Benefits and Challenges of the Use of Human Milk for Premature Infants

William Rhine, M.D.
Professor, Stanford School of Medicine
Medical Director, Neonatal ICU, Lucile Packard Children’s Hospital
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• Dr. Rhine has indicated that he has nothing to disclose
Talk Objectives

• Review the benefits of human milk for all infants
• Describe the role of human milk in meeting the unique physiologic and nutritional needs of premature infants
• Share strategies for optimizing the use of human milk for premature infants
• Review nutritional monitoring of premature infants
Clinical Impact of Human Milk for Term Infants—Short-term

- Respiratory – URI (60% reduction), LRI (72-77% reduction), RSV bronchiolitis (74% reduction)
- SIDS – 36% reduction
- Otitis media – 23-50% reduction (77% reduction in recurrent OM)
- Allergies – atopic dermatitis (27-42% reduction)
- GI – gastroenteritis (64% reduction)

Clinical Impact of Human Milk for Term Infants—Long-term

- GI – celiac disease (52% reduction); inflammatory bowel disease (31% reduction)
- Allergy – asthma (26-40% reduction)
- Obesity – 24% reduction
- Diabetes – Type 1 (30% reduction); Type 2 (40% reduction)
Clinical Impact of Human Milk for Term Infants–Long-term

- Cancer – leukemia (15% reduction AML, 20% reduction ALL)
- Cardiovascular – reduced BP by 3.2 mmHg - more than weight loss (2.8 mmHg), alcohol reduction (2.1 mmHg), salt restriction (1.3 mmHg), exercise (0.2 mmHg)
- Neurodevelopmental outcomes – improved IQ scores and teacher ratings
- Maternal benefits include reduction in diabetes, HTN, breast and ovarian cancer

Gold Standard of Growth for Premature Infants

• The ideal goal of providing nutrition to premature infants is to approximate the \textit{in utero} growth of a normal fetus of the same post-conceptional age
  – Body weight and length
  – Body composition and organ development

Unique Nutritional Aspects of the Premature Infant

• Higher organ: muscle mass ratio
• Higher rate of protein synthesis and turnover
• Greater oxygen consumption during growth
• Higher energy cost due to transepidermal water loss
• Higher rate of fat deposition
• Prone to hyperglycemia
• Higher total body water content
Unique Nutritional Aspects of Premature Infants - Brain Growth

Brain growth over 8 weeks:
- At 28 wks. 100% Increase
- At term 40% Increase
- At 3 mo. 25% Increase

Preventing Feeding-Related Morbidities in Premature Infants

- Necrotizing enterocolitis
- Osteopenia/rickets of prematurity
- Vitamin and mineral deficiencies
- Feeding intolerance
- Prolonged TPN and related cholestasis
- Nosocomial infections
- Prolonged hospitalization
Optimal Growth of Premature Infants Influences Long-term Health and Disease

- Premature infants receiving breast milk are less likely to have excessive growth
- Adverse effects of excessive growth acceleration:
  - Obesity
  - Elevated blood pressure
  - Insulin resistance and diabetes
  - Cardiovascular mortality

Clinical Benefits of Human Milk for Preterm Infants

• Improve Host Defense – reduced infections
• Promote Gastrointestinal Development
• Provide Special Nutritional Needs
• Improve Neurodevelopmental Outcome
• Support Physically & Psychologically Healthier Mother
Human Milk Provides Protection from Infection in Premature Infants

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>Fortified BM</th>
<th>Formula</th>
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<tbody>
<tr>
<td>Oxygen Rx (days)</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>NEC</td>
<td>1.6%</td>
<td>13%</td>
</tr>
<tr>
<td>Late-onset sepsis</td>
<td>31%</td>
<td>48%</td>
</tr>
<tr>
<td>NEC or sepsis</td>
<td>31%</td>
<td>54%</td>
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GI Benefits of Human Milk for the Premature Infant

• Gastrointestinal development
  – Reduces intestinal permeability faster
  – Induces lactase activity
  – Multiple factors to stimulate growth, motility and maturation of the intestine
  – Human milk empties from the stomach faster than artificial milks
  – Less residuals and faster realization of full enteral feedings
Nutrition of Premature Infants: Cognitive Development

- Many studies have evaluated impact of receiving breast milk (especially fortified) on cognitive development, specifically higher IQ or Bayley score (MDI improved 0.53 per 10ml/kg/day of breast milk).
- Benefit was strongest for children of low birth weight and in males.
- Improvement in developmental achievements associated with breast milk persisted at least through adolescence.
- Postnatal growth lag and suboptimal HC associated with neurological and sensory handicaps and poor school performance.

Human Milk Fortification

- Expressed human milk has variable nutritional content, and does not provide adequate nutrition for premature infants
- Must fortify human milk to provide adequate energy, protein, minerals and vitamins for the growing premature infant
- Starting fortifier before being on full feeds (40-100 ml/kg/day total fluids) will allow for transition from parenteral to enteral nutrition without accumulating deficits
## Human Milk Fortification

<table>
<thead>
<tr>
<th></th>
<th>HM</th>
<th>Pro</th>
<th>Sim</th>
<th>Enf</th>
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<tbody>
<tr>
<td><strong>Energy (kcal)</strong></td>
<td>67</td>
<td>83</td>
<td>79</td>
<td>81</td>
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<tr>
<td><strong>Protein (g)</strong></td>
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<td>2.3</td>
<td>2.3</td>
<td>2.5</td>
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<tr>
<td><strong>Carbohydrate (g)</strong></td>
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<td>7.3</td>
<td>8.2</td>
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<tr>
<td><strong>Fat (g)</strong></td>
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<td>4.9</td>
<td>4.1</td>
<td>4.9</td>
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<tr>
<td><strong>Calcium (mg)</strong></td>
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<td>110</td>
<td>138</td>
<td>115</td>
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<tr>
<td><strong>Phosphorus (mg)</strong></td>
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<td>59</td>
<td>78</td>
<td>63</td>
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<tr>
<td><strong>Osmolality§</strong></td>
<td>290</td>
<td>&lt;360*</td>
<td>385</td>
<td>325</td>
</tr>
</tbody>
</table>

*estimated

**HM**=Human Milk; **Pro**=Prolacta; **Sim**=Similac; **Enf**=Enfamil

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Human Milk Fortification

• Babies randomized to receive human milk-based fortifier had 50% reduction in medical NEC (p<0.03) and 90% reduction in surgical NEC (p<0.007) compared to bovine-based

• No difference in feeding intolerance or NEC in those infants receiving human milk-based fortifier starting at 40 mL/kg/day of feeds vs. 100 mL/kg/day

Reduced NEC with HM-Based Fortifier

Human Milk-Based Fortifier Cost/Benefits

• Recent cost analysis predicts savings of 3.9 NICU days and $8,167 per patient, based on cost estimates of medical and surgical NEC within California 2007 dataset

• Factors that influence costs include patient selection, duration of fortifier use, and baseline NEC rate

• Calculator program to estimate unit-specific costs/benefits available at vtoxford.org NICQpedia

• Estimated cost per patient at LPCH=$3,750

Use of Human Milk for Premature Infants—Optimizing Commitment

- Need to start education around human milk and pumping before delivery—by Obstetrical Services and during Neonatology consultations
- Hospital policy support of WHO/UNICEF Ten Steps to Successful Breastfeeding (<5% of hospitals support 9-10 steps) for all babies
- Resource allocation includes facilitating breast pump availability, appropriate milk storage
- Post partum and NICU staff education and support of breastfeeding and pumping, as directed by adequate lactation consulting services

Human Milk Availability - Recent Studies

• Best way of optimizing milk production is a combination of hand expression and breast pump  

• This combination also increases the caloric content of human milk available to premature infants  

• Bundle of practices to improve breast milk availability can be found at cpqcc.org – these were associated with relative 13% improvement in % of VLBW infants being sent home on breast milk  
Challenges to the Use of Mother’s Breast Milk for Premature Infants

• Neonatal transports
• Maternal diseases/colonization
• Maternal medications
• Concerns about CMV
• Safety of transport and storage of maternal milk
Alternatives to Specialty Fortifiers

• Protein fortifiers-liquid formulation recently available; lack many nutrients including Ca$^{+2}$ and phosphorus that may be necessary for optimal fortification of breast milk

• Thickeners-recent warning by FDA against use of Simply Thick thickener for VLBW infants due to association with NEC; expressed concern that xanthan gum may affect GI flora

Nutritional Care/Outcomes in Premature Infants-LPCH at Stanford

- Feeding pathway and nutrition bundle used at Stanford described by McCallie et al.
- Encourage use of human milk and fortification
- “Early” TPN
- GI priming/trophic feeds
- Defined feeding advance schedule
- Standardized fortification
- Consensus around residuals, feeding intolerance

Human Milk Use and Fortification at LPCH

- Over 90% of the mothers of our VLBW infants provide breast milk; if mother’s milk not available, we recommend banked breast milk.
- Per FDA recommendations, we seek to avoid powdered fortifier products, which until recently limited options.
- In past 2+ years we have used Prolacta fortifier up to 1500 gm/34-35 weeks gestational age, then transitioned to other liquid fortifiers.
- 85% of inborn VLBW infants are discharged on at least some breast milk.
LPCH vs. VON
Inborn Growth Velocity

Graph showing the growth velocity for LPCH and VON from 2007 to 2011, with data points for inborn, rate, 75th percentile, and 25th percentile.
LPCH vs. VON
Inborn NEC
Nutritional Practices Supporting Breast Milk-Individual Patient Level

• Careful monitoring of nutrition
  – Intake-fluid volume, calories, protein
  – Growth-measuring weight, length (using board), head circumference

• Adjust intake volume to anticipate growth instead of reacting to decreases in growth rate

• Track breast milk production - use pumping log

• No definitive evidence about selection and benefits of nutrition lab monitoring, e.g. alkaline phosphatase
Nutritional Practices Supporting Breast Milk-Individual Patient Level

• Should aim for weight gain of 15-18+ gm/kg/day during growth phase after weight nadir
• Premature infants being discharged home should have careful follow-up of their nutrition and growth
• Nutritional supplementation for premature infants should be continued for 3-6 months to optimize growth and development
Nutritional Practices Supporting Breast Milk-NICU Level

• Average weight gain for VLBW infants*
• NEC rate for VLBW infants*
• Track and benchmark percentage of babies starting on human milk (mom’s or banked)
• Track and benchmark percentage of babies discharged on human milk*
• Other nutritionally-related measures include day of first feed, TPN days, length of stay*

* Data available on VON, Pediatrix NICU databases
Alternatives to Mother’s Breast Milk

• Banked breast milk-usually in conjunction with HMBANA milk bank
  – Usually selected population for use, e.g. VLBW infants
  – Informed assent/consent should be obtained describing pros and cons of donated milk compared to formulas

• Special premature formulas-superior to term formulas as far as growth; nutritional content better meets the needs of premature infants
Summary

• Nutrition is critically important for the optimal growth and development of premature babies
• Ideal food for premature infants is mother’s breast milk that should be fortified, or donated breast milk (fortified prn), or else premature specialty formula
• Successful use of breast milk depends on institutional promotion and support and maximizing availability
• Should have standardized approach based on providing optimal nutrition, mainly human milk for premature infants; at Stanford this has been associated with improved growth velocity and reduced NEC