NICU Practices that Impact the Properties of Pumped Human Milk

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Human Milk for Healthy Term Infants

- Human Milk has evolved to ideally grow the human infant, with exception of Vitamin D for some populations
  - High lactose and lipid
  - Low protein

- Compared to other species, the infant is fed frequently because the milk is relatively “dilute”

- Infants consume 600-800 mLs/d during established lactation

- Feeding directly from the breast optimizes adequacy and safety of milk

- Little is known about exclusive bottle feeding of pumped milk in term infants

- The breast has not evolved to meet the volume, nutritional, and milk-removal needs and limitations of premature and other compromised NICU infants

- Infants may consume as little as 1/10th of a mother’s daily milk volume if the mother is producing enough milk to protect lactation over the long-term

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The Mammary Gland is a Body Organ with Marked Within-and Between Mother Variability

The Two Breasts are Independent Organs, not really a “Matched Pair”

This marked variability is inconsistent with NICU attempts to standardize and default to an “average”

Human milk is 20 calories per ounce.

No problem! Let’s add fortifier and make it 24 or 28 calories!
“Default” Caloric Values for Pumped Human Milk do not Reflect the Evidence About Within and Between-Mother Differences

The Reality
- MOM varies with the stage of lactation:
  - Colostrum and transitional MOM are completely different from mature MOM in composition, including electrolytes
  - MOM composition varies from the beginning to the end of a pumping, with calories increasing as much as 3-fold
  - MOM composition varies according to the fullness of the breast at the time of pumping
  - Pumped MOM varied from 14.3 to 43.9 calories/ounce
- Just because something is “in the MOM” doesn’t mean that it is there for the infant

Optimizing Mothers’ Own Milk Feedings for NICU Infants

Human Milk Feedings in the Neonatal Intensive Care Unit
Paula P. Meier
d, Maha L. Patel, Harold B. Higgins, Yvonne Cheek, Tricia J. Johnson, Beverly Rozman

Evidence-Based Methods That Promote Human Milk Feeding of Preterm Infants
An Expert Review

Diet and Nutrition in Critical Care, 2015
Clinics in Perinatology, 2017
Prioritizing NICU Practices that Optimize the Quality and Safety of MOM

- Target early colostrum feeding of own mothers’ milk
- Implement storage, handling, fortification and feeding practices that optimize human milk integrity and minimize contamination
- Implement practices that avoid feeding low-lipid pumped HM


Colostrum is the transition from intrauterine to extrauterine nutrition in all mammals, including the human

- The fetus swallows large amounts of amniotic fluid during the last trimester in pregnancy.
- Amniotic fluid contains large quantities of growth factors and other protective proteins that support the growth, maturation and protection of the GIT.
- Colostrum is more like amniotic fluid than mature milk in composition, and supports the rapid growth, maturation and protection of the GIT.
Distinct Gene Expression at Different Stages of Lactation

- Colostrum
- Transitional Milk
- Mature Milk

Growth Factors Target Enterocytes to Markedly Increase Surface Area and Stimulate Epithelial Cell Migration and Turnover in the GIT

Colostrum Stimulates this Growth and Maturation More Effectively than Mature Human Milk

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Bioactive Proteins are Highest During the Early Lactation Period—Mirror the Biology of the Newborn


Total Protein is Higher in Preterm Milk than Term Milk and Stays High Over 1st Month of Lactation


From Evidence to Practice: Accuracy and Consistency of Messaging for Families

- Special small colostrum container
- Families number pumpings from 1-60
- Bedside nurse quickly identifies the order in which colostrum should be fed to the infant
- Colostrum is fed from first feed through 130 to 150 mL/kg/d
From Evidence to Practice

- Special 11 mL container for colostrum
- Families number pumpings from 1-60
- Bedside nurse quickly identifies the order in which colostrum should be fed to the infant
- Colostrum is fed from first feed through 130 to 150 mL/kg/d

Pilot study that randomly assigned colostrum vs placebo to 12 VLBW infants
- Colostrum infants demonstrated different oral microflora patterns that were different from control infants
- These differences persisted for 48 hours after the intervention ended

Prioritizing NICU Practices that Optimize the Quality and Safety of MOM

- Target early colostrum feeding of own mothers' milk
- Implement storage, handling, fortification and feeding practices that optimize human milk integrity and minimize contamination
- Implement practices that avoid feeding low-lipid pumped HM

All pumped milk fed in the NICU should be stored in industrial freezers that are temperature monitored and tamper-proof.

Table 3
Safe handling of pumped human milk for preterm infant feeding in the neonatal intensive care unit

<table>
<thead>
<tr>
<th>Objective</th>
<th>Best Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Maximize nutritive and bioactive components</td>
<td>- Feed freshly pumped, never-frozen, HM to greatest possible extent</td>
</tr>
<tr>
<td></td>
<td>- Freshly pumped, unfortified HM can be refrigerated for up to 96 h</td>
</tr>
<tr>
<td></td>
<td>- Do not pasteurize mother’s own HM</td>
</tr>
<tr>
<td></td>
<td>- Implement mechanism for identifying pumped colostrum and transitional HM so it can be fed in the order it is pumped during advancement of enteral feedings</td>
</tr>
<tr>
<td></td>
<td>- Alternate colostrum and transitional HM with freshly pumped HM after 72 h postnatal initiation if colostrum and transitional HM collections have been previously frozen</td>
</tr>
<tr>
<td>C. Minimize number of temperature changes (e.g., serial refrigeration)</td>
<td>- Live cells in the milk are destroyed with freezing</td>
</tr>
<tr>
<td></td>
<td>- Thawed frozen milk should be fed within 24 hours after thawing</td>
</tr>
<tr>
<td></td>
<td>- Milk can be refrozen one time</td>
</tr>
<tr>
<td></td>
<td>- Viral load in milk (such as CMV) is reduced, but not destroyed</td>
</tr>
<tr>
<td></td>
<td>- The bioavailability and the concentration of some protective components are reduced</td>
</tr>
<tr>
<td></td>
<td>- Lipase is not inactivated at -20°C, so milk can partially self-digest, giving “sour” odor and taste</td>
</tr>
<tr>
<td></td>
<td>- Milk can be frozen for up to a year</td>
</tr>
</tbody>
</table>

Fresh (Refrigerated) or Frozen Milk

**Fresh**
- Maximally preserves nutritional and bioactive components
- Live cells in the milk phagocytize bacteria and the bacterial colony count in expressed milk decreases over the first several hours
- Can be kept at NICU bedside for 4 hours after expression
- Can be safely fed for 96 hours after expression (per new research) when refrigerated at 4°C (standard nursery refrigeration temperatures)

**Frozen**
- Live cells in the milk are destroyed with freezing
- Thawed frozen milk should be fed within 24 hours after thawing
- Milk can be refrozen one time
- Viral load in milk (such as CMV) is reduced, but not destroyed
- The bioavailability and the concentration of some protective components are reduced
- Lipase is not inactivated at -20°C, so milk can partially self-digest, giving “sour” odor and taste
- Milk can be frozen for up to a year
Magnet for NICU Refrigerators and Freezers

- Summarizes major storage principles for families and staff

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**Refridge**

Refrigerator Storage of Expressed Human Milk in the Neonatal Intensive Care Unit

Meredith Slusser, DO, Chanana N. Grojic, PhD, Debra Polak, RN, Richard M. Clark, PhD, and Richard J. Schorlie, MD

*Journal of Pediatrics* 156: 26-28, 2010

Figure 2. Gram positive bacterial colony counts declined over 96-hour storage (P < 0.05)

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**Refreeze**

Effect of Environmental Conditions on Unpasteurized Donor Human Milk

David J. Rechman, Martin E. Lee, and H. Berry

*Breastfeeding Medicine* 1: 24-26, 2006

**Table 2. Microbial Analysis of Frozen and Thawed Breast Milk**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>CFU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>8°C for 4 hours</td>
<td>8.6 × 10^3</td>
</tr>
<tr>
<td>8°C for 24 hours</td>
<td>3.5 × 10^3</td>
</tr>
<tr>
<td>23°C for 4 hours</td>
<td>1.0 × 10^3</td>
</tr>
<tr>
<td>23°C for 8 hours</td>
<td>3.7 × 10^2</td>
</tr>
<tr>
<td>Repeated freeze-thaw</td>
<td>1.1 × 10^2</td>
</tr>
<tr>
<td>Control</td>
<td>1.1 × 10^2</td>
</tr>
</tbody>
</table>
Refill

Pooling Expressed Breastmilk to Provide a Consistent Feeding Composition for Premature Infants

Bacterial counts among individual samples highly variable
• High bacterial counts (>100,000 cfu/mL occurred more commonly (14.7%) in individual than in pooled (8.6%) samples
• 24-hour pooling of milk reduced nutrient and caloric variability without increasing bacterial counts

Reuse

There are no data that indicate it is unsafe to reuse mothers’ own milk from a bottle when a NICU infant approaches discharge
• In contrast, there are multiple studies indicating that maternal milk bacteria are influenced by the infant’s oral microbiome and the NICU environment
• Refrigeration and rewarming may slightly reduce some bioactive components, but does not make the milk unsafe for feeding.

Prioritizing NICU Practices that Optimize the Quality and Safety of MOM

• Target early colostrum feeding of own mothers’ milk
• Implement storage, handling, fortification and feeding practices that optimize human milk integrity and minimize contamination
• Implement practices that avoid feeding low-lipid pumped HM

Variability in Mature Pumped MOM

• Clinical emphasis is on protein, but MOM protein varies very little within or between mothers. PROTEIN IS LOW
• The primary component in MOM that varies most is lipid, which is 55% of total calories.
• Lactose is the primary osmotic driver of MOM volume, and high-volume producers typically have slightly more lactose as a percentage of calories

Greer et al., J Pediatr 1987; 110: 745-745

Variability in Lipid

• Variability in MOM lipid is not well-understood by clinicians.
• Often thought of as foremilk and hindmilk, with concern about feeding too much lipid.
• In the NICU, multiple practices work to compromise lipid in MOM

J Perinatology 2002
Breastfeeding Medicine, 2006

Evidence-Based Methods That Promote Human Milk Feeding of Preterm Infants

An Expert Review

Table 4: Factors influencing the human milk lipid received by the preterm infant

<table>
<thead>
<tr>
<th>Factor</th>
<th>Impact</th>
<th>Best Practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long intervals between pumpings</td>
<td>Low-low lipid, high lactone HM</td>
<td>If sufficient HM volume, freeze low lipid HM for use after NICU discharge and feed HM collected after shorter interpump intervals</td>
</tr>
<tr>
<td>Long intervals between pumpings</td>
<td>High-low lipid, high lactone HM</td>
<td>HM can be pooled over a 24 h period in the same storage container to decrease this within-mother variability</td>
</tr>
<tr>
<td>Short intervals</td>
<td>Low-low lipid, high lactone HM</td>
<td></td>
</tr>
</tbody>
</table>
In the NICU many MOM intolerance issues can be attributed to high-lactose, low-lipid MOM

- When lipid is low, infants receive a greater proportion of total MOM calories as lactose
- Imbalances between lipid and lactose can manifest in symptoms of enteral feed intolerance
- Mothers are often counseled about their “diet” or are told infants don’t “tolerate” human milk
- Feeding low-lipid MOM is not just about calories but about PUFAs, mucins and other nutritional and bioactive components

How does the interval between pumpings affect MOM lipid and calories?

1.0 = Extent of milk storage capacity, after which milk synthesis stops in the individual breast

Less fullness = higher lipid milk

Reviewed in Kent, J Midwifery and Women’s Health, 2007; 52: 564-570

Slow Weight Gain in a 30-Week Preemie

- A former 24-week infant who is currently 6 weeks old has gained only an average of 5 grams daily over the past 5 days on fortified mothers’ milk
- The neonatologist requests a “consult” about how to continue to feed the mother’s milk and achieve adequate weight gain
Slow Weight Gain in a 30-Week Preemie

- The Mother’s pumping log shows she pumps about 800 mLs of milk each day
- 6 pumpings
- Volume stable for several weeks

Slow Weight Gain in a 30-Week Preemie

- The mother does not pump during the night
- Gets the “most milk” in the morning (250 mLs) and stores it in a 250-mL container
- Pumps every 2-3 hours during the day, removes 70-100 mLs each pumping and stores it in 120 mL containers
- All milk is kept in NICU

Slow Weight Gain in a 30-Week Preemie

- The NICU nurse notes that the 240-mL container holds enough milk for the infant’s entire 24-hour volume requirements
- She chooses to refrigerate and “feed” this 240 mL, and freeze the remaining 5 containers for use later in NICU stay or after discharge
How does the interval between pumpings affect MOM lipid and calories?

1.0 = Extent of milk storage capacity, after which milk synthesis stops in the individual breast

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Reviewed in Kent, J Midwifery and Women’s Health, 2007; 52: 564-570

Slow Weight Gain in a 30-Week Preemie

• The lactation specialist suspects that the early AM milk is low in lipid (and high in lactose)
• Serial creamatocrit measures on milk collected over the course of the day reveal:
  – AM milk = 17 Cal/oz
  – Later milk = 28-31 Cal/oz
• Management Plan:
  Feed milk pumped later in the day and save large containers for use after NICU discharge

Case Study: Slow Weight Gain and Loose Stools in Twins of Mother Taking Atypical Anti-Psychotics

• A set of previous 30-week premature infants is approaching discharge, when one gained weight slowly for 1 week and the other developed loose stools
  • The neonatologist requested a consult to determine if the mothers’ atypical anti-psychotics were causing the symptoms
  • Prior to this time, the infants had grown appropriately
Case Study: Slow Weight Gain and Loose Stools in Twins of Mother Taking Atypical Anti-Psychotics

- An individualized assessment with the mother confirmed the lactation team’s suspicions based on this mother’s lifestyle and milk output patterns.

- The mother had 4 other young children, all of whom had been full-term and breastfed for almost a year.

- Her pumping was erratic due to the children’s schedule

- She pumped >1500 mLs per day at unequal intervals

- The team suspected that these infants were receiving a low-lipid, high-lactose milk and showing symptoms of mild lactose intolerance.

- This suspected diagnosis was based on the fact that:
  - Anti-psychotic medications lower dopamine concentrations, which removes inhibition to prolactin, increasing the milk yield
  - The irregular breast emptying yielding high-volume, low-lipid milk on some occasions during the day

- Creamatocrit measures confirmed this speculation.
- Breast fullness was sporadic due to mother’s schedule—not to overnight sleeping or a single long predictable stretch during the day.
- Mother sorted appropriate milk for the last 2-3 days for her infants and began to prioritize the feeding of milk that was pumped after no longer than 3 hour interval.
- Infants’ problems were corrected.
- Maternal medication was not the cause of the infants’ symptoms, but was related to the high milk output on the part of the mother.
Milk Lipid Content Increases Over the Minutes of Breast Emptying

Lipid globules are released with milk ejection and total lipid increases with duration of breast emptying.

Not Emptying Breasts Thoroughly

Compromises total volume and lipid content.

Pumping Directly into Milk Storage Containers

- Is convenient and may reduce bacterial contamination when compared with transferring milk
- For mothers with more milk in 1 breast than the container holds, there is potential for inadvertent separation of foremilk and hindmilk
- All milk is considered equal at 20 calories per ounce, but is likely closer to 15 and 30 calories per ounce
Fat in the milk has separated during freezing and thawing.

Fat globules adhere to grooves in storage container after milk is thawed.

Fat globules adhere to grooves in storage container lid.

Position of Infusion Syringe

Fat has separated from the aqueous portion of the milk and is not delivered to the infant.
Position of Infusion Syringe

Lipid Loss in Infusion Tubing

Milk lipid adheres to infusion tubing, with greatest loss during slowest continuous gavage feedings


Human Milk Fortifiers Evolved to Concentrate Macro-and Micro-Nutrients into a Feed Volume that is Safe for Premature Infants

Healthy term infants consume 400-1300 mLs/day, but preterm infants are fluid-restricted
More is Better Approach to Fortification

- Addition of large amounts of iron inhibited the antibacterial impact of HM against major microbes
- Iron binds with lactoferrin, a powerful antimicrobial and anti-inflammatory component of HM

**Table 3: Bacterial Growth x 10^7 at 3 Hours**

<table>
<thead>
<tr>
<th></th>
<th>H. c. coli</th>
<th>Staph</th>
<th>GBS</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human milk</td>
<td>32</td>
<td>15.9±6.8</td>
<td>21.5±3.2</td>
<td>31±25</td>
</tr>
<tr>
<td>Human milk+SFHM</td>
<td>20</td>
<td>15.4±3.5</td>
<td>19.5±5.6</td>
<td>20±52</td>
</tr>
<tr>
<td>Human milk+BHM</td>
<td>20</td>
<td>20.5±5.8</td>
<td>30±3.3</td>
<td>6.9±3.5</td>
</tr>
</tbody>
</table>

Pasteurization results in large losses of lactoferrin


Acidification of Liquid HMF

**Table 1. The effects of acidification on HM contents (mean ± s.d.)**

<table>
<thead>
<tr>
<th></th>
<th>Control HM</th>
<th>Acidified HM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>6.8±0.1</td>
<td>4.5±0.1</td>
<td></td>
</tr>
<tr>
<td>White cells, 10^5 ml^-1</td>
<td>14.5±11.9</td>
<td>3.6±5.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Total proteins, g dl^-1</td>
<td>1.3±0.1</td>
<td>1.3±0.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Lipase, UI^-1</td>
<td>22±120</td>
<td>86±98</td>
<td>0.01</td>
</tr>
<tr>
<td>Free fatty acids, μM</td>
<td>8030±3082</td>
<td>6080±2881</td>
<td>0.09</td>
</tr>
<tr>
<td>Creamatocrit, %</td>
<td>5.5±1.6</td>
<td>7.5±1.6</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Abbreviation: HM, human milk.


Dose-Response Relationship Between Amount of Fortifier in HM and Oxidative Stress in VLBW infants

Value is 6-fold higher than normal adult level

Antioxidants are abolished with storage and processing

Summary

• Oftentimes, clinicians report that they do not have the same outcomes of human milk feeding that are reported in the literature.
• Sometimes this is due to NICU practices that compromise the potential impact of human milk on these outcomes.
• The evidence for best practices is available, but not routinely implemented due to cost and/or ideological constraints.
• Of primary importance are:
  – Protecting mothers’ own milk volume through evidence-based practices rather than substituting second-best donor milk and referring to all as “human milk feeding”
  – Prioritizing the collection, storage and early feeding of mothers’ fresh colostrum to the maximum extent
  – Using fresh rather than frozen (or pasteurized) milk
  – Understanding the role of human milk lipid and its variability in pumped human milk
  – Recognizing NICU practices that result the feeding of low-lipid, low-calorie pumped milk
  – Becoming better consumers of human milk fortifiers
  – Recognizing the benefits as well as the inflammatory impact of bovine-based human milk fortifiers

Fecal Calprotectin Concentrations Pre- and Post-Fortification of Human Milk with Bovine Products


Human Milk “Processes and Escorts” Milk-Borne Antigens to the Recipient Infant in Concentrations that are 10,000 Times Lower than in Formula-fed Infants

Verhasselt, 2010

• The milk components that process and escort are reduced or abolished with storage and pasteurization
• Bovine protein (in fortifiers) is an “antigen”