Mammalian lactation patterns and milk composition have evolved over millions of years to support the survival, growth, and development of mammalian offspring.

- Largest brain of all mammals
- Because the brain is large, the head is large
- If the human fetus were to remain in utero and reach the maturity of other mammals, the head would be too large for normal delivery
- Thus, the human is the most “immature” of all mammals at the time of term birth

Human Milk has evolved to:

- Grow the human body slowly
- Lowest protein of all mammalian milk
- Grow the human brain rapidly in a highly specific manner
- High lactose and triglycerides for energy
- Uniquely concentrated fats that facilitate optimal structural development and myelinization
- Protect, develop and program many body systems through synergistic functions: immunomodulatory, anti-inflammatory, gut-colonizing, and epigenetic mechanisms
Breastfeeding and Early White Matter Development

133 Term Infants followed with neuroimaging and neurodevelopmental testing from 10 months-4 years of age

- Relationship between duration of breastfeeding, white matter microstructure, and neurodevelopmental testing

<table>
<thead>
<tr>
<th>Participants</th>
<th>Infant Malformations</th>
<th>White Matter Scores</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breastfeeding</td>
<td>WBBX 3rd percentile 80%</td>
<td>80%</td>
<td>8.24</td>
</tr>
<tr>
<td>Infant Malformations</td>
<td>0.13</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>White Matter Scores</td>
<td>0.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p Value</td>
<td>0.68</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rush University Medical Center, Chicago

- Regional perinatal center responsible for 25,000 live births
- 72-bed NICU
- Family-centered care
- 24-hour visitation
- Care by parent
- Parents attend medical rounds

RUSH MOTHERS’ MILK CLUB
Practice and Research Initiatives

- Imbedded in the NICU is the lactation/human milk feeding program
- Practice: Families receive state-of-the-art, evidence-based lactation care by the entire NICU staff
- Research: Families and infants serve as subjects in the team’s internally and externally funded research projects

Proactive Lactation Care is Provided by all NICU Personnel

Toolkit for Translating the Evidence about Human Milk for NICU Infants into Best Clinical Practices

Welcome to the Rush Mothers’ Milk Club

CONSERVE Human Milk

My Milk Things for Me
Initial Visits to New Mothers Take about 1 Hour

Each BPC Maintains a Photo Album of Her or His NICU Baby from Birth through Current Age

Discussion focuses on impact of human milk on the infant's outcome

BPCs assist with the first pumping session for all new NICU mothers

• Proper use of the pump is taught
• Breast shield sizing is done
• Pump hygiene is reviewed
• Pump rental is organized

Weekly Mothers’ Milk Club Luncheons Provide a Forum to “Share the Science” about Human Milk and Lactation

Original Research about the Impact and Effectiveness of Breastfeeding Peer Counselor Practice

Beverly Rossman, PhD, RN

Journal of Human Lactation

The Role of Peer Support in the Development of Maternal Identity for "NICU Moms"
Helping Mothers Establish and Maintain an Abundant Milk Supply is a Major NICU Priority

Helping a new mother use the breast pump at her baby’s bedside in the NICU

Stages of Lactation and Implications for Breast Pump Dependent Mothers

Initiation

Coming to Volume

Maintenance

The Rush Mothers’ Milk Club breastfeeding peer counselors shipping 273 kilograms of pumped milk to a piglet laboratory for research purposes

Initiation of Lactation: Mechanisms and Best Practices

• Profound hormonal, anatomical and milk composition changes
• Mammary gland transitions from “preparing to make milk” (secretory differentiation) to “synthesizing and secreting milk (secretory activation, lactogenesis II)
• “One-time event that is either achieved or not achieved
• Interference impacts the “initiation of lactation”, not “the milk supply”

Prolactin

Progesterone

Endocrine Control of Lactogenesis I and II


Coming to Volume: Mechanisms and Best Practices

• Period between the onset of lactogenesis II and achieving a threshold milk volume that is sufficient to maintain lactation
• Autocrine control of lactation begins
• Milk must be removed effectively and efficiently in order to be replaced
• Problems that interfere with milk removal can have a long-lasting impact on lactation performance
Suckling-Induced Prolactin Surge

Pumping Begins

Prolactin concentration increases 2-3 times over baseline (more rapid milk synthesis)

If available milk is not removed, the feedback inhibitor of lactation (FIL) works at the level of the individual breast to down-regulate milk synthesis

FIL


Evidence to Practice: Coming to Volume is a critical period, so it should be approached proactively and interventions during this time should be given funding priority

Every mother is seen every day during this period to ensure milk expression is progressing optimally

Nutrition Begins Pre-Birth with the Swallowing of Amniotic Fluid in Utero

- High concentrations of growth factors target the GIT epithelial cells
- Weight of intestinal mucosa per kg of body weight increases 146%
- Fetus swallows up to 750 mL/d

Colostrum is the transition from intrauterine to extrauterine nutrition in mammals

- In composition and bioactivity, colostrum is more like amniotic fluid than it is like mature milk:
  - ≥13 identified growth factors target GIT
  - Growth factors function synergistically, in that the combined effect is greater than that of individual factors
  - Epidermal Growth Factor (EGF) is > 1000 times higher in colostrum than maternal serum
  - EGF is absorbed intact from the GIT, and may affect growth of distal organs
  - EGF receptors in infant GIT and lungs
  - 68 cytokines in human colostrum, changing over first few days after delivery


**Distinct Gene Expression at Different Stages of Lactation**

- Colostrum
- Transitional Milk
- Mature Milk

**Oropharyngeal Administration of Colostrum**

- Cytokines in colostrum may be absorbed via the OFALT system and provide systemic protection
- Oligosaccharides may interfere with adherence of pathogens to mucous membranes in the oral cavity and oropharynx and protect from VAP
- BOTH mechanisms would be additive to intestinal effects of colostrum

Rodriguez, Meier, Greer, Zeller, 2009; Rodriguez et al., 2010; Rodriguez et al, 2011; Seigel et al., 2013; Lee et al, 2015

**Several lines of evidence suggest that health and neurodevelopmental outcomes for premature infants have their origins in the immature gut**

- Colonization with commensal bacteria
- Down-regulation of inflammation and oxidative stress
- Programming immunomodulatory and metabolic pathways

Keunen et al., 2015; Collado et al., 2012; Al-aasmah et al., 2012

Copyright Rush Mothers' Milk Club, 2011.

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Several lines of evidence suggest that artificial milks exert a separate, detrimental effect on the growth, maturation and integrity of the gut epithelium.


Martin et al. Human milk is a source of lactic acid bacteria for the infant gut. J Pediatr 2003; 143: 754-8

Cabrero-Rubio et al. The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery. AJCPEN 2012, 61(3): S4-551.


The Rush Research Team
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Lou Fogg, PhD
Judy Janes, RN, IBCLC
Paula Meier, PhD, RN
Kousiki Patra, MD

Health Outcomes and Cost of Human Milk Feedings for VLBW Infants
• Prospective cohort study
• 630 VLBW Infants enrolled Feb, 2008-Jan, 2013
• Variables Included:
  • Dose and Exposure Period of HM Feedings
  • Health Outcomes
    • Enteral feed intolerance
    • Late onset sepsis
    • Necrotizing enterocolitis
    • Chronic lung disease
    • Retinopathy of prematurity
    • Perventricular leukomalacia
    • Growth velocity (wt, length, HC)
• Cost of NICU Care
• Maternal and Institutional Costs of Providing HM

NIH grant: NRO10009, 2007, Meier, PI

Health Outcomes and Cost of Human Milk Feedings for VLBW Infants*
• 95% of eligible infants were enrolled
• 98% received some HM from the mother (3 mLs - 28,229 mLs)
• Days 1-14:
  • Median Cumulative HM-PCT = 100%
  • 76.8% received exclusive HM
• Days 1-28:
  • Median Cumulative HM-PCT = 98%
  • 59.7% received exclusive HM
• NICU hospitalization:
  • Average HM-DD = 61 mL/kg/d
  • Average HM-PCT = 48.6%

NIH grant: NRO10009, 2007, Meier, PI

### Characteristics of the Mothers

- **Age:** 27.2 ± 6.5
- **Education:** 13.2 ± 2.8
- **Pre-pregnancy BMI:** 28.7 ± 7.5
- **Black:** 30.1
- **Hispanic:** 27.7
- **Caucasian:** 26.7
- ** Cesarean delivery:** 65%
- ** Major morbidity:**
- ** Hypertension:** 31.3%
- ** Diabetes:** 8.3%
- ** Mental Health Dx:** 17.1%

### Characteristic (N = 430)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD or N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant Birthweight (g)</td>
<td>1046 ± 256</td>
</tr>
<tr>
<td>Infant Gestational Age (wks)</td>
<td>28.0 ± 2.4</td>
</tr>
<tr>
<td>Length of NICU Stay (d)</td>
<td>73.8 ± 41.9</td>
</tr>
<tr>
<td>Male Gender</td>
<td>229 (53%)</td>
</tr>
<tr>
<td>Maternal Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>223 (52%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>114 (27%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>83 (19%)</td>
</tr>
<tr>
<td>Maternal WIC Eligibility</td>
<td>298 (70%)</td>
</tr>
</tbody>
</table>

### Any Formula (< 100% HM-PCT) During Days 1-14 Post-Birth Increases the Risk of NEC

- The Risk of NEC was modeled using a propensity score to control for variables that impact NEC (e.g., days NPO, antibiotic use, TPN, etc.)
- Various HM variables were added to the statistical model AFTER controlling for the risk of NEC. Formula by day of life 14 increases risk of NEC (OR = 3.0, p = 0.03)
- Each additional 1 ml/kg/d of HM during days 1-14 decreases NICU costs by $560.

<table>
<thead>
<tr>
<th>Decision Variable</th>
<th>Marginal effect (in USD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEC</td>
<td>$43,897</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HM-DD for Days 1-14</td>
<td>-$560</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Model controls for birth weight, race, gender, and propensity score.
Exposure Period of NICU Hospitalization: Human Milk Reduces the Incidence of Chronic Lung Disease (CLD) and the Duration of Hospitalization

- 203 symmetrically-grown AGA VLBW infants
- CLD and PGF measured at 36 wks PMA (or prior to NICU DC, if earlier)
- Dose of HM grouped into quartiles (% of enteral feedings = HM during the NICU)
- 43% reduction in the risk of CLD with each increasing HM quartile over the NICU hospitalization

Patel et al., podium presentation, ESPGHAN, Jerusalem, June 2014

Does High-Dose HM feeding in the NICU translate into long-term health and neurodevelopmental outcomes?

- Direct Impact
  - Nutrition: LCPUFAs, cholesterol, IGF-1, glutamine
  - Gut-colonizing
  - Anti-inflammatory, anti-oxidant
  - Oligosaccharides, stem cells
  - Immunomodulatory
  - Metabolic programming

- Indirect Impact
  - Reduction in NEC, sepsis, CLD

Neurodevelopmental Outcome at 20 months, CA N = 241

<table>
<thead>
<tr>
<th>HM-DD Quintiles</th>
<th>1 (n 37)</th>
<th>2 (n 46)</th>
<th>3 (n 50)</th>
<th>4 (n 53)</th>
<th>5 (n 52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HM-DD (mL/kg/d)</td>
<td>0-7</td>
<td>7-27</td>
<td>27-79</td>
<td>80-116</td>
<td>116-156</td>
</tr>
<tr>
<td>Cognitive</td>
<td>90 ± 13</td>
<td>94 ± 11</td>
<td>94 ± 13</td>
<td>94 ± 11</td>
<td>98 ± 12</td>
</tr>
<tr>
<td>Language</td>
<td>77 ± 16*</td>
<td>81 ± 13</td>
<td>83 ± 17</td>
<td>85 ± 16</td>
<td>87 ± 15*</td>
</tr>
<tr>
<td>Motor</td>
<td>88 ± 12</td>
<td>87 ± 17</td>
<td>90 ± 14</td>
<td>92 ± 12</td>
<td>93 ± 11</td>
</tr>
</tbody>
</table>

* p<0.05

Human Milk from an Economic Perspective

Cost of Human Milk vs Formula and Donor Human Milk Feeding

- The “upstart” costs of a human milk feeding program in the NICU are thought prohibitive
- Mothers do not maintain adequate milk output because of the lack of evidence-based lactation services that are specific to breast pump dependent mothers
- Is provision of these services cost-effective?

Johnson et al., 2013

Tricia Johnson, PhD

Economic Benefits and Costs of Human Milk Feedings: A Strategy to Reduce the Risk of Prematurity-Related Morbidities in Very-Low-Birth-Weight Infants

- The institutional cost of providing variable ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

- The Institutional Cost of Providing Variable Ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

- The Initial Maternal Cost of Providing Variable Ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

- The Initial Maternal Cost of Providing Variable Ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

- The Initial Maternal Cost of Providing Variable Ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

- The Initial Maternal Cost of Providing Variable Ratios of Human Milk for Very Low Birth Weight Infants in the Neonatal Intensive Care Unit
Donor Milk is a “Do no Harm” Option

Bioactive and Nutritional Limitations in Donor Human Milk

<table>
<thead>
<tr>
<th>Component</th>
<th>Pasteurization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular</td>
<td>Abolished</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>57-80% reduction</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>Up to 48% reduction</td>
</tr>
<tr>
<td>(sIgA, IgG)</td>
<td></td>
</tr>
<tr>
<td>Antioxidant</td>
<td>Significant reductions</td>
</tr>
<tr>
<td>Properties</td>
<td></td>
</tr>
<tr>
<td>Adiponectin</td>
<td>33% reduction</td>
</tr>
<tr>
<td>Insulin</td>
<td>46% reduction</td>
</tr>
<tr>
<td>Soluble CD14</td>
<td>88% reduction</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Different profile</td>
</tr>
<tr>
<td>Amylase</td>
<td>15% reduction</td>
</tr>
<tr>
<td>Lipase</td>
<td>Abolished</td>
</tr>
</tbody>
</table>


Leptin concentration decreases dramatically with the duration of lactation


Supporting Breastfeeding in the Neonatal Intensive Care Unit
Rush Mother's Milk Club as a Case Study of Evidence-Based Care

In Your Hands

February 2013

www.rushmothersmilkclub.com