D2: USE OF BANKED DONOR MILK IN THE NICU

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OBJECTIVES

- Understand how banked milk is obtained & processed.
- Understand how banked milk differs from fresh milk.
- Understand benefits of banked milk versus formula for feeding premature infants.

ABSTRACT/OUTLINE

- The history of human milk banking in the USA.
- Indications for use of banked donor milk (BDM) for premature infants.
- How BDM is obtained.
- Where BDM is used.
- Concerns & questions regarding the use of BDM.
- Benefits ascribed to BDM.
- The interplay between lactation support & milk banking.
Banked Donor Milk in the NICU – The 21st Century

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MOTHERS’ MILK BANK OF SAN JOSÉ, CA
Conflict of Interest Statement

- Medical Director, Mothers’ Milk Bank of San José.
  - An unpaid position.
  - MMB-SJ loses money on every ounce distributed.
- MMB-SJ does provide some support for research.
Unique Abbreviations

- BDM = Banked Donor Milk
- MAT = Maternal Milk
- PTF = Pre-Term Formula
- PDF = Post-Discharge Formula
- HMBANA = Human Milk Banking Association of North America
- HMF = Human Milk Fortifier
- H2MF = Human-milk derived HMF
- NEC = Necrotizing Entero-Colitis
Starting Points

• Breast is best – undisputed for term infants.
• Widely accepted for preterm infants, but some concerns remain regarding:
  ○ Vertical transmission of disease;
  ○ Protein intake;
  ○ Calcium-Phosphorus intake.
• Role of donor milk controversial still:
  ○ Safety;
  ○ Nutritional content;
  ○ Cost-benefit analysis.
Historical Regulation of Milk Banking

- 1943: AAP formal guidelines for milk banks.
- 1953: AABB Guidelines
- Today: CDC/FDA and Advisory Board provide ongoing review of data and resources for screening and procedural advice.
Map of US Milk Banks of HMBANA
Hospitals Served by HMBANA in 2006
HMBANA BDM Total Distribution

HMBANA Annual Total Distribution Rates 2000-2009 (oz)

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
409,877 511,651 501,143 515,660 580,768 745,329 900,260 1,122,725 1,441,070 1,508,735
HMBANA Recipients

Outpatient 44%

Inpatient 56%
Distribution by MMB - SJ

Mothers’ Milk Bank of San José
Total Distribution 2000-2010

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DHM Use at LPCH

Yearly Distribution at LPCH

- 2004: 0
- 2005: 7256
- 2006: 5104
- 2007: 5896
- 2008: 6305
- 2009: 5051
- 2010: 4611
Who Donates Milk?

- Approved by donor’s Obstetrician.
- Approved by infant’s Pediatrician if breastfeeding.
- Potential donors screened like blood banks.
- Questionnaire on health, habits, travel, etc;
- Cannot be on medications except for
  - Asthma inhalers;
  - Replacement hormones [e.g., thyroid];
  - Mini-pill OCP.
- Serologic testing
HMBANA Donor Exclusions

- Positive blood test result for HIV, HTLV, Hepatitis B or C, or Syphilis;
- She or her sexual partner is at risk for HIV;
- She uses illegal drugs;
- She smokes or uses tobacco products;
- She has received an organ or tissue transplant or a blood transfusion in the last 6 months;
- She regularly has more than two alcoholic drinks per day;
- She has been in the United Kingdom for more than 3 months or in Europe for more than 5 years between 1980-1996;
- She was born in or has traveled to Gabon, Niger, Cameroon, Chad, Congo, or Equatorial Guinea.
Heat treatment destroys CMV\(^1\):
- Holder Pasteurization @ 62.5° C;
- “Flash” Pasteurization @ 72° C.

Freeze/thaw may not eliminate CMV:
- Freezing for 1 year, then freeze/thaw x 3 did NOT eliminate infectious virus\(^1\);
- 5 of 36 CMV positive mothers transmitted CMV to 6 babies despite freezing\(^2\);
- 2 of 23 CMV positive mothers transmitted CMV to 2 babies despite freezing & Cesaerean delivery\(^3\).

Positive Serologic Screens

Table 1: Positive serological screening tests of potential human milk donors

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>RPR</th>
<th>HIV</th>
<th>HTLV</th>
<th>Hep B</th>
<th>Hep C</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>115</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>2001</td>
<td>165</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4 (2.4)</td>
</tr>
<tr>
<td>2002</td>
<td>180</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>5 (2.8)</td>
</tr>
<tr>
<td>2003</td>
<td>163</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>5 (3.1)</td>
</tr>
<tr>
<td>2004</td>
<td>219</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>12 (5.5)</td>
</tr>
<tr>
<td>2005</td>
<td>249</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>8 (3.2)</td>
</tr>
<tr>
<td>All</td>
<td>1091</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>17</td>
<td>3</td>
<td>36 (3.3)</td>
</tr>
</tbody>
</table>

Hep B, hepatitis B; Hep C, hepatitis C; HTLV, human T cell lymphotropic virus; N, number tested; RPR, rapid plasma reagin test for syphilis.

“In conclusion, at least 3% of potential donors to a human milk bank, a relatively low-risk population, were found to test positive for the rapid plasma reagin (RPR) test for syphilis, HIV, hepatitis B, hepatitis C, HTLV-1 or HTLV-2, on screening serology. Although screening tests overestimate the number of true positives, the prevalence of these viruses in the unscreened adult population at large would likely be higher than in our donors. The use of unpasteurised donor human milk from untested women may pose a significant health risk to exposed infants.”

“Use of the following medications is acceptable: human insulin, thyroid replacement hormones, nasal sprays, asthma inhalers, topical treatments, eye drops, progestin-only birth control products, and low-dose estrogen birth control products, ...”
HMBANA Donor Exclusions

- “Regular use of over-the-counter medications or systemic prescriptions.”
- “Regular use of mega dose vitamins and/or herbal products used as medication, including vitamin/herb combinations.”
Medication Usage Among Potential Milk Bank Donors

- Single Regional Milk Bank.
- Retrospective review.
- Covered 2 Calendar Years
  - 2007-08.
- De-identified records
  - N = 2118.

Potential Donor Pool

- Total screened = 2118.
- 1129 (53.3%) reported medication use.
  - 736 (34.7%) on acceptable medications.
- 393 (18.6%) excluded by HMBANA Criteria.

Potential Milk Donors

N = 2118

No Meds
989 (46.7%)

Acceptable Meds
736 (34.7%)

Meds
1129 (53.3%)

Excluded
393 (18.6%)

Most Common Medications Causing Exclusion

1. Fenugreek  [N = 79/393; 20%]
2. Ibuprofen   [N = 74/393; 19%]
3. Acetaminophen  [N = 50/393; 13%]
4. Antidepressants  [N = 31/393; 7.9%]
5. Allergy Rx    [N = 28/393; 7.1%]

Breakdown of Anti-Depressants

- Sertraline – 20
- Fluoxetine – 4
- Escitalopram – 3
- Citalopram – 1
- Amitriptyline – 1
- Paroxetine – 1
- Bupropion – 1

“Because of the low levels of sertraline in breastmilk, amounts ingested by the infant are small ...”

“Most authoritative reviewers consider sertraline one of the preferred antidepressants during breastfeeding”.

LactMed Record 328
“The average amount of drug in breastmilk is higher with fluoxetine than with most other SSRIs and the long-acting, active metabolite, norfluoxetine, is detectable in the serum of most breastfed infants during the first 2 months postpartum and in a few thereafter.”

“Adverse effects such as colic, fussiness, and drowsiness have been reported in some breastfed infants. Decreased infant weight gain was found in one study, but not in others.”

“No adverse effects on development have been found in a few infants followed for up to a year.”

LactMed Record #323
“Infants receive citalopram in breastmilk and it is detectable in low levels in the serum of some.”

“A few cases of minor behavioral side effects such as drowsiness or fussiness have been reported ...”

“... no adverse effects on development have been found in infants followed for up to a year.”

LactMed Record #322
“... maternal doses of escitalopram up to 20 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months.”

“...escitalopram appears to be preferable to racemic citalopram during breastfeeding because of the lower dosage and milk levels ....”

“One case of necrotizing enterocolitis was reported in an breastfed newborn whose mother was taking escitalopram during pregnancy and lactation, but causality was not established.”

LactMed Record #404
What’s in Banked Donor Milk?

Table 1. Selected Components of Human Milk After Freezing and Pasteurization

<table>
<thead>
<tr>
<th>Function</th>
<th>Percentage Activity</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA and sIgA</td>
<td>Binds microbes in the baby’s digestive tract to prevent their passage into other tissues</td>
<td>67-100</td>
</tr>
<tr>
<td>IgM</td>
<td>Antibodies specifically targeted against pathogens to which the mother has been exposed</td>
<td>0</td>
</tr>
<tr>
<td>IgG</td>
<td>Antibodies specifically targeted against pathogens to which the mother has been exposed</td>
<td>66-70</td>
</tr>
<tr>
<td>Lactoferrin (iron-binding capacity)</td>
<td>Binds iron required by many bacteria and thus retards bacterial growth</td>
<td>27-43</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Attacks bacterial cell walls and thus destroys many bacteria</td>
<td>75</td>
</tr>
<tr>
<td>Lipoprotein lipase</td>
<td>Partly responsible for lipolysis of milk triglycerides to release monoglycerides and free fatty acids</td>
<td>0</td>
</tr>
<tr>
<td>Bile salt activated lipase</td>
<td>Partly responsible for lipolysis of milk triglycerides to release monoglycerides and free fatty acids</td>
<td>0</td>
</tr>
<tr>
<td>Monoglycerides produced by lipolysis of milk triglycerides</td>
<td>Disrupts the membrane coating of many viruses and protozoans, destroying them</td>
<td>100</td>
</tr>
<tr>
<td>Free fatty acids produced by lipolysis of milk triglycerides</td>
<td>Disrupts the membrane coating of many viruses and protozoans, destroying them</td>
<td>100</td>
</tr>
<tr>
<td>Linoleic acid (18:2Δ6)</td>
<td>Essential fatty acid; metabolic precursor for prostaglandins and leukotrienes</td>
<td>100</td>
</tr>
<tr>
<td>ɑ-linolenic acid (18:3Δ3)</td>
<td>Essential fatty acid; metabolic precursor for docosahexaenoic acid; important for eye and brain development</td>
<td>100</td>
</tr>
</tbody>
</table>

* These biologically active components do not occur in commercial formula.
** Some manufacturers are now adding docosahexaenoic acid and other supplemental fats to selected infant formula preparations.

Banked Donor Milk: Benefits & Concerns

World Association of Perinatal Medicine: Consensus

Table 2: Recommendations regarding the use of donor human milk in the feeding of preterm infants.

- Growing clinical evidence has placed human milk (HM) feeding as a basic right for preterm infants.
- Mother’s own milk is the first choice in preterm infant feeding and strong efforts should be made to promote lactation.
- When mother’s milk is not available, fortified donor human milk is the recommended alternative for this group of infants.
- Concerns regarding the nutritional and immunological quality of donor milk and slow growth of preterm infants fed HM should not be a barrier to its use.
- Optimization of donor HM processing (particularly pasteurization) and of fortification are required.
- Recent developments in pasteurization techniques appear to retain the bioactivity of human milk, and individualized fortification of HM provides improved protein intakes and growth. Thus, implementation of these techniques in human milk banks and utilization of individualized fortification are recommended.
- Donor milk banking should be protected, promoted, and supported as an extension of national breastfeeding policies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross</td>
<td>0.21 (0.02 to 1.93)</td>
</tr>
<tr>
<td>Lucas and Cole</td>
<td>0.23 (0.03 to 2.00)</td>
</tr>
<tr>
<td>Svenningsen et al</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Tyson et al</td>
<td>0.39 (0.01 to 9.41)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0.25 (0.06 to 0.98)</td>
</tr>
</tbody>
</table>

**Figure 2** Relative risk of confirmed necrotising enterocolitis in infants randomised to donor human milk versus formula milk.

Cochrane review of 8 trials.

Formula feeding had increased risk of NEC:
- RR 2.5 (1.2, 5.1);
- NNH 33.

**BDM vs PTF & NEC: Cochrane ‘07**

Is BDM Cost Effective?

• “Three models of cost analysis are presented to show savings that could accrue to a health care system or individual family if banked donor milk were provided as first feedings when mother’s milk is not available. The cost of using banked donor milk to feed premature infants is inconsequential when compared to the savings from NEC prevention.”


• “A reduction in length of stay, necrotizing enterocolitis and sepsis may result in a relative saving of approximately $11 to the NICU or healthcare plan for each $1 spent for pasteurized donor milk”.

Impact of Fortification

- RCT - fortified maternal milk vs Preemie formula
  - N = 108
  - milk frozen, stored, & thawed
- Fortified milk benefits:
  - earlier discharge
  - decreased NEC
  - decreased late-onset Sepsis
  - better Ca & Phos absorption
- Preemie formula benefits:
  - faster weight gain
  - better fat & energy absorption


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BDM vs PTF Supplementation?

- RCT of N = 243 infants < 30 weeks gestation
  - All patients started on Maternal Milk
  - Randomized if maternal supply inadequate
- Donor Milk group had slower weight gain
- Maternal Milk group had less Sepsis & NEC
- “...DM conferred little short-term protective advantage to extremely premature infants.”

DHM vs PTF - Advantage?

- All patients received ~ 50% Maternal Milk.
- “Intent to treat” analysis - some in Donor group got formula for “poor weight gain”.
- Rate of NEC not significant, but:
  - Maternal Milk 6%
  - Donor Milk 6%
  - Preterm Formula 11%
- Big difference in Skin-to-skin, SES, Visits.

Protein intake with human milk

- Varying numbers in the literature.
- Questions regarding analytic methods.
- Questions regarding collection methods.
- Biologic variability.
The “DARLING” Study

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Milk volume and composition*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 mo (n = 58)</td>
</tr>
<tr>
<td>Volume consumed by infant (g/d)</td>
<td>811 ± 133</td>
</tr>
<tr>
<td>Volume produced (g/d)</td>
<td>895 ± 200</td>
</tr>
<tr>
<td>Protein (g/L)</td>
<td>5.2 ± 1.3</td>
</tr>
<tr>
<td>Lipid (g/L)</td>
<td>38.2 ± 7.0</td>
</tr>
<tr>
<td>Lactose (g/L)</td>
<td>74.4 ± 1.5</td>
</tr>
<tr>
<td>Gross energy (kcal/L)</td>
<td>697 ± 67</td>
</tr>
</tbody>
</table>

Approximately 1.2 gm/dL Protein

Analysis of Donor Milk

<table>
<thead>
<tr>
<th>Protein</th>
<th>Lactose</th>
<th>Kcals/oz</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.24 gm/dL</td>
<td>7.23 gm/dL</td>
<td>20.5</td>
</tr>
<tr>
<td>± 16%</td>
<td>± 6.7%</td>
<td>± 10%</td>
</tr>
</tbody>
</table>

Rivera A. Personal Communication.
## Can Milk Provide Enough Protein?

<table>
<thead>
<tr>
<th><strong>Milk Protein Content</strong> (gm/dL)</th>
<th><strong>Fluid Intake</strong> (mL/kg daily)</th>
<th><strong>Protein Intake</strong> (gm/kg daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>150</td>
<td>1.8</td>
</tr>
<tr>
<td>1.2</td>
<td>180</td>
<td>2.16</td>
</tr>
<tr>
<td>1.2</td>
<td>200</td>
<td>2.4</td>
</tr>
</tbody>
</table>

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NICU Standard Feeding Orders

- Colostrum 0.5 mL q 6 h buccal when available.
- Maternal milk xx mL q 3 h ....
- When not available may use banked donor milk.
- Document parental assent before using BDM or H2MF.
Why use Donor Breast Milk?

- According to WHO/UNICEF (1980): "In situations where mother’s own milk is not available, provisions of pasteurized, screened donor milk is the next best option particularly for ill or high risk infants."

- The American Academy of Pediatrics policy statement of 1997: "Human milk is the preferred feeding for all infants, including premature and sick newborns, with rare exceptions. The ultimate decision on feeding of the infant is the mother’s."

- Pediatricians should provide parents with complete, current information on the benefits and methods of breastfeeding to ensure that the feeding decision is a fully informed one. When direct feeding is not possible, expressed human milk, fortified when necessary for the premature infant, should be provided.

- Before advising against breastfeeding or recommending premature weaning, the practitioner should weigh thoughtfully the benefits of breastfeeding against the risks of not receiving human milk."
What is Donor Breast Milk?

- Milk Bank collects, and distributes donated breast milk.
- Potential donors are screened just like blood donors, and milk is pasteurized to kill all known bacteria and viral pathogens. No infections have ever been linked to milk from the Banks.
Donor milk offers all of the benefits of human milk for the infant or child, including optimal nutrition, easy digestibility, and growth factors to promote maturation and healing of tissues, immunologic protection and infection-fighting components. For some children this is the only source of nutrition that allows them to grow and develop without allergic symptoms. In the past 30 years, there has never been a documented disease or illness transmission through processed human milk.
How Does the Milk Bank Operate?

- Breastfeeding mothers who are willing to express extra milk for donation and who meet the health criteria are told how to safely express, store, and pack their breast milk.
- Once the breast milk arrives at the Milk Bank, it is pooled with milk from several different donors. It is heat treated (pasteurized) to destroy any bacteria or viruses that may be present. It is then cultured and frozen.

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Milk Banking Supports Lactation!

- **Directly reinforces importance of human milk:**
  - Doctors value this enough to pay for BDM while PTF free!
  - Other women pumping for your child – you can too!!
- **Preemies leave hospital having never taken formula!**
- **Mother’s aware of temporary supply:**
  - They will need to bring-up their production.
  - Segue to mother’s own milk prior to discharge.