tr>
<td></td>
<td>Less than high school</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>Childbirth history</td>
<td>Previous children</td>
<td>12 (44%)</td>
</tr>
<tr>
<td></td>
<td>First child</td>
<td>15 (56%)</td>
</tr>
<tr>
<td>Completed some prenatal care</td>
<td>Yes</td>
<td>27 (100%)</td>
</tr>
<tr>
<td># Prenatal care visits</td>
<td>Range (mean)</td>
<td>2-13 (6.3)</td>
</tr>
<tr>
<td>Type of delivery</td>
<td>Vaginal</td>
<td>21 (78%)</td>
</tr>
<tr>
<td></td>
<td>Caesarian</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>Term (&gt;37 weeks)</td>
<td>20 (74%)</td>
</tr>
<tr>
<td></td>
<td>Preterm</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>Birth weight</td>
<td>&gt;2500g</td>
<td>19 (70%)</td>
</tr>
<tr>
<td></td>
<td>&lt;2500g</td>
<td>6 (22%)</td>
</tr>
<tr>
<td></td>
<td>&lt;1500g</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Newborn outcome</td>
<td>Normal discharge</td>
<td>20 (74%)</td>
</tr>
<tr>
<td></td>
<td>Hospitalized in NICU</td>
<td>7 (26%)</td>
</tr>
</tbody>
</table>
Learning about the Milk Bank and Donation.

**Donors.** Women described learning about the milk bank from one or more of multiple sources: (1) their mothers or female friends; (2) health professionals, either during prenatal care, or, more often, in the hospital after delivery; (3) personal experiences in which they witnessed other women who could not breastfeed and thus went to the milk bank for assistance and supplementary donor milk; and (4) media sources, particularly television. Health care professionals were the principal source of information about the milk bank; doctors, nurses, and nutritionists who visited women following delivery offered what many women interpreted as “medical advice” about donation and the milk bank. Depending on the individual, health professionals encouraged donation or suggested that women receive help learning how to breastfeed correctly by visiting the milk bank and learning proper technique.

One donor, whose daughter was born preterm, hospitalized in the NICU, and unable to feed directly from the breast, learned about the milk bank when the pediatrician came to her bedside:

“When I was admitted to the hospital, I didn’t know there was one [a milk bank], no. And the doctor herself told me to come and look for the milk bank, because she said that I needed to breastfeed my daughter. And she told me. She said to me ‘Now you need to begin breastfeeding, extracting milk, breastfeeding your daughter. So go to the bank –
to the milk bank.' And so I came here and that was how I learned about it.” – First-time donor, 38 years old; child interned in the NICU

Other women experienced excess breast milk production and did not know what to do or where to go to alleviate the pain and discomfort associated with overly full, leaking breasts. Multiple women said they had either thought of or begun to throw excess milk away, prior to learning about the possibility of donation. In-patients with excess production received information about donation from health care professionals, while one outside donor learned about the milk bank from a friend.

“...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

“...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

“...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

“It was the nurses [who told me]. My breasts were really hard and really full, and they were hurting. They were so full, so I said, ‘I’m going to express it into a cup and then I’m going to throw it away.’...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

“...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

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“My friend who was here just now, who’s with my daughter, she told me. ‘Ah, if you have lots of milk, you donate it.’ She said to donate. And she came to me yesterday, I think, when I was expressing some milk. She said to me ‘Go, you go donate.’ And I said ‘How am I going to donate?’ Then she said, ‘Oh, you have to donate.’ And I said, ‘I think, for me, there’s no way to donate because I don’t know where to go.’ And I took out some milk and threw it away into the sink. But now that I’m here – that I’ve been able to donate, I’m going to keep donating.” – First-time donor, 18 years old

Women also learned about milk banks and breast milk donation through social contacts and experiences in which they saw or knew women who could not breastfeed their children and were in need of donor milk.

“In the hospital where I was staying, there was a girl who didn’t have any milk. She cried because her son was hungry, because the doctors kept telling her to try harder, but she really didn’t have any milk. There are women who have this problem. So she took her son and went to the milk bank. She got there and there wasn’t any milk. And I thought, if I could breastfeed that child, I would. That experience stayed with me, and when I got home I said, ‘I am going to start donating milk.”’ – Returning donor, 19 years old

“There was a little boy in the NICU and before I got there [to the milk bank], the woman was hurrying around trying to make his milk, and there was only a little bit left. She turned around and said ‘Go find that other mother! His milk is running out already.’” – First-time donor, 28 years old

“...But I was thinking, and at the same time that I was thinking about expressing it and throwing it away, the girl [the nurse] came in. And I said, ‘My breasts are really full,’ and she said, ‘Why don’t you donate?’” – First-time donor, 23 years old

Non-Donors. Among women who were non-donors, none reported knowing another woman who had relied upon donor milk to feed one of her children. Like donors, many non-donors learned about the milk bank from health care professionals visiting
their rooms after delivery. Importantly, non-donors reported that they learned about the milk banks as a place to receive breastfeeding support, rather than a place to donate breast milk.

One non-donor went to the milk bank on the recommendation of the pediatrician, because she had been unable to breastfeed her son successfully in the first 24 hours following birth.

“If the pediatrician hadn’t told me, I would have gone home thinking that I wasn’t going to have any milk. I was going to go to the doctor as soon as I was discharged to see what I could give to my son to drink. Totally not knowing, totally misinformed, you know? I really didn’t know. And I was sad, saying ‘Oh my God, I don’t have any milk.’” – Non-donor, 31 years old

Several non-donors learned about the milk banks when she visited the hospital for prenatal care.

“The doctor told me to go there if I had any difficulties [breastfeeding]. She talked to all of us and said that if we had any problems, we could go to the bank and ask questions, and the women there would explain everything to us.” – Non-donor, 21 years old

Contemplating and Journeying to the Milk Bank. After learning about the milk bank, women had to decide whether or not to visit it. This process could be considered contemplation: women processed what they had heard, along with any remaining fears, doubts, or uncertainties about donation and the milk bank. Following a period of contemplation, most women described a journey to the milk bank, either to donate or to receive help with breastfeeding, or both. “Journeying” took the form of a woman leaving her hospital room or her home and visiting the milk bank in the hospital; the milk bank is not far from the labor and delivery floor, but it is tucked away at the end of a hallway, and many women indicated that they did not know where the bank was prior to visiting it for the first time. Women described learning about breastfeeding technique and donation, as well as how the bank distributed donated milk. The journeying phase – or lack thereof – was a critical aspect of each woman’s narrative, whether she was a donor, a non-donor who had visited the bank for breastfeeding assistance, or a non-donor who had not visited the bank.

Donors. Donors expressed lingering uncertainties about the bank, even after they received information from health care professionals in the hospital. Women worried about experiencing pain if they were to donate.

“Ah, they say it hurts when you extract [milk]…there was fear of feeling pain, you know? Nobody wants to feel pain.” – First-time donor, 28 years old
Some donors expressed uncertainty about the destination of the milk they donated to the milk bank. They worried that the bank would throw their milk away, while others were skeptical of what the bank did to the milk. Even while receiving information about where donor milk was distributed, some donors expressed fear of donating their own milk.

“So I asked them [the nurses], ‘Where does my milk go?’ We need to know where it goes, because it’s not okay for you to take something out and then just throw it away. And that’s when she explained to me, ‘No, the milk goes to children in the NICU, to the children who are born underweight.’” – First-time donor, 23 years old

Multiple donors identified infants hospitalized in the NICU – born preterm or low birth weight – as those most likely to receive donor milk. They referenced information they had received from the milk bank staff, or from health care professionals who visited them in their rooms, when indicating why and for whom donor milk was collected. Still, the excerpt above illustrates an uncertainty about donation, stemming not from fear of pain, but rather from a lack of “direct contact” with the donation process. That is, women deposited their milk at the bank and left, unaware of who benefited from their donation.

Finally, other women were skeptical about their ability to donate at all. They were unsure that one could actually provide milk for another child, despite learning about donation as in-patients.

“I didn’t even know. I thought that you couldn’t – that you couldn’t even give your milk to another child. I don’t know, I thought it would be bad. Only the mother’s milk is good for her baby. That’s what I thought…and I changed a lot, you know, because it’s important that we know this, about giving milk to other children. It’s important.” – First-time donor, 23 years old; child interned in NICU

Another woman, an outside donor – a woman who had not given birth at HMHP but learned about the milk bank in her community and came to the bank to donate -- experienced excess production and engorged, painful breasts. She began expressing some of her milk into her kitchen sink. Though her friend recommended that she go to the hospital and donate, she had doubts about how the milk bank processed and handled donor milk.

“I was a little afraid...afraid of giving my milk to someone [at the bank] and them doing something to it, you know? And I thought, ‘I don’t think so, I’m not going to donate,’ you know?” – First-time donor, 18 years old

Apprehension and uncertainty course through all of these narratives, whether the doubts relate to donation being painful, the destination of donor milk, or the process by which the bank prepares donor milk.
Non-Donors. Like donors, non-donors also expressed fear of pain if they were to donate milk. One non-donor befriended a donor when she went to the milk bank to receive breastfeeding assistance from the staff. She asked the donor questions about donation and to receive additional information about whether donation is painful.

“I was afraid – I thought that it would hurt. I can’t tolerate being in pain. And she [the donor] said ‘No, it doesn’t hurt, no.’ So she explained to me a little bit about it, that she was going there to give some milk to her own child, and she quickly told me about it. I asked her ‘Does it hurt?’ And she said no.” – Non-donor, 20 years old

Some non-donors also suggested that they would have inadequate milk supply for their own children if they donated milk to the bank.

“Yesterday, a girl said to me, ‘I’m not going to donate milk because I won’t have any milk for my son...She thought that if she donates [to others] the milk that feeds and nourishes her son, that when her son breastfed she wouldn’t have any milk for him.’” – Returning donor, 34 years old

“I’m not even producing enough milk for me! There’s not enough milk even to feed my own son – how am I going to donate milk? There’s no way.” – Non-donor, 18 years old

Many non-donors had never visited the milk bank, especially those who had not had difficulty initiating breastfeeding and did not require assistance from milk bank staff.

“It didn’t even occur to me. I didn’t even think about it – I’m being sincere. I haven’t once thought about donating.” – Non-donor, 36 years old

“I can’t say that I’m not afraid. It’s because I haven’t seen it [the milk bank] yet – I don’t know what it’s like. I just have to go there to see it – that’s the only way I’m going to know.” – Non-donor, 20 years old

This – the journeying phase – was a critical difference between women who donated milk to the bank and those who did not. All donors described how their own agency culminated in donation. While they had prior knowledge of the milk bank, they had to visit the milk bank themselves to understand what it does and decide if they wanted to donate. Milk donation requires a degree of self-determination and activity that often begins out of necessity – what can be termed as pragmatic reasons for donation – and, upon contact with the milk bank, transforms into altruistic reasons for donation.

Reasons for donation and beneficiaries of the donation process. Donors expressed very different reasons for donation, depending upon whether they were donating to their own children or to other children. All 17 donors first considered donation out of necessity. Women donating to other children experienced overproduction and painful, engorged breasts, and they were unable to feed their own infants as a result, while
women donating to their own children did so because their infants were in the NICU and donation was the only way they could feed their infants and continue producing breast milk. Therefore, in all cases, initial reasons for donation were pragmatic, sometimes even self-serving.

**Women Donating to Their Own Infants.** Seven women were donating milk to their own infants, with five of them donating to other infants in addition to their own. All seven of these women had infants hospitalized in the NICU. At HMHP, mothers of infants in the NICU appear to be targeted specifically to encourage donation to their own infants (*auto-ordenha*). In this context, donation is deemed a medical necessity – a way to provide milk for at-risk infants and to ensure that mothers can produce milk if their infants cannot feed directly. Women who donate breast milk to their own children have very different reasons for donating than do women who donate breast milk to others: through donation, they are able to provide sustenance to their infants, who are often born preterm, LBW, or who have been hospitalized in the NICU with post-partum complications like infections.

The advice four women – all of whom had infants hospitalized in the NICU – received from health professionals was akin to a “prescription.” They were told to go donate to the milk bank “every three hours.” They donated to provide breast milk for their children, as well as to encourage milk production while their infants could not feed directly.

“I come here every day, every three hours. And right now I’m donating to my daughter. In reality it’s only for her right now. She’s still not able to feed directly, and she’s not able to latch on to my breast. So I’m doing this donation every three hours. It’s a way that lets me breastfeed my child. If [the milk bank] didn’t exist, how would I be able to breastfeed her?” – *First-time donor, 38 years old; child interned in the NICU*

“I never thought that I was going to do it [donate milk]. I only do it because I’m here [in the hospital] – because I have milk and I’m here, and he’s not able to breastfeed yet.” – *First-time donor, 32 years old; child interned in the NICU*

Another donor, whose daughter went to the NICU shortly after birth with an unknown infection, described the need to introduce her daughter to breast milk.

“[I’m donating] so that she doesn’t get hungry, and so that she can taste the flavor of my milk. So that when I can breastfeed her, she’ll be able to latch on directly and not reject it.” – *First-time donor, 19 years old; child interned in the NICU*

Women who donated milk to their hospitalized children consistently identified a biomedical need as their reason to donate: it was a pragmatic decision -- encouraged by health care professionals and milk bank staff – that improved the health and wellness of their fragile newborns.
“It’s so that the baby can recuperate as fast as possible. Because it’s only with this [milk] that she’s able to live. So I’m extracting it and giving it to her so she can get better faster.” – First-time donor, 38 years old; child interned in the NICU

Women Donating to Other Infants. Ten women donated milk only to other infants, and all of them reported that their initial impetus was to alleviate their own pain or discomfort.

“Why did I only think of donating now? Because I was in a lot of pain. And I wanted to empty my breasts fast so the pain would go away. I think people only think of doing something when it’s for our own benefit. Look at me. I already had two daughters and I never donated. Why did I go donate today [with my third daughter]? Because I couldn’t take the pain anymore.” – First-time donor, 28 years old

donors to other children, particularly those who donated as in-patients following the births of their children, described initial contact with the milk bank as a medical necessity – but one that was significantly different from that of mothers donating to their infants in the NICU. These women emphasized that overproduction of milk made it difficult for them to properly breastfeed their own children.

“He wasn’t latching on, and my breasts were full – full of milk, and I didn’t know what was happening. I thought I didn’t have any milk. The nurse went with me to the milk bank...My breasts were full, really full, and I was shocked by how much milk I had [when I donated]. I said, ‘Wow, I didn’t even know I had this much milk.’ I felt much better afterwards...and now he’s latching on the right way.” – First-time donor, 23 years old

Upon contact with the milk bank, many donors described learning about the dual benefits of milk donation, both for themselves as well as for the recipients. Milk bank employees inform potential donors about the process of milk donation, emphasizing that donated milk is distributed to high-risk neonates. One outcome of the physical journey to the bank, therefore, is an understanding of the role of milk donation in the lives of sick infants.

“I saw that it didn’t hurt much, and that there were other people in need. So if I have a lot, why not donate it? Why would I throw it away? During the time that I’m throwing it away – that’s the time that other children are in need of it and they won’t have it.” – First-time donor, 23 years old

“I’m doing what I couldn’t do before, when I didn’t have this knowledge – like the way she [the milk bank employee] oriented me. I had heard about it, but I didn’t know how important it was. Now I’m going to do it so that other babies can be fed with my milk.” – First-time donor, 29 years old
Another woman expressed regret that she had not donated before. When she went to the bank because she was in pain due to excess production, she received information from the milk bank staff and learned where donor milk goes and why it is important.

“Look, I used to think like this: ‘Oh, this doesn’t affect my child at all.’ But then I went there, and I talked to the girl, and she was explaining it to me. Now I’m going to be anxious, thinking, ‘Wow, I had the opportunity to donate two times and I didn’t donate.’ To help another life.” – First-time donor, 28 years old

In addition, donors frequently referenced both pragmatic and altruistic reasons for donation, bringing them together and rendering them inseparable from one another.

“Oh, I know it’s for the people who need it, you know? And because I have more, I can go there and donate. I got some relief [from full and painful breasts], and I can give some to another person.” – First-time donor, 22 years old

“Because I experienced some relief, and I’m helping other children. It’s really great, knowing that you’re helping to give someone life.” – First-time donor, 32 years old

Many donors employed a collectivist, empathetic rhetoric, emphasizing that they might require donor milk some day. They donated because they would like someone else to do the same for them.

Mothers often mentioned the importance of “imagining themselves in another’s situation” and “always thinking of the person next to you.” Their motivations for donation, and their understanding of its benefits, were grounded in a belief that donation was an essential act done on behalf of women who were unable to breastfeed their own children. Women reflected that they themselves could one day be unable to breastfeed, and thus it was imperative to empathize with fellow women who could not. They created a community in which donors and recipients were interchangeable entities.

“I was lucky enough to have milk, but there are mothers whose milk dries up. And it doesn’t cost anything to go there and do a little bit [for someone else]. I would like people to do that for me. It’s reciprocal – you do some and then receive some. I’m doing my part. That other person is going to do their part, and the other their part, and it’s just like that. All of us, together.” -- First-time donor, 32 years old; child interned in the NICU

“One hand washes another. Today it’s another child who needs it – tomorrow it could be your child.” – Returning donor, 19 years old

One mother, whose son relied on donor milk when she had difficulty producing breast milk, became a donor to her son and other children when her milk supply
increased. As both a donor and a recipient, she detailed the “benefits” she received through her contact with the milk bank:

(As a recipient): “Sometimes, I was sad, but at the same time I was happy. Because I could see that he was hungry, and I wanted to know if he could have something to eat. So I was happy because of that. To know that he was hungry, but that in a little while his stomach would be full. I was happy. What [the other mothers] did for me was a really good, beautiful act.” – First-time donor, 23 years old; child interned in the NICU

(As a donor, when her son was in the NICU): “It helped me, because my breasts were full and I didn’t have – my son wasn’t with me and I couldn’t give it to him. He wasn’t around to breastfeed, you know? And that’s when the girl [the nurse] told me that I could give my milk to another mother, and I thought that was really important. Because I was suffering with full breasts and they were able to extract it, and I felt better already. I felt relief from pain.” – First-time donor, 23 years old; child interned in the NICU

Finally, women emphasized that acquiring knowledge about who receives donor milk is likely to promote continued donation, as they now have experiential evidence of how donation benefits themselves and others.

“One time I was here extracting milk, and a woman came in who had to take out one milliliter of milk. And she was having a lot of difficulty extracting that one milliliter. Such a small amount. That’s when I thought ‘Wow, difficulty extracting such a small amount of milk. That little bit could be mine. That little bit of milk could be all of the mothers who are here.’ And that’s when I decided to extract [and donate].” – First-time donor, 29 years old

Several women viewed donation as a self-empowering, positive experience, one in which their own agency and determination would benefit other mothers and children. When asked who would benefit from donation, mothers frequently referenced at-risk preterm infants, as well as the mothers of these children, but they often mentioned themselves as well. Many cited relief from painful, full breasts; multiple women, however, also said they felt happy and proud that they helped other people.

“Oh, I can’t really explain it. It seemed like somebody needed it [my milk]. The first time I came and donated, it made me feel good, and I said, ‘I’m helping a child!’…And when I continued to come, I kept thinking that I was helping someone. That’s why I came.” – Returning donor, 34 years old

“I feel good about myself. As a human being I feel like – mission accomplished. Satisfied. I feel really good. When I go donate, and when I leave there, I see the container that I’ve filled [with milk] and I feel really good. I know that now [someone] is guaranteed lunch, dinner…I feel really happy.” – First-time donor, 33 years old
**Role of the Milk Bank in the Hospital.** Integral to spreading information and educating expecting mothers about milk banks and milk donation is a firm understanding of what the milk bank does within the hospital.

Twelve of the 27 women (44%) described receiving help with breastfeeding technique at the milk bank, including eight of the 17 donors (47%). Non-donors who visited the bank also received information about breast milk donation.

**Donors.** Women emphasized that the milk bank existed not only to encourage and facilitate donation, but also to educate women about breastfeeding, to encourage breastfeeding, and to help resolve mothers’ early difficulties with feeding.

“Oh, they help a lot, even with mothers who are experienced and already have more than one child. Sometimes when I’m here expressing milk, a mother will arrive, desperate, who doesn’t know what to do because the child doesn’t want to latch on, doesn’t want to take in milk...And they [the milk bank staff] put them here and explain how you have to place the child on your lap.” – *First-time donor, 19 years old*

“The first time that I went there, they taught me how to do a massage, how the breasts get really hard and engorged, and how to breastfeed. After that, I went back to donate...But after I went there, I learned everything correctly, and now I know [how to breastfeed].” – *First-time donor, 23 years old*

The second excerpt underscores an important part of the milk bank’s mission: This woman, a first-time mother, first went to the milk bank to receive help with breastfeeding difficulties related to engorgement and pain. After learning about how to breastfeed and receiving information about donation, she then returned to the milk bank to donate. For her, the milk bank provided two unique services: assistance with breastfeeding technique and donation. She went to seek help and later became a donor, demonstrating the fluidity with which the milk bank assumes different roles at different times. A few weeks later, the same woman was back at the HMHP milk bank, long after she had been discharged with her newborn son. She returned with a severe case of engorgement and mastitis, and she sought relief at the milk bank. Weeks after she left the hospital and had ceased donating, she returned to the same place that helped her in the days following her son’s birth. She identified the milk bank’s role in ensuring the health and well-being of young infants and new mothers:

“If there was no milk bank, how would we know about these things? How would a child who can’t – the mother has no way of giving [milk] or sustaining her child during the three days that she’s here, or even more time if there’s some problem. If there were no milk bank, how would these children breastfeed? How would these children know how to live?” – *First-time donor, 23 years old*
**Non-donors.** Non-donors who visited the milk bank for breastfeeding assistance identified the bank as a place to learn about breastfeeding, primarily, as well as about donation:

“They teach us to breastfeed our children and also teach us ways to stimulate milk [production], and even about donation. They talk about donating your own breast milk. They tell you – if you want to, they don’t demand it. They say ‘If you want to, you can go and donate.’” – *Non-donor, 30 years old*

It is important to note that *donors* emphasized the role of the bank in providing breast milk to at-risk infants in the NICU, while *non-donors* focused on the role of the milk bank to educate new mothers about breastfeeding technique and stimulation of milk production.

**A model of milk donation.** Interviews with donors were utilized to create a “model of donation,” which details the rather linear process undertaken by most participants when they were deciding to donate milk to the hospital’s milk bank. The donors’ narratives involved several “steps”: (1) Learning about the possibility of donating breast milk from peers, health professionals, or personal experiences in hospitals; (2) Contemplating breast milk donation, including experiencing fear, uncertainty, or doubt about it; (3) Exploring the logistics of donation by “journeying” to the milk bank to learn more about it; (4) Donating milk to the bank while receiving information about proper breastfeeding technique; and (5) Getting positive reinforcement for breast milk donation through imagining who benefits from their donations. This process is illustrated in the model below.

**Figure 2. A Model of Milk Donation.**
Discussion

Our qualitative study of breast milk donors and non-donors at a public hospital in Rio de Janeiro, Brazil, illustrates that the milk bank is an integral part of in-hospital breastfeeding promotion and in ensuring that mothers are equipped to handle the responsibilities of breastfeeding when they are discharged. The overarching responsibility of the bank is to promote breastfeeding and human milk nutrition for all infants, by 1) a mother’s own milk – direct from the breast, 2) donation to one’s child, or 3) donor milk. The 17 donors interviewed reported that their initial reasons for donation grew out of medical necessity: pain, discomfort, overproduction, or an inability to breastfeed their child directly precipitated the first visit to the milk bank. Women who donate to their own infants hospitalized in the NICU can provide their children breast milk through a nasogastric tube while the infants are still unable to breastfeed. Furthermore, all women who visit the milk bank – donors and non-donors – are encouraged to solicit help with difficulties breastfeeding. Thus, milk donation is another aspect of a strategy to promote breastfeeding for all women and infants – one of the stated goals of a Baby-Friendly Hospital.

These results build upon three studies of breast milk donors in Brazil; despite methodological differences, all three found that the most commonly reported reasons for donation were overproduction of milk/breast engorgement and a desire to help others.\textsuperscript{139,140,142} Our study offers additional information on the process women went through when deciding whether or not to donate breast milk, as well as some insight into why non-donors elect not to donate breast milk. Furthermore, it illustrates the many roles the milk bank assumes in the hospital, both for donors and non-donors.

That Thomaz et al. found an association between higher educational level and more “altruistic” reasons for donation – that is, knowing the needs of the infants who receive the milk\textsuperscript{142} – is interesting, given that only seven of 17 donors (41\%) in the current study completed high school, and none attended college. Such a finding suggests that the milk bank may serve an important role in educating women about why donation is important, irrespective of the educational level of women in this smaller, qualitative study. The model of breast milk donation we propose emphasizes that pragmatic reasons for donation (overproduction, pain, recommendation of a health care professional) are often the initial motivation for donors. Contact with the milk bank and additional information about the purpose and destination of donor milk can encourage altruistic reasons for donation (helping others).

The extensive literature on motivation for blood donation offers insight into the interplay between what we have termed “pragmatic” and “altruistic” reasons for breast milk donation. For example, treatment for patients with hemochromatosis – an inherited disease in which too much iron accumulates in the body, leading to organ dysfunction and potentially fatal consequences like hepatic cirrhosis – includes therapeutic phlebotomy to rid the body of excess iron.\textsuperscript{146} This is akin to women donating excess
Voluntary blood donation, however, at first appears more altruistic than does milk donation in the context we describe in this article; there are far fewer people with hemochromatosis than there are blood donors who donate for other reasons. Indeed, Richard Titmuss argued in his seminal work *The Gift Relationship: From Human Blood to Social Policy* that blood donation is a unique form of giving—what he terms “creative altruism”—because it is a gift exchange that occurs between complete strangers and in which there is no expectation that the giver receive a gift in return. In addition, blood donation can be painful to the donor, and the blood itself is quickly replenished by the donor but may be life-sustaining to the recipient. The same can be said of the model of breast milk donation described in this paper, with the caveat that several non-donors feared that they would lack sufficient milk to feed their infants if they were to donate milk. This reluctance may constitute a unique barrier to breast milk donation. Titmuss also contends that blood donation is perhaps the closest thing to a free human gift, one that spurs community cohesion in pursuit of the common good for society at large, and he argues against a market-driven blood-banking model that could endanger the “creative altruism” of voluntary blood donors.

Despite the emphasis on altruism, Titmuss and many others have questioned whether voluntary blood donation is truly an altruistic act. Rapport and Maggs note that Titmuss himself conceded that there is no such thing as a purely altruistic act; rather, donors are carrying out an act of “self-love” in giving blood to anonymous others. Andreoni refers to this as “impure altruism” or “warm-glow” giving in his economic assessment of donor behavior, arguing that people help other people at least partially because it is personally rewarding. Ferguson et al. extend this idea to blood donation by categorizing benefits to the blood donor as an “emotional warm glow” experienced after donation. They conclude that blood donation is an act of benevolence, not altruism, with benevolence defined as a situation in which both the donor and the recipient benefit from the act of donation. A meta-analysis of self-reported reasons for blood donation found that donors cited altruistic and collectivist motivations (helping others, helping the community), as well as what they termed “indirect reciprocity”—including improved self-esteem, motivation to help someone else after having received donor blood in the past, and a belief that donating now increases one’s chances of receiving help in the future if needed.

The findings here suggest that breast milk donation might also be classified as an act of benevolence rather than one of true altruism. Multiple donors expressed sentiments akin to “warm glow”: they felt better about themselves as a result of donation, and they believed that their donation was instrumental to the health and wellbeing of at-risk infants. In addition, many women also invoked the notion of reciprocity (“I would want someone to donate milk if I needed it”) at the same time that
they expressed altruistic motivations. The initial impetus to donate — to relieve pain or discomfort — further supports the notion that milk donation offers tangible benefits to both the donor and the recipient. Furthermore, milk donation allows mothers of hospitalized infants to give milk directly to their own children — another self-serving aspect to milk donation that can offer a “warm glow” of another sort (being able to provide sustenance to one’s child, even under difficult circumstances).

Lee et al. proposed that the “high cost” of blood donation — anxiety, fear, and pain — may explain differences in donor behavior among people who donate time, money, and blood. They suggest that blood donors may possess internal, even moral, reasons to donate, which allow them to overcome initial fear of donation. Many participants in this study — donors and non-donors alike — expressed fear of donation, specifically fear of experiencing pain when expressing milk. For many donors, overcoming that fear of pain and other uncertainties associated with donation was integral to the decision to donate breast milk.

But there is an additional layer to the relationship between pain and breast milk donation: Donors in this study indicated that donating excess milk relieved pain associated with engorged breasts. Thus, milk donation may be associated with “high costs,” like blood donation, but it may also lead to “high rewards.” Recruitment campaigns that target these “benevolent” aspects of milk donation — focusing on how donation benefits both the donor mother and the recipient child — may be more successful than campaigns targeting altruism alone, as has been suggested in the blood donation literature.

Policy and Health Implications

Our proposed model of breast milk donation includes the “contemplative phase,” which contains potential deterrents that may reduce a woman’s likelihood of donating. Several non-donors in this study identified fear of pain and concern about inadequate milk supply as deterrents to donation; many non-donors had not visited the milk bank or learned about the utility of donor milk in the hospital. In their meta-analysis of motivations and deterrents for blood donation, Bednall and Boyce found that some non-donors believed they did not have sufficient blood, they were unaware of the need for blood and did not know where the donation site was, and they expressed fear of needles or physical injury associated with donation. Educational campaigns that address these fears and uncertainties, as well as that focus on the role the milk bank has in breastfeeding promotion, may be effective in increasing awareness about donation and utilization of milk banks.

Conversely, factors that seemed to enable donation in the contemplative phase were breast engorgement and encouragement of health care professionals. Therefore, a critical driver in breast milk donation is excess milk production — something that all of the donors to other children experienced, while none of the non-donors reported
overproduction. That not all women will experience excess milk production seems likely to limit the amount of donor breast milk collected. The role of health care professionals in encouraging breast milk donation should be considered an important aspect of a strategy to promote breast milk donation among new mothers.

Finally, participants – donors and non-donors alike – identified the milk bank as a “hub” of breastfeeding promotion and education within the hospital. Indeed, milk bank employees appear to serve as on-site “lactation consultants,” in that they provide women assistance and education about breastfeeding.154 In this study, the bank was a critical aspect of a hospital-wide effort to encourage exclusive breastfeeding among new mothers, suggesting that a milk bank can be utilized as part of the breastfeeding promotion strategies of a Baby-Friendly Hospital. Furthermore, previous donors and users of milk banks could be utilized as community health workers to educate pregnant women about the role of milk banks in the hospital, as well as to teach women where to go if they have early difficulties with breastfeeding. Strengthening connections between milk collection units, communities with primary care posts that do not have collection units, and larger milk banks could improve women’s knowledge about milk donation and spur donation efforts. This strategy could increase knowledge about donation among new mothers who are not in the hospital, facilitating “outside donations” either by way of a local milk collection unit or a visit to a nearby hospital with a milk bank.

Limitations

Several limitations to this study make generalizability difficult, even within Brazil. It is a small qualitative study carried out in a Baby-Friendly Hospital with an on-site milk bank, meaning there were fewer barriers to donation and breastfeeding initiation than there would have been in a community setting in Rio de Janeiro or elsewhere. Furthermore, Brazil has an extensive, entrenched network of human milk banks that are supported by the national health care system1, and thus it is difficult to extrapolate these results to other countries and health care systems where the reality can be very different. It is important, however, to use Brazil as a case study for how milk banking can be utilized to promote breastfeeding. In addition, all women in the study completed prenatal care, with an average of greater than six visits. Some women reported learning about breastfeeding and infant nutrition during prenatal care, and all women displayed knowledge of the importance of breastfeeding during infancy. In addition, all women delivered their infants in a maternity hospital setting, and all received post-partum care from doctors, nutritionists, and nurses. Thus, these results may not apply to other populations, particularly those in which women do not have access to or complete prenatal care, and in which breastfeeding education is more limited.
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