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Randomized Trial of Donor Human Milk Versus Preterm Formula as Substitutes for Mothers' Own Milk in the Feeding of Extremely Premature Infants

Richard J. Schanler, MD*‡; Chantal Lau, PhD§; Nancy M. Hurst, MSN‖; and Elliot O'Brian Smith, PhD¶

ABSTRACT. *Objective.* **Compared with preterm formula (PF), mother's milk (MM) is associated with lower rates of late-onset sepsis (LOS) and necrotizing enterocolitis (NEC) among premature infants. Because not all mothers of premature infants produce sufficient milk to supply their infants throughout hospitalization, we reasoned that pasteurized donor human milk (DM) would be a suitable alternative.**

Methods. **Extremely premature infants (<30 weeks of gestation) whose mothers intended to breastfeed were assigned randomly to receive either pasteurized DM or PF if the supply of their own MM became insufficient during the study (birth to 90 days of age or hospital discharge). Infection-related events (LOS, NEC, meningitis, presumed sepsis, or urinary tract infection) that occurred after the attainment of a milk intake of 50 mL/kg, dietary intake, growth, skin-to-skin contact, and duration of hospital stay were compared. The primary analysis compared groups DM and PF on an intent-to-treat basis. If no differences were noted, then these groups were combined and compared with the reference group, group MM. If differences were noted, then the subsequent analyses compared each group with group MM.**

Results. **Of 243 infants, 70 (29%) received only MM; group DM included 81 infants and group PF included 92 infants. Because of poor weight gain, 17 infants (21%), all in group DM, were switched to PF. There were no differences in birth weight, gestational age, multiple births, and age at attainment of feeding of 50 mL/kg among groups. There were no differences between group DM and group PF in LOS and/or NEC, other infection-related events, hospital stay, or number of deaths. Group DM received a greater intake of milk and more nutritional supplements but had a slower rate of weight gain, compared with group PF. Compared with groups DM and PF, group MM had fewer episodes of LOS and/or NEC and total infection-related events and a shorter duration of hospital stay. Group MM also had fewer Gram-negative organisms isolated from blood cultures than did the other groups.**

Conclusions. **In this randomized, blinded trial of feeding of extremely premature infants, we found that, as a substitute for MM, DM offered little observed short-term advantage over PF for feeding extremely premature infants. Advantages to an exclusive diet of MM were observed in terms of fewer infection-related events and shorter hospital stays.** *Pediatrics* **2005;116:400–406;** ***human milk, pasteurized human donor milk, premature infant feeding.***

ABBREVIATIONS. DM, donor human milk; PF, preterm formula; MM, mother's milk; LOS, late-onset sepsis; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; OR, odds ratio; CI, confidence interval.

In a previous study of the time of initiation and method of feeding for premature infants, the benefits observed were overshadowed by the type of milk fed (mother's milk [MM] versus preterm formula [PF]).[1] The more human milk consumed, the lower were the rates of late-onset sepsis (LOS) and necrotizing enterocolitis (NEC) and the shorter was the hospitalization.[2] Because not all mothers were able to supply sufficient milk to meet their premature infants' needs throughout the hospitalization, many infants received PF. We reasoned that, if the MM supply is inadequate, then pasteurized donor human milk (DM) might be substituted for PF, to preserve the protective effects of MM. The objective of this study was to compare the incidence of LOS and/or NEC, the duration of hospitalization, and the growth of extremely premature infants assigned randomly to receive either pasteurized DM or PF if the supply of their own MM was inadequate.

METHODS

Study Design

Study infants whose mothers expected to breastfeed were enrolled within 4 days after birth, stratified according to gestational age (23–26 vs 27–29 weeks) and receipt of prenatal steroids, and assigned randomly to receive either pasteurized human DM or PF if their own MM was unavailable during hospitalization. The study groups were defined on the basis of whether the infants received their MM partially (with either DM [group DM] or PF [group PF]) or exclusively (group MM). Caregivers were blind to group assignment. The major outcome was the incidence of LOS and/or NEC, comparing groups DM and PF, with group MM as

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a reference. The duration of the study was from enrollment at 4 days to 90 days of age or discharge from the hospital, whichever occurred sooner. Data on daily milk intake, growth, duration of hospitalization, parental involvement through visiting and skin-to-skin contact, incidence of infection-related events (LOS, NEC, presumed sepsis, meningitis, urinary tract infection), and death were collected.

A nutrition support protocol was used to ensure that milk advancement and use of parenteral nutrition were consistent for all study infants.[3] Administration of small quantities of MM (~20 mL/kg per day) was initiated in the first week after birth and continued for ~3 to 5 days before the volume was advanced.[1] Milk intake was increased by ~20 mL/kg daily to 100 mL/kg, at which time human milk fortifier (Enfamil Human Milk Fortifier; Mead Johnson Nutritional Division, Evansville, IN; or, after February 2000, Similac Human Milk Fortifier; Ross Laboratories, Columbus, OH) was added. Subsequently, the volume of fortified human milk (4 packets per 100 mL of human milk) was advanced by 20 mL/kg daily until 160 mL/kg per day was achieved. If no MM was available and the infant was assigned to the DM group, then a similar advancement and fortification protocol was followed with DM. If the infant was assigned to the PF group, then Enfamil Premature Formula (100 kJ/oz; Mead Johnson Nutritional Division, Evansville, IN) was used, and the same volume increments were followed. For the first 2 days, the PF group received half-strength PF. For all infants, after complete enteral tube feeding was achieved, adjustments in milk intake between 160 and 200 mL/kg per day were recommended by dietitians, to ensure an average weekly weight gain of ≥15 g/kg per day. The criteria for hospital discharge were uniform, ie, satisfactory weight gain while receiving full oral feeding, maintenance of adequate thermal stability, and resolution of acute medical conditions.

Each mother supplied milk only for her infant (MM). A milk bank is operated at Texas Children's Hospital exclusively for this purpose.[4] To provide quality control, milk was received from mothers and stored, prepared, and distributed daily to the nurseries through this bank. Milk was cultured initially for routine bacterial pathogens, and medical, medication, and habit histories were obtained from mothers. The milk bank prepared all syringes of milk for study infants (MM, DM, and/or PF). Lactation counselors from the Texas Children's Hospital Lactation Program routinely instructed mothers regarding the mechanical expression of milk and methods for milk supply maintenance and collection, storage, and transport of milk. Lactation management was similar among the study groups.

The DM was purchased (approximately $3.50/oz) from the Mother's Milk Bank, Presbyterian/St Luke's Medical Center (Denver, CO), and the Lactation Center and Mother's Milk Bank, WakeMed (Raleigh, NC). The milk banks followed the recommendations for donor screening and for milk collection and storage published by the Human Milk Banking Association of North America.[5] All DM was obtained from mothers of premature infants, passed the screening process, and was subjected to the classical Holder pasteurization process (62.5°C for 30 minutes).[6,7] DM was cultured for bacterial pathogens; sterile milk was frozen at −20°C until used.

Study Population

A total of 243 extremely premature infants (23–29 weeks of gestation) from the nurseries of Texas Children's Hospital were recruited between August 1997 and July 2001 because their mothers intended to breastfeed. Infants were considered protocol violators if they were unable to adhere to the enteral nutrition support protocol for >1 week, but the infants remained in the groups to which they were assigned originally.

The proposed sample size for the study was based on our original data, which indicated that the incidence of LOS and/or NEC was 30% among infants receiving predominantly fortified MM, compared with 55% among infants receiving either a mixture of fortified MM and PF or PF only.[2] Therefore, 70 infants per group were needed to detect this difference in LOS and/or NEC. The calculation was based on a type I error of .05 and a power of 0.80. Final group determination was made at the end of the study, on the basis of whether the participants had received the assigned supplement (DM or PF). Therefore, enrollment continued until group MM had 70 infants. Infants at <30 weeks of gestation at birth were enrolled because this group has the highest incidence of LOS and/or NEC.[8] Randomization was performed by the research nurse coordinator with sealed opaque envelopes grouped, in an unbalanced blocked design, according to the stratification variables of gestational age and receipt of prenatal steroids. The study was approved by the Baylor Institutional Review Board for Human Subject Research. Informed written consent was obtained from parents before enrollment.

Outcome Measures

LOS was defined as occurring ≥5 days after birth and included clinical signs and symptoms consistent with sepsis in association with the isolation of a causative organism from a culture of blood obtained from a peripheral vein.[9] In addition, all cases of LOS had documentation of treatment with antibiotics for ≥7 days. A diagnosis of presumed sepsis was made if the clinical presentation and treatment plan were the same but no organism was isolated from the blood culture. Infection at other sites, including cerebrospinal fluid and urine (obtained through bladder puncture or sterile catheterization), was recorded. NEC was defined as clinical signs with the presence of pneumatosis intestinalis on abdominal radiographs (Bell stage II).[8,10] Abdominal radiograph diagnoses were corroborated by the investigator and a radiologist. NEC was treated with antibiotic therapy for ≥10 days and orogastric decompression for ≥5 days. Body weight was measured at the same time each day, with electronic scales. Head circumference and crown-heel length were measured every 2 weeks, with methods published previously.[1]

Data Analyses

The primary analysis, addressing the incidence of LOS and/or NEC, compared groups DM and PF on an intent-to-treat basis. Because we sought to relate this outcome to milk exposure, only cases of LOS and/or NEC that occurred after the infant attained a milk intake of ≥50 mL/kg were analyzed for the primary outcome. If no differences were noted, then these groups were combined and compared with the reference group, group MM. If differences were noted, then the subsequent analyses compared each group with the reference group, group MM. Any variables with baseline differences were treated as covariates in the analyses. Skewed data (eg, length and head circumference) were logarithmically transformed before analyses. The χ^2 test, Fisher's exact test, and logistic regression analysis were used to test for differences in categorical variables, and analysis of variance and linear regression analysis were used for continuous variables. Data are expressed as mean ± SD.

RESULTS

Of 243 infants enrolled, 7 were never fed but remained in the study group to which they were assigned (Table 1). At the discretion of the attending physician and in consultation with the principal investigator, 17 infants (21%), all in group DM, were switched to PF because of poor weight gain. Nevertheless, all infants remained in their originally assigned group for analyses. There were no differences in birth weight, gestation, number of infants with gestational age of <27 weeks, gender, incidence of multiple births, 5-minute Apgar scores of <7, intraventricular hemorrhage, patent ductus arteriosus, and duration of parenteral nutrition between group DM and group PF or between these groups and reference group MM. Because differences in the receipt of prenatal steroids were noted, this variable was used as a covariate in the analyses of study outcomes (Table 1).

Study infants fed ≥50 mL/kg of milk had an overall incidence of LOS and/or NEC of 36% and a rate of all infection-related events of 44%. No differences between group DM and group PF for any infection-related event or death were noted either after the study infants attained a milk intake of ≥50 mL/kg

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TABLE 1. Characteristics of Study Infants

	Group DM (n = 81)	Group PF (n = 92)	Group MM (n = 70)	Group DM Versus Group PF, P	Group MM Versus Combined Groups DM and PF, P
Birth weight, g, mean ± SD	947 ± 233	957 ± 267	999 ± 259	.76	.31
Gestational age, wk	27 ± 2	27 ± 2	27 ± 2	.99	.23
Receipt of prenatal steroids, n (%)	62 (77)	76 (83)	66 (94)	.43	.011
Male gender, n (%)	46 (57)	46 (50)	35 (50)	.32	.61
Apgar score at 5 min of <7, n (%)	14 (17)	22 (24)	9 (13)	.31	.12
Mechanical ventilation, d	14 ± 14	19 ± 24	12 ± 15	.076	.10
Chronic lung disease, n (%)	12 (15)	25 (28)	9 (13)	.048	*
Duration of central venous catheter use, d	24 ± 18	24 ± 18	21 ± 15	.97	.46
Age achieved feeding of ≥50 mL/kg, d	18 ± 10	18 ± 11	16 ± 8	.77	.21
Hospital stay, d	87 ± 53	90 ± 56	75 ± 37	.66	.04

* Group MM versus group DM versus group PF: P = .013 (group MM versus group DM: P = .42; group MM versus group PF: P = .044).

(Table 2) or throughout the entire study. With respect to infection-related events, however, groups DM and PF differed significantly from reference group MM. Overall, fewer infection-related events were found in group MM (Table 2). Compared with groups DM and PF, group MM had significantly fewer LOS episodes (odds ratio [OR]: 0.47; 95% confidence interval [CI]: 0.25–0.90). Group MM also had fewer repeat LOS episodes (OR: 0.45; 95% CI: 0.24–0.86) and repeat episodes of LOS and/or NEC (OR: 0.18; 95% CI: 0.04–0.79). The number of episodes of LOS and/or NEC, as well as all infection-related events, were correlated negatively with the cumulative intake of MM (r = −0.1 to −0.2; P < .02). No such associations between infection-related events and the intake of DM or PF were observed. LOS also correlated positively and independently with the duration of parenteral nutrition (r = 0.4; P < .001), the time to attain full tube feeding (r = 0.4; P < .001), the time to attain complete oral feeding (r = 0.2; P < .01), the duration of mechanical ventilation (r = 0.2; P < .01), and the use of central venous catheters (r = 0.3; P < .01).

Pathogens isolated from blood cultures were similar for groups DM and PF (Table 3). Significantly fewer pathogens, especially Gram-negative organisms, were isolated for group MM, compared with the other groups.

There was a significant difference in the incidence of chronic lung disease (oxygen need at postmenstrual age of 36 weeks) between group DM and group PF (Table 1). Chronic lung disease, however, did not affect the relationships among groups when used as a covariate in the analyses of study outcomes. There were differences in the highest stage of retinopathy of prematurity (ROP) attained during hospitalization. Group MM (median: stage 1 ROP) did not attain as high a stage of ROP, compared with group DM (median: stage 2 ROP) and group PF (median: stage 1 ROP) (P = .04). ROP stage 3 was noted less frequently in group MM (5.6%) than in group DM (19%) or group PF (14%) (OR: 0.29; 95% CI: 0.08–1.0; P = .05). There were no significant differences in the numbers of infants who required ROP surgery during hospitalization.

The cumulative amounts of MM received throughout the study in group DM (2.4 ± 2.7 L/kg) and group PF (2.8 ± 2.9 L/kg) were similar (P = .38). By design, group MM received significantly more MM (5.6 ± 3.1 L/kg) than did groups DM and PF (P = .001). Average milk intake differed between group DM and group PF (166 ± 10 and 159 ± 11 mL/kg per day, respectively; P < .001) and in comparison with group MM (162 ± mL/kg per day; P < .001). There were no differences among groups in the type of

TABLE 2. Infection-Related Events Among Study Infants Who Received ≥50 mL/kg of Milk

	Group DM (n = 78)	Group PF (n = 88)	Group MM (n = 70)	Group DM Versus Group PF, P	Group MM Versus Combined Groups DM and PF, P
LOS, n (%)				.97	.022
1 episode	23 (29)	26 (30)	16 (23)		
>1 episode*	7 (9)	7 (8)	1 (1)		
NEC, n (%)	5 (6)	10 (11)	4 (6)	.27	.39
Meningitis, n (%)	3 (4)	6 (7)	4 (6)	.50	.90
Presumed sepsis, n (%)	3 (4)	5 (6)	1 (1)	.72	.29
Urinary tract infection, n (%)	7 (9)	9 (10)	4 (6)	.79	.59
LOS and/or NEC, n (%)				.42	.034
1 episode	23 (29)	20 (23)	18 (26)		
>1 episode†	8 (10)	14 (16)	2 (3)		
Death, n (%)	3 (4)	3 (3)	2 (3)	.88	.77
Sum of death and/or infection-related events, cases per 100 infants	77 ± 103	85 ± 111	47 ± 70	.62	.012

* Group MM significantly lower than groups DM and PF (OR: 0.45; 95% CI: 0.24–0.86): P = .015.
† Group MM significantly lower than groups DM and PF (OR: 0.18; 95% CI: 0.04–0.79): P = .023.

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TABLE 3. Bacterial and Fungal Isolates From Blood Among Study Infants

	Group DM (n = 78)	Group PF (n = 88)	Group MM (n = 70)	Group MM Versus Combined Groups DM and PF, P
Gram-positive, n (%)	38 (49)	44 (50)	27 (39)	.083
Coagulase-negative *Staphylococcus*, n (%)	21 (27)	23 (26)	17 (24)	
Enterococcus sp, n (%)	3 (4)	9 (10)	5 (7)	
Staphylococcus aureus, n (%)	8 (10)	3 (3)	2 (3)	
Staphylococcus epidermidis, n (%)	6 (8)	9 (10)	3 (4)	
Gram-negative, n (%)	11 (14)	19 (22)	4 (6)	.008
Citrobacter sp, n (%)	1 (1)	1 (1)	0	
Enterobacter sp, n (%)	0	3 (3)	1 (1)	
Escherichia coli, n (%)	5 (6)	5 (6)	1 (1)	
Klebsiella sp, n (%)	4 (5)	7 (8)	1 (1)	
Pseudomonas sp, n (%)	0	2 (2)	0	
Serratia sp, n (%)	1 (1)	1 (1)	1 (1)	
Candida sp, n (%)	3 (4)	2 (2)	1 (1)	.425
All pathogens, n (%)	34 (44)	37 (42)	20 (29)	.028

human milk fortifier used throughout the study. Group DM received more acetate (41% vs 22% of infants; P = .002) and sodium (70% vs 52%; P = .014) supplements than did group PF. Fewer energy supplements (oil, protein, and/or glucose polymers) were given to group MM (33% infants) than to group DM (59%) or group PF (50%) (P = .002). Differences in growth were noted among groups (Table 4). The rates of weight gain differed between group DM and group PF, and rates also differed when each group was compared with group MM. There were no differences among groups in head circumference gain. Groups DM and PF had similar increments in crown-heel length, but the increment was significantly less in group MM (Table 4). The duration of hospitalization did not differ between group DM and group PF but was significantly shorter (by 1 week) for group MM (Table 1). The duration of hospital stay was significantly related positively to the presence of LOS and/or NEC and negatively to gestational age and birth weight, which together accounted for 21% of the variability in hospital stay.

There were differences in social characteristics among groups for the 187 mothers (Table 5). There was a progression in maternal age, marital status, family income, and educational attainment from group DM to group PF to group MM. LOS and NEC were not associated with maternal demographic factors. Differences were observed in parent-infant interaction, such as skin-to-skin contact (Table 5). Skin-to-skin contact was correlated positively (r = 0.47; $P < .001$) with intake of MM, negatively with PF ($r = -0.25$; $P < .001$), and not with DM ($r = -0.08$; P = .18). Skin-to-skin contact was not correlated with the number of infection-related events.

DISCUSSION

The protective effects of human milk benefit premature infants through lower rates of LOS, NEC, urinary tract infection, diarrhea, and upper respiratory tract symptoms, compared with feeding formula.[2,8,11–14] In most cases, the protective effects are associated with partial, and not necessarily exclusive, feeding of human milk; usually, this milk is given early in the postnatal period, before any formula is received.[2,8] Moreover, some of the beneficial effects are observed among infants partially fed DM.[8,15] Increased awareness of the protection afforded premature infants through feeding with human milk led to reconsideration of the use of pasteurized DM if MM milk is unavailable.[16] This seems to be a rational consideration, because many mothers are unable to

TABLE 4. Growth Parameters

	Group DM (n = 78)	Group PF (n = 88)	Group MM (n = 70)	Group DM Versus Group PF, P	Group MM Versus Combined Groups DM and PF, P
Weight gain for entire study, g/kg per d	17.1 ± 5.0	20.1 ± 6.7	18.8 ± 5.8	.001	*
Weight gain from 150 mL/kg per d to end of study, g/kg per d	18.1 ± 5.1	20.7 ± 7.1	19.7 ± 5.9	.011	†
Head circumference increment for entire study, cm/wk	0.9 ± 0.9	0.9 ± 0.8	0.8 ± 0.5	.91	.42
Head circumference increment from 150 mL/kg per d to end of study, cm/wk	0.9 ± 0.5	0.9 ± 0.5	0.7 ± 0.5	.68	.13
Length increment for entire study, cm/wk	1.2 ± 0.8	1.0 ± 1.0	0.6 ± 0.4	.59	.03
Length increment from 150 mL/kg per d to end of study, cm/wk	1.0 ± 0.4	1.3 ± 0.9	0.6 ± 0.4	.29	.03

Values are mean ± SD.
* Group MM versus group DM versus group PF: P = .005; group MM versus group PF: P = .19; group MM versus group DM: P = .07.
† Group MM versus group DM versus group PF: P = .03; group MM versus group PF: P = .36; group MM versus group DM: P = .10.

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TABLE 5. Social Characteristics

	Group DM	Group PF	Group MM	Group DM Versus Groups PF, *P*	Group MM Versus Combined Groups DM and PF, *P*
	n = 65*	*n* = 72*	*n* = 50*		
Maternal age, y, mean ± SD	25.4 ± 6.8	29.0 ± 7.1	30.2 ± 5.9	.006	†
Single head of household, *n* (%)	23 (35)	10 (14)	3 (6)	.003	‡
Mother attended college, *n* (%)	24 (37)	33 (46)	30 (60)	.29	.026
Household income of >$100,000, *n* (%)	2 (3)	2 (4)	6 (12)	.73	.032
	n = 78§	*n* = 88§	*n* = 70§		
Parents visit >50% of hospital stay, *n* (%)	51 (65)	63 (72)	69 (98)	.33	<.001
Skin-to-skin contact					
Mother, *n* (%)	56 (69)	60 (65)	65 (93)	.58	<.001
Father, *n* (%)	21 (26)	22 (24)	33 (47)	.79	.001
Episodes of maternal skin-to-skin contact, *n*, mean ± SD	5.0 ± 7.5	5.2 ± 7.7	11.6 ± 12.6	.87	<.001
Duration of maternal skin-to-skin contact, min, mean ± SD	318 ± 673	349 ± 596	962 ± 1452	.75	<.001

* Mothers.
† Group MM versus group DM versus group PF: $P = .001$; group MM versus group PF: $P = .37$; group MM versus group DM: $P = <.001$.
‡ Group MM versus group DM versus PF: $P < .001$; group MM versus group PF: $P = .17$; group MM versus group DM: $P = <.001$.
§ Infants.

provide sufficient milk for their premature infants. Indeed, the current study found that only 27% of mothers were able to sustain their lactation to meet the needs of their extremely premature infants. However, few contemporary studies have identified beneficial effects of DM, compared with either MM or PF. Previous reports suggested that DM was nutritionally inferior and led to slower growth and more abnormalities in bone mineral metabolism.[17–20] In contrast, data summarized from earlier reports suggested that, compared with formula, DM feeding was associated with a lower relative risk of NEC, albeit with borderline statistical significance.[15] Therefore, in the era of human milk fortification and close monitoring of nutritional status for the increasingly large population of extremely premature infants, a comparison of DM and PF is warranted.

In this randomized blinded trial of feeding of extremely premature infants, we found that infants fed DM had similar rates of LOS, NEC, and other infection-related events, compared with infants fed PF. In addition, despite receiving greater milk intakes and more nutritional supplements in attempts to meet targeted rates of weight gain, infants fed DM had lesser gains in weight, and significantly more of these infants were switched to a PF diet because of poor weight gain. Therefore, as a substitute for MM, DM offered no observed short-term advantage over PF for feeding of extremely premature infants.

The overall incidence of LOS and/or NEC was less than the 50% expected from our previous study, perhaps because of changes in neonatal care since our last study.[2] Factors that affected LOS rates were evenly distributed among the study groups.[21,22] There were no differences between group DM and group PF in birth weight, gestational age, duration of mechanical ventilation, use of central venous lines, parenteral nutrition, or achievement of full feedings. The fact that these factors were similar among groups is partly a result of our study design, which focused the investigation on a relatively homogeneous population of infants. We also chose to evaluate infants after they had received a specific cumulative dose of milk (≥50 mL/kg), in an attempt to control for the confounding observation that extremely premature infants who are ill do not receive feedings as readily as healthier, more mature infants. Although the ages at achievement of this 50-mL/kg milestone were similar among the groups, use of this milestone strengthens the relationship between diet and infection-related events.

The current study also confirms and expands on our previous observations that premature infants fed their own MM have lower rates of LOS and/or NEC, compared with those fed PF. This study details the advantages of exclusive MM feeding, compared with earlier studies depicting the advantages of predominantly MM feeding.[2,11,12] Importantly, LOS and/or NEC and the sum of other infection-related events were correlated negatively with the quantity of MM fed but not with the quantity of DM or PF. This observation suggests a dose-response relationship. Because groups DM and PF received ~50% of their milk as MM, it seems that a greater dose of MM is needed to enhance protection of extremely premature infants. Because substitutes for MM are not optimal, the data suggest that alternative strategies should be sought to enhance MM production, to provide an adequate supply throughout hospitalization. Creating such a strategy is a major endeavor, and supportive data on which to base such a plan are limited.[23,24] Indeed, when groups DM and PF were compared with group MM, significant social differences were noted. Group MM mothers were older, were more educated, had a higher income, visited the nursery more often, and practiced skin-to-skin contact with their infants more frequently. These observations suggest that social factors may affect infant outcomes, either by enhancing maternal mo-

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tivation to provide milk or through other, as-yet-unidentified mechanisms.

Some but significantly less chronic lung disease was observed in groups MM and DM, and less ROP was observed in group MM. These observations suggest antioxidant protection from MM, protection that may remain despite pasteurization. Although this study was not designed to evaluate these observations as primary outcomes, additional studies in this area are warranted, to determine whether presumed antioxidant protection is a short-term outcome of feeding human milk.

It is a concern that DM conferred little short-term protective advantage to extremely premature infants. DM usually is obtained from women who delivered term infants, late in lactation.[15,25] The milk is low in protein content because of these characteristics and is also low in fat and total energy contents because of the losses that result from the collection, preparation, and processing.[25] To eliminate some of the nutritional concerns, this study specifically used DM obtained from women who delivered prematurely and DM was fortified in the same way as MM. However, the process of pasteurization reduces the content and function of several host defense proteins and cellular elements.[26,27] To compensate for nutritional limitations of DM, some investigators devised an elaborate protocol to prepare "high-concentration" DM.[25] A short-time, high-temperature, human milk pasteurization protocol that can provide sterile milk but involves less loss of important bioactive factors was also described.[28] Costs and time are major limitations of these technologies.

Lastly, certain human milk factors, such as long-chain polyunsaturated fatty acids and cytokines (eg, interleukin-10), are not affected by pasteurization.[29,30] The presence of certain milk constituents has been implicated in improved long-term visual and cognitive development among premature infants.[31] Slower neonatal growth may not imply long-term deficits but may be associated with leaner body composition.[32,33] However, we did not investigate long-term outcomes. Therefore, we conclude that beneficial short-term outcomes for extremely premature infants are not supported by the substitution of pasteurized DM for MM.

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"LACTIVISTS" TAKE THEIR CAUSE, AND THEIR BABIES, TO THE STREETS

"The calls for a 'nurse-in' began on the Internet mere moments after Barbara Walters uttered a negative remark about public breast-feeding on her ABC talk show, 'The View.' . . . The protest, inspired by similar events organized by a growing group of unlikely activists nationwide in the last year, brought about 200 women to ABC's headquarters yesterday. They stood nursing their babies in the unmistakably public venue of Columbus Avenue and West 67th Street. They held signs reading, 'Shame on View,' and 'Babies are born to be breastfed.' Ms. Walters, who remarked a few weeks ago on the show that the sight of a woman breast-feeding on an airplane next to her had made her uncomfortable, said through a spokesman that 'it was a particular circumstance and we are surprised that it warrants a protest.' . . . But the rally at ABC is only the most visible example of a recent wave of 'lactivism.' Prodded by mothers who say they are tired of being asked to adjourn to the bathroom while nursing in a public space, six states have recently passed laws giving a woman the right to breast-feed wherever she 'is otherwise authorized to be.' . . . In interviews and Internet discussions, hundreds of women recount being asked to stop nursing in public spots, . . . [b]ut the new generation of lactivists compare discomfort with seeing breast-feeding in public to discomfort with seeing interracial couples or gays holding hands. . . . 'It's like any other prejudice. They have to get used to it,' said Rebecca Odes, co-founder of 'The New Mom' blog, who attended the ABC protest."

Harmon A. *New York Times.* June 7, 2005

Noted by JFL, MD

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Randomized Trial of Donor Human Milk Versus Preterm Formula as Substitutes for Mothers' Own Milk in the Feeding of Extremely Premature Infants

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