Optimizing Human Milk Nutrition for Growth

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Conflict of Interest Disclosures

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• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation
Optimized steps

• Human milk alone is insufficient for the optimal growth of the preterm infant
  • Use of liquid human milk fortifiers
  • Adjustable fortification strategy
• Developing “current good human milk practice” (CGHMP) guidelines
• Rational use of donor human milk
• Oral colostrum care
Goal of Feeding Preterm Infants

Provide nutrients to approximate the rate of growth and composition of weight gain for a normal fetus of the same post-conceptional age and to maintain normal concentrations of blood and tissue nutrients.

Human milk feeding alone is insufficient to meet the nutritional demands of the very preterm infant.
Postnatal Malnutrition and Growth Retardation: An Inevitable Consequence of Current Recommendations in Preterm Infants?

AFTER 1 WEEK
Energy deficit = 300 kcal/kg
Protein deficit = 12 g protein/kg

AFTER 5 WEEKS
Energy deficit = 813 kcal/kg
Protein deficit = 23 g protein/kg

Embleton et al., Pediatr, 2001;107:270-273
BABY FRIENDLY HOSPITAL INITIATIVE

- Started in 1991 after Innocenti Declaration
- Evidence based Ten Step plan for quality improvement
- Multidisciplinary approach
- Education for parents
- Education of all staff
- Minimize formula exposure
- Initial self assessment
- QI process

UCSD was home to the birth of BFHI concept (Audrey Naylor) but it took another 15 years to get our designation

1990 Innocenti Declaration on Breastfeeding Promotion
SPIN PROGRAM MISSION STATEMENT

To create a Center of Excellence in neonatal nutrition focused on the provision, analysis, and research of human milk to improve nutritional and long-term health outcomes of premature babies.
Team Building to Make More Milk

IMPORTANT TO BRIDGE TWO DISCIPLINES
The SPIN Program Ten Steps

1. Have a NICU nutrition/human milk policy
2. Educate all mother/baby staff in SPIN 10-steps
3. Educate NICU families about optimal premature infant nutrition
4. Prevent extrauterine growth restriction
5. Standardize enteral feeding procedures
6. Target 100% human milk nutrition
7. Maximize mothers’ milk production
8. Optimize milk quality and safety
9. Encourage skin-to-skin care and breastfeeding
10. Plan a nutritional discharge from NICU
Diffusion of Innovation

Rogers EM, 1962 Law of Diffusion of Innovation
Inpatient care
MILK “TRAFFIC” CHAIN

- Mother pumps
- Milk in bottle
- Milk in storage container
- Milk in NICU freezer
- Milk in cooler for transport
- Milk in home freezer
- Milk thawed
- Milk measured
- Milk fortified
- Milk in tubing
- Milk drawn into syringes
- Milk in baby (finally!)

MORE MILK MEANS MORE RESPONSIBILITY
Expanding variety of human milk fortifiers

• Bovine based
  Powder
  – Intact whey protein, standard amount of protein
  Liquid
  – Partially hydrolyzed whey, higher protein
  – Intact whey protein, standard protein
  – Extensively hydrolyzed casein, higher protein

– Protein module
  – Intact whey protein powder (no longer recommended!)
  – Liquid protein (extensively hydrolyzed casein)

• Human based
  – Donor human milk derived (dialyzed, reconstituted)
Powder vs Liquid

**Powder**
- non-sterile
- difficult to mix
- needs to warm up significantly to get into solution
- minimal volume displacement

**Liquid**
- sterile
- greater solubility
- ease of use for staff and parents
- volume displacement
Less bovine: protein hydrolysis

- Whole bovine proteins
  - Immunogenicity: 5 stars

- Partially hydrolyzed whey or casein proteins
  - Immunogenicity: 1 star

- Extensively hydrolyzed whey or casein proteins
  - Immunogenicity: 1 star

- Amino acids only
  - Immunogenicity: not possible
Newer liquid human milk fortifiers

- new ultra-concentrated liquid fortifiers
- Base protein
  - Partially hydrolyzed whey OR
  - Extensively hydrolyzed casein
- Protein amount: ~20% more protein than older standard fortifier
- Differentiating properties
  - Acidified to mildly low pH
  - Additional lutein, DHA and ARA

Effects of liquid bovine based human milk fortifiers

- Higher weight and linear growth rate were similar to or better than control intact bovine powder
- Strict adherence to protocol further improved overall growth including head circumference with one of the fortifiers
- No differences in measures of feeding tolerance or days to achieve full feeding volumes
- Higher levels of prealbumin, albumin, and blood urea nitrogen
- Similar incidence of sepsis or NEC

Commercial development in donor human milk products

• Prolacta Biosciences
  • Donor human milk derived HMF
  • Donor human milk
  • Donor human milk derived cream
  • Donor human milk derived ready to feed
  • [Donor human milk derivatives – oligosaccharides]

• Medolac
  • Mother’s milk cooperative
  • Donor human milk with prolonged shelf life
  • [Donor human milk derived HMF-coming?]
Standardizing care is better care

• Why should we standardize?
  • reduce variability
  • generate a steadier average
  • obtain interpretable results
  • “in the absence of evidence practice varies widely”

• What should we standardize?
  • nutrient delivery
  • energy targets
  • nutrient targets
  • growth goals
Standardized feeding protocol

• Any plan is better than no plan
• In the absence of strong evidence, practice variability increases
• Standardized care is better care
• Eliminate the outliers (attending-of-the-day!)
Retrospective evidence for protocol feeding

Key Elements to a Great Feeding Protocol

• Established consensus from medical faculty
• Visible, nurse-driven advancement
• Linear advancement
• Trophic feeding for extremely preterm infants
• Incorporate timing of fortification and vitamins
<table>
<thead>
<tr>
<th>Weight: 1050 grams</th>
<th>Advances by Approximately 13mL/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date &amp; Time Advances are q 12hrs</td>
</tr>
<tr>
<td>1st day of feedings</td>
<td></td>
</tr>
<tr>
<td>2nd day of feedings</td>
<td></td>
</tr>
<tr>
<td>3rd day of feedings</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td></td>
</tr>
</tbody>
</table>
What is the correct rate of feeding?

• Should all preemies be fed the same rate?
  • Literature supports very fast rate of feeding up to 35mL/kg/day

• How much trophic feeding is good?
  • Berseth et al. study suggests that 10 days was better

• When is the earliest day to start feeding?
  • Little data to support day 1 feeding

• When not to feed?
  • More theoretical basis to stop feeds
Routine Human Milk Analysis in the NICU

- Human milk is best, but:
  - Varies in composition by
    - mothers
    - time of day, week, month
    - timing of pumping
    - delivery system
  - Current fortification methods are BLIND!
  - Error margin at least 50%
Caloric variability of human milk
Human milk protein declines with time

Ideal Features of a Milk Analyzer

- Point-of-care
- Accurate
- Measures Protein, Fat, and Carbohydrates
- Uses only a small volume of milk
- Affordable
- Fast
- Small footprint
Custom Fortification of Human Milk

Spectroscopic milk analysis

Pros
• Precise and accurate
• Bedside application
• Addresses individual macronutrients

Cons
• Very expensive
• Requires regular personnel
• Cannot differentiate types of proteins
• Cannot readily test fortified milk

Adjustable fortification method
(Using BUN)

Pros
• Simple biochemical measure that has been shown to improve weight gain

Cons
• Indirect measure of needs

Arslanoglu et al. J Perinatol. 2006;26:614-21
Target fortification of breast milk: how often should milk analysis be done?

• Per feed or even daily measurements may be impractical due to excess workload, adding 5-10 min per sample including measurement and calculations

• Stable correction of macronutrient contents possible with 2x/week measurements of daily pooled milk

• No answer yet for what is more physiologic: feed-to-feed variability or stable intake over each day

Nutrient content: individual vs pooled approach

Calories vary by 29%

Stellwagen et al 2013 Breastfeeding Medicine 8:205-9
Is pooled milk better than standard methods?

- Bacterial counts over $10^5$ were more common in individual samples
  - Individual 14%
  - Pooled 9%
- 83% of pooled milk had same or less bacteria
- Mothers preferred 1 liter bottle
- Should make tracking mom’s 24-hour milk volume easier

Stellwagen et al 2013 Breastfeeding Medicine 8:205-9
Benefits of pooling human milk

- 24 hour pooling of mother’s milk:
  - Provides a more consistent calorie product for baby
  - Allows for more accurate fortification
  - Permits measuring, labeling, fortifying, drawing up feeds from one container
  - May minimize milk fat loss
  - May allow for more fresh milk use

Stellwagen et al 2013 Breastfeeding Medicine 8:205-9
Improving Milk Processing In NICU: Milk Technician

- Milk technician position: dietary tech
- Collect morning milk order
- Use standard recipe to mix 24 hour feedings
- Milk feeding put in syringes, or large bottle once orally feeding
- Milk analysis will be incorporated into practice to further improve optimal milk product
- Benefits of milk tech:
  - Ease RN workload
  - Consistent preparation
  - Minimize milk transfers
  - Encourage use of fresh milk
Factors in nutrient loss in human milk

• oxidation
• refrigeration
• freezing
• heating
• photo-degradation
• adherence to the tubing system
Loss of triglycerides and carotenoids in human milk after processing

- Assessment of milk factors with heating, freezing, and tube feeding
- Triglycerides and carotenoids were stable with freezing, refrigeration, microwave heating
- Tube feeding led to 33% loss in triglycerides
  - Represents 11 Kcals/100 mls of milk
  - And 16% of calories
  - Despite measures to decrease fat loss
- Carotenes also fell significantly during tube feeding
- Infant formula did not show fat loss with tube feeding

Tacken 2009
Donor human milk
Primary goal of donor human milk practice:

Avoid using donor human milk!

Mother’s own milk (MOM) is still the best!
History of Donor Milk

- Wet nursing
- Commercial refrigeration since 1850’s
- 1909: the first milk bank was established in Vienna, Austria
- 1910: milk bank in Boston
- North American history in milk banking is 100 years old
- Boston “Wet Nurses Directory” 1910-19
- 1919: milk bank in Germany
- 1943: Milk Bank in Brazil
  - AAP guidelines (*J Pediatrics* 1943;23:112-128)
  - 1947: “Lactarium” in Paris
- 1974: Canada’s first milk bank in Vancouver
- By early 1980’s 23 banks in Canada and 30 in US

Donor Milk Banking in North America

Existing Milk Banks

Cities Served by Milk Banks

http://hmbana.org/index/locations
Processing of Donor Human Milk

1. **Screening** (Questionnaire and Blood)
2. Expression of milk
3. Freezing, storage, and transport
4. Thawing and Bacterial culture
5. Batching
6. Pasteurization
7. Culture of batch
8. Freezing
9. Thawed for use

The process involves several steps, starting with screening and expression of milk, followed by freezing, storage, and transport, then thawing and bacterial culture, batching, pasteurization, culture of batch, freezing, and finally thawing for use.
Infectious Screens

- HIV 1&2
- HTLV 1&2
- HBsAg
- Hep C
- VDRL or RPR
- PPD (as appropriate to population)
- Bacteriologic Screening
Human Milk Processing / Handling

• Guidelines established by the Human Milk Banking Association of North America

• (HMBANA) written in cooperation with:
  • Centers for Disease Control (CDC)
  • American Academy of Pediatrics (AAP)
  • Food and Drug Administration (FDA)
Sterilizing Human Milk

• Holder Pasteurization
  • 62.5 degrees Celcius x 30 min
  • used by most non-profit milk banks

• High Temperature Short Time
  • 72 degrees Celcius x 15 seconds
  • used by commercial milk bank

DONOR MILK CONSENT

Adapted from CPQCC VLBW Nutrition Toolkit 2005, and HMBANA.org

CONSENT FOR USE OF DONOR MILK IN THE INFANT SPECIAL CARE CENTER

In the absence of your own breast milk, your infant’s health care team recommends and will prescribe, heat-processed, donor human milk for your infant if your infant meets one of these criteria:

- Birthweight less than 1500 grams
- Your child has had some type of bowel injury such as necrotizing enterocolitis (NEC) or gastrochisis
- Your physician has requested the use of donor milk for other reasons that he/she feels potentially adds further health benefits for your infant.

Donor milk will generally be provided until mother’s milk volume becomes sufficient or your infant reaches 32-34 weeks gestation at which point your infant will be switched over to the appropriate standard infant formula in the absence of mother’s milk.

In the absence of the infant’s own mother’s milk, donor milk offers many of the benefits of human milk for the infant, including:

- Infection-fighting factors
- Reduced incidence of NEC, a severe inflammatory bowel condition in premature infants
- Active growth and developmental hormones
- Improved digestion
- Ideal nutrition

Donor milk banks receive milk from lactating mothers who have been carefully screened for health behaviors and communicable diseases, including AIDS, hepatitis B, hepatitis C, and syphilis. Additionally, they must not smoke, drink or take any medications regularly.

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Donor milk is transported to the milk bank frozen. The milk from several donors is pooled together after thawing, and then heat-treated to kill any bacteria or viruses. The milk is processed and then refrozen. The milk is only sent to hospitals after it has tested to ensure the absence of dangerous viruses and bacteria.

Although every precaution is taken, there is a very small chance that an infectious agent may nevertheless be transmitted to your child by the milk, and your child could become sick. Please discuss any concerns you have regarding the use of donor human milk with your baby’s health care team.

My baby’s physician/nurse practitioner has described the need for donor human milk for baby and has told me about the potential risks and expected benefits, as well as other methods of nutrition available and their risk and benefits. My physician/nurse practitioner has given me the chance to ask questions about the use of donor human milk and all of my questions have been answered to my satisfaction.

<table>
<thead>
<tr>
<th>I accept the use of donor human milk for my child.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature of Guardian ___________________ Date _________________</td>
</tr>
<tr>
<td>Signature of Witness ________________________ Date _________________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I understand that use of cow’s milk-based formulas may increase my child’s risk of infection, intestinal complications, or allergies, but decline the use of donor human milk for my child.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature of Guardian ___________________ Date _________________</td>
</tr>
<tr>
<td>Signature of Witness ________________________ Date _________________</td>
</tr>
</tbody>
</table>

*If one twin is less than 1500 grams and one more, both twins can receive donor human milk for first feedings*
Lactation support
Maternal support in the hospital

- Encourage all mothers to pump
- Standardize approach to pumping mother
- Provide up to date education
- Early initiation of pumping
- Hospital grade pump
- Proper flange fit

- Consider “Plus” Card
- Start log book
- Teach hand expression
- Clear volume goals
- Review home instructions for pumping prior to discharge
- Discharge with adequate pump

Meier 2010
How to approach the reluctant mother

Start with general discussion of nutrition for preemies
Try and include partner
If possible, first discussion before baby is born
Discuss infection, NEC, brain and body growth
So you can see that we need your milk for your baby

We would like you to pump for your baby
We will help you
We will get you (or give you) a pump
Avoid discussing breastfeeding in these early stages
Over time we aim for pumping until the baby goes home
Mother’s Milk Log Book

Log book to track first week, no volume concerns yet
When milk volume picks up, mothers start to record and add 24-hour volume
Use the milk!

- If mother sees her milk is being used she is more likely to keep pumping
- Minimize NPO time
- Address concerns about milk quality
How to help the mother with a low milk supply

1. Pump type
2. Procedure for pumping
3. Pain
4. Pills
5. Power pumping
6. Schedule
7. Six or more
8. Stress
9. Sleep + eat/drink
10. Skin-to-skin
Early pumping strategy for higher milk production

Herbals? Teas? Acupuncture? Do they work?

- Traditionally used
- Scant evidence
- Placebo effect
- Couldn’t hurt?
Galactogogues (Dopamine Antagonists): Do they work?
The best way to increase milk supply is to never let it get low
Handling of milk
What milk to use first?

1. Colostrum should be used first
   - First 2-4 weeks
   - Higher protein
   - More immunologic properties
   - Label early milk

2. Fresh milk

3. Frozen milk
### Fresh or frozen?

<table>
<thead>
<tr>
<th>Benefits of fresh milk</th>
<th>Benefits of frozen milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Live cellular elements</td>
<td>o Minimize CMV</td>
</tr>
<tr>
<td>o Better fat preservation (MFG)</td>
<td>o Longer storage time</td>
</tr>
<tr>
<td>o Bacteria counts fall over 4 days</td>
<td>o Bacteria counts stable</td>
</tr>
<tr>
<td>o Better for baby</td>
<td>o Easier for NICU</td>
</tr>
</tbody>
</table>
Refrigerator storage of expressed human milk in the NICU

- Expressed milk refrigerated at 4°C and sampled for 4 days (96 hours)
  - Assessed for pH, WBC count, osmolality, bacterial counts, sIgA, lactoferrin and fat
  - pH fell from 7.2-6.7
  - WBC fell by 16%
  - Total protein fell by 5%
  - Gram+ bacterial colony counts fell
  - 3-fold increase in free fatty acids, from active lypolysis
  - No changes in Osm, sIgA, fat, gram- bacteria, lactoferrin

- Cold human milk retains optimal nutrient profile and a safe content for 96 hours after expression

Slutzah 2009
Suggested plan for fresh milk use

- Mom pumps and pools 24 hours of milk
- She is told how much milk is needed for 24 hours of feeds
- Mother pours off extra milk and freezes it at home
- She brings in fresh milk daily
- Milk tech fortifies in bottle
- Syringes or bottles are filled from bottle
CMV transmission in breastmilk

- Most women are CMV positive (80%)
- Post-delivery large amounts of virus are present in milk for 4-6 weeks
- Premature infants can rarely become ill with CMV illness
- Freezing diminishes viral content by killing live WBC
- Pasteurization prevents viral transmission
- No consensus exists on how to deal with this issue
Mother’s rules for transport

- Use cooler
- Blue ice (2-3 is best)
- Bring milk directly to unit
- Tell mom to keep her hospital bin full so we never run out
Storage of milk
Mother’s rules for milk storage

- Rule of 3’s for milk storage:
  - 3 hours at room temperature
  - 3 days in the refrigerator
  - 3 months in the freezer
  - 12 months in the deep freeze
- Provide coolers and blue ice
Processing milk
Where do you process your human milk?

- Bedside in the NICU like we used to do?!
- Milk lab
- Formula prep area
Thawing milk

- What method is best?
  - Water bath
  - In fridge
  - Dry heater

- Does it affect milk components?

- Best practical way to thaw
New options for thawing at bedside

**The Penguin**

The Penguin Nutritional Warmer™ comes in two sizes: a single well for individual bedsides and a four well for prep areas or pods. The unit has 3 modes: WARM room temperature or refrigerated milk to body temperature; THAW frozen milk to refrigerated temperature; or WARM frozen milk to body temperature. The Penguin vibrates as it’s warming to keep breast milk from separating and also holds the temperature for 30 minutes.

**Therma-Liner™**

The patented Therma-Liner™ minimizes the risk of infection or cross-contamination by keeping the feeding separated from the tap water with a “bag in a bag” design.
Safety
NICU RN Workflow

- Correct milk/correct baby
- RN Double check
- Bar coding systems
- Misadministration policy

(All mismatch numbers include both breast milk and formula feedings.)

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total infant-feeding mismatches in the NICU &amp; milk preparation room</td>
<td>387</td>
</tr>
<tr>
<td>Infants have the same last name. (These mismatches would most likely have become breast milk errors.)</td>
<td>9</td>
</tr>
<tr>
<td>Infants have similar last names, similar first letter(s) sound, or length of name (possibility of becoming an error).</td>
<td>28</td>
</tr>
<tr>
<td>Last names have no similarity (slight chance of becoming an error).</td>
<td>220</td>
</tr>
<tr>
<td>There are multiples of the same family. (These are less concerning as an error, but we chose to distinguish each infant separately in the event they were receiving very different milk preparations.)</td>
<td>112</td>
</tr>
<tr>
<td>Total number of milk mismatches during the preparation of EBM feedings in the milk preparation room—data available from July 1, 2008–January 23, 2009 (7 months). The last names of the EBM containers were similar; if the alarm had not been triggered, the error would have affected more than one feeding. The label applied by the technician would appear correct to the nurse, and the error would not be discovered.</td>
<td>18</td>
</tr>
</tbody>
</table>

The average number of infant feedings prepared monthly in the milk preparation room is 8,686, ranging from 7,697 to 9,884 (census dependent).
COLOSTRUM

- Nutrition
- Lactoferrin
- Lysozyme
- Immunoglobulins
- Oligosaccharides
- Cytokines
- Cellular immunity
## Bacteria in Breast Milk

<table>
<thead>
<tr>
<th>Phyla</th>
<th>Genera</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firmicutes</td>
<td>Staphlococcus, Streptococcus, Veillonella, Gemella,</td>
</tr>
<tr>
<td></td>
<td>Enterococcus, Clostridia, Bifidobacterium,</td>
</tr>
<tr>
<td></td>
<td>Lactobacillus</td>
</tr>
<tr>
<td>Actinobacteria</td>
<td>Propionibacterium, Actinomyces, Corynebacterium</td>
</tr>
<tr>
<td>Proteobacteria</td>
<td>Pseudomonas, Sphingomonas, Serratia, Escherichia,</td>
</tr>
<tr>
<td></td>
<td>Enterobacter, Ralstonia, Bradyrhizobium</td>
</tr>
<tr>
<td>Bacteroidetes</td>
<td>Prevotella</td>
</tr>
</tbody>
</table>

**Figure 1** During the course of lactation, there is an overall decrease in bacterial diversity compared with colostrum samples. The composition of the microbiota shifts from skin- and enteric-associated organisms to infant oral and skin organisms.
Microbiota of Colostrum

L. Fernández et al. / Pharmacological Research 69 (2013) 1–10

Fig. 2. Potential sources of the bacteria present in human colostrum and milk. DC: dendritic cell.
Recommendation For Initiation Of Premature Infant Nutrition Program

- Form multidisciplinary group
- Leadership must support process
- Enlist support of medicine, nursing, nutrition, OT/PT, lactation
- Conduct self-assessment
- Decide on goals
- Create timeline for new initiatives
- Meet regularly and update staff about activities
- Patience with process of change
- Collect data about outcomes
SPIN: Supporting Premature Infant Nutrition

Premature infants who receive human breast milk have the best outcomes—medically, nutritionally, and developmentally.

The Supporting Premature Infant Nutrition (SPIN) program was developed to address the challenges of helping mothers produce sufficient breast milk for their premature infants, and to improve the manner in which neonatal intensive care unit (NICUs) support optimal nutrition and growth in their most vulnerable population of patients.

Resources for Parents
These resources may be helpful for NICU parents:
- Breastfeeding guide
- Pump logs
- Videos: Tips and one mom’s journey
- SPIN Mommas mentoring program

Resources for NICU Staff
Other hospitals are welcome to use or adapt these resources:
- Feeding advancement tables
- Lactation support letter
- Discharge plans
- Materiel education materials

More than a half million babies are born premature each year in the U.S. Treatment is costly, but as Dr. Sanjay Gupta reports in this CBS video, "Power of a Mother's Milk," one new strategy is as old as life itself: breastfeeding.