Necrotizing Enterocolitis

- Necrotizing enterocolitis (NEC) is the most common and serious GI disorder affecting neonates, occurring in 5-8% of very-low-birth-weight premature infants. Babies with NEC present with abdominal distension, feeding intolerance, and an abnormal x-ray.
Necrotizing Enterocolitis
Economic Burdens of NEC

- Mortality
- Morbidity
  - Strictures
  - Short gut syndrome
  - Intestinal Transplantation
  - Quality of life
Preventing NEC?

- Cause of NEC is multifactorial.
- Infants fed their own mother’s milk have approximately 50% reduction in NEC.
- Donor human milk has also been shown to reduce NEC in at risk infants.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Excess Risk* (%) (95% CI)</th>
<th>Comparison Groups</th>
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</thead>
<tbody>
<tr>
<td><strong>Among full-term infants</strong></td>
<td></td>
<td></td>
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<tr>
<td>Acute ear infections (otitis media)</td>
<td>100 (56, 233)</td>
<td>EFF^ vs. EBF^ for 3 or 6 mos</td>
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<tr>
<td>Eczema (atopic dermatitis)</td>
<td>47 (14, 92)</td>
<td>EBF &lt;3 mos vs. EBF ≥3 mos</td>
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<tr>
<td>Diarrhea and vomiting (gastrointestinal infection)</td>
<td>178 (144, 213)</td>
<td>Never BF^ vs. ever BF</td>
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<tr>
<td>Hospitalization for lower respiratory tract diseases in the first year</td>
<td>257 (85, 614)</td>
<td>Never BF vs. EBF ≥4 mos</td>
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<tr>
<td>Asthma, with family history</td>
<td>67 (22, 133)</td>
<td>BF &lt;3 mos vs. ≥3 mos</td>
</tr>
<tr>
<td>Asthma, no family history</td>
<td>35 (9, 67)</td>
<td>BF &lt;3 mos vs. ≥3 mos</td>
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<tr>
<td>Childhood obesity</td>
<td>32 (16, 49)</td>
<td>Never BF vs. ever BF</td>
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<tr>
<td>Type 2 diabetes mellitus</td>
<td>64 (18, 127)</td>
<td>Never BF vs. ever BF</td>
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<tr>
<td>Acute lymphocytic leukemia</td>
<td>23 (10, 41)</td>
<td>Never BF vs. &gt;6 mos</td>
</tr>
<tr>
<td>Acute myelogenous leukemia</td>
<td>18 (2, 37)</td>
<td>Never BF vs. &gt;6 mos</td>
</tr>
<tr>
<td>Sudden infant death syndrome</td>
<td>56 (23, 96)</td>
<td>Never BF vs. ever BF</td>
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<tr>
<td><strong>Among preterm infants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>138 (22, 2400)</td>
<td>Never BF vs. ever BF</td>
</tr>
<tr>
<td><strong>Among mothers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>4 (3, 6)</td>
<td>Never BF vs. ever BF (per year of breastfeeding)</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>27 (10, 47)</td>
<td>Never BF vs. ever BF</td>
</tr>
</tbody>
</table>

* The excess risk is approximated by using the odds ratios reported in the referenced studies.
^ CI = confidence interval.
^ EFF = exclusive formula feeding.
^ EBF = exclusive breastfeeding.
^ BF = breastfeeding.
Preventing NEC?

- However human milk alone does not supply all nutrients needed for preterm infants.
- Fortification is necessary.
- Most fortifiers are bovine derived.
- Prolacta© is a commercially available human milk fortifier, but it is very expensive.
Preventing NEC?

- A recent study of exclusive human milk plus human derived fortifier compared to human milk plus bovine derived fortifier found:
  - 50% reduction in the incidence of NEC, and
  - 90% reduction in surgical NEC in the group fed an exclusive human milk based diet.
- NNT to prevent one case is 10; to prevent one case of surgical NEC or death is 8.
“Human milk is a complex, specialized and sophisticated human infant support system that provides protection, information, and nutrition to the nursing infant.”
Protective Bioactive Factors

- Bifidus factor
- Lysozyme
- Cytokines and Interleukins
- Lactoferrin
- Nucleotides
- Oligosaccarides
- Vitamins A, C, E
- Prolactin
- Cortisol, Thyroxine, Insulin, Growth Factors:

Purposes:
- Promote gut maturation and development of intestinal host-defense
- Promote growth of gut probiotics
- Antibacterial, antiviral effects
- Enhance development of T- and B-cells
- Anti-inflammatory and scavenge free radicals
Breastmilk contains live cells

**Macrophages** – phagocytosis and killing of bacteria and fungi, amplification of T-cell reactivity

**PMN’s** – Likely primary function is as defense in mammary tissue

**T and B Lymphocytes**
- Exclusively breastfed infant has larger thymus
- T’s and B’s in breastmilk are reactive against organisms that can invade the intestinal tract
Admissions to NICU 501-1500 Grams

Year | Admissions to NICU 501-1500 Grams
--- | ---
2002 | 75
2003 | 78
2004 | 72
2005 | 80
2006 | 70
2007 | 65
2008 | 90
2009 | 68
2010 | 70
Infants With Birthweight < 1500 Grams
Breastfeeding Status at Time of Discharge
Any Exposure to Breast Milk

2002 2003 2004 2005 2006 2007 2008 2009 2010
Infants < 1500 Grams
Formula Only at Time of Discharge

0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
2002 2003 2004 2005 2006 2007 2008 2009 2010
Necrotizing Enterocolitis
Infants < 1500 Grams
Necrotizing Enterocolitis

Graph showing the percentage of necrotizing enterocolitis cases from 1991 to 2013 for different categories: GBMC, VON, VON 25, and VON 75.
Infants 501-1500 Grams Discharged Home
Any Human Milk by Birth Year
Infants 501-1500 Grams Who Died – Any Human Milk by Birth Year

GBMC

1 Network Quartiles (0)
Economic Burdens of NEC

- There were 499 infants in Maryland who developed NEC between 2005 and 2009.
- There were 85 cases of NEC in 2010.
- VLBW infants with NEC increase length of stay in NICU from 11 to 48 days.
- Excess NICU costs are $74,000 for one case of medical NEC and as much as $198,000 for a case surgical NEC.
Human Milk Benefits

Infants <=28 Weeks GA fed 100% human milk reduced NICU stay by 3.9 days: $8,167 (95% CI $4,404-$11,930) (p<0.0001). Cost of formula, fortifier, HM included.*

100% HM yielded a 63% lower rate of NEC and an 86% reduction of surgery for NEC.**

• We presented our data to Women’s Board of the Hospital for Women at GBMC in 2012.

• The Board generously provided a 3 year challenge grant to develop and institute a human milk bank for vulnerable babies in NICU.

• The Milk Bank began to operate January 2014 after licensure and inspection by the State of Maryland.
CRITERIA FOR USING BANKED DONOR HUMAN MILK:

- An infant needs to meet at least one of the following criteria to qualify.
  - Infants under 1250 gms
  - Infants under 29 weeks
  - Extreme feeding intolerance
  - Status post neonatal necrotizing enterocolitis
Fortification with PROLACTA®

- Prolacta is added to human milk as a fortifier for infants receiving human milk when feedings have been advanced to between 40 and 100 mL/kg/day. Prolact+4 is initially used to fortify the milk to 24 kcal/oz.
If there is poor growth on human milk fortified with Prolact+4, consider using Prolact+6 at 160mL/kg for 1 week.

If there continues to be poor growth, options include the following:

- OPTION 1: Increase milk and Prolact+6 to 170–175mL/kg
- OPTION 2: Use human milk and Prolact+8 at 150mL/kg
- OPTION 3: Use human milk and Prolact+10 at 130mL/kg
TRANSITIONING OFF PROLACTA

- Transition off Prolacta at 33 – 34 weeks PMA and weight approaching 1800g

- If mother’s own milk is available, transition to mother’s milk plus liquid Human Milk Fortifier over 3-4 days

- If mother’s own milk is not available, transition to 24 calorie premature formula or a 22 calorie formula 3-4 days:
To Date:

- 16 babies birth weight 501-1250 grams have received an exclusive human milk diet.
- Birth weights ranged from 580 to 1220 grams.
- Gestational age ranged from 23.1 to 33.2 weeks.
- There has been 0 cases of medical NEC, and 1 case of surgical NEC.
Challenges going forward:

- Maternal acceptance?
- Continued funding?
- Reimbursement?
- Legislation?
- Supply of donor milk?
In our regular nursery:

- 88% initiated breastfeeding in the hospital
- 59% breast fed exclusively while in the hospital (41% supplemented)
Newborn Nursery

Exclusive Breastfeeding

Date

% of Exclusive Breastfeeding


GBMC