Addressing the Nutritional Emergency of the Preterm Infant

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- Jae Kim
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- Speaker bureau for Abbott Nutrition

The Nutritional Emergency of the Preterm Infant

Why is this an emergency?

- Estimated placental transfer (second and beginning of third trimester)
- 8 to 10 mg/kg/min of glucose
- 3.6 to 4.8 g/kg/day of amino acids

Leaving the placental pipeline

Why is this an emergency?

- Estimated placental transfer (second and beginning of third trimester)
- 8 to 10 mg/kg/min of glucose
- 3.6 to 4.8 g/kg/day of amino acids

Define the problem
- Why is this an emergency?
- Consequence of emergency?
- Brain development
- Metabolism
- Growth
- Bones

Matching In Utero Growth

Zeigler et al., 1986

<table>
<thead>
<tr>
<th>WEIGHT CLASS</th>
<th>GROWTH (G/KG/DAY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-700</td>
<td>21</td>
</tr>
<tr>
<td>750-995</td>
<td>29</td>
</tr>
<tr>
<td>1000-1200</td>
<td>19</td>
</tr>
<tr>
<td>1250-1600</td>
<td>10</td>
</tr>
<tr>
<td>1600-1800</td>
<td>19</td>
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</tbody>
</table>

Zeigler et al., 1986
Vulnerable Period of Brain Growth

- 5% gain every 48 to 72 hours

Dobbing and Sands. Early Hum Dev 1979;3:79

Human brain-growth velocity expressed as a percentage of adult brain weight gained per month

http://en.citizendium.org/images/d/d6/Journalpmed.gif

Postnatal Malnutrition and Growth Retardation: An Inevitable Consequence of Current Recommendations in Preterm Infants?


Extrauterine Growth Failure
Consequences of the emergency


Extrauterine Growth Restriction: Never Catching Up


CATCH-UP GROWTH OF HEAD CIRCUMFERENCE OF VERY LOW BIRTHWEIGHT, SMALL FOR GESTATIONAL AGE PRETERM INFANTS AND MENTAL DEVELOPMENT TO ADULTHOOD

Brandt et al. J Pediatr 2003;142:463-8

Duration of Extrauterine Growth Restriction

- 36 wk corr (Lemons, 2001)
- 36 wk corr (Morley, 2000)
- 8 years (Morley, 2000)
- 10 years??
AAP Recommendations

- The Committee on Nutrition of the American Academy of Pediatrics have recommended a caloric intake of 120 kcal/kg/day for children enterally fed and 80 to 100 kcal/kg/day for those parenterally fed, with a protein intake of 3.5 to 4 g/kg/day

Brain growth needs specific nutrition

- Protein
- Fats
  - LCPUFA
  - Fish oil
- Choline

High Energy and Protein Diet Increases Brain Growth in Term and Preterm Infants After Perinatal Brain Injury

- measured noninvasively with transcranial magnetic stimulation (TMS)
- axon diameter growth is a marker for growth of the pyramidal neuron as a whole
- there is a positive linear correlation between axonal diameter growth and the horizontal spread of the dendritic tree of layer pyramidal neurons of the motor cortex

Human milk and brain development

- Preterm infant feeding study
  - STANDARD = unsupplemented donated banked breast milk or a standard term formula
  - HIGH = great macro and micronutrients: 2.0g protein, 80 kcal/dl milk
  - 50 adolescents
  - IQ difference of 8.3 points
  - MRI scans were obtained (mean age 15 y 9 mo)
Effect of Early Human Diet on Caudate Volume and IQ

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th></th>
<th>P-value</th>
<th>95% confidence intervals</th>
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</thead>
<tbody>
<tr>
<td>Caudate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>3701(475)</td>
<td>4305(717)</td>
<td>&lt;.002</td>
<td>-805 to -187</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>3896(569)</td>
<td>4575(742)</td>
<td>&lt;.001</td>
<td>-880 to 235</td>
<td></td>
</tr>
</tbody>
</table>

Standard-nutrient (n=18)
High-nutrient (n=20)

STANDARD = unsupplemented donated breast milk or a standard term formula
HIGH = great macro and micronutrients: 2.0g protein, 80 kcal/dl


Early nutritional intervention and neurodevelopment

<table>
<thead>
<tr>
<th></th>
<th>VIQ</th>
<th>PIQ</th>
<th>FSIQ</th>
<th>VIQ</th>
<th>PIQ</th>
<th>FSIQ</th>
<th>VQ</th>
<th>FO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>94.8 (2.0)</td>
<td>96.1 (2.1)</td>
<td>94.4 (2.3)</td>
<td>95.5 (1.8)</td>
<td>94.1 (2.4)</td>
<td></td>
<td></td>
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<tr>
<td>High</td>
<td>101.0 (2.0)</td>
<td>96.8 (2.1)</td>
<td>98.9 (2.0)</td>
<td>101.5 (1.7)</td>
<td>97.0 (2.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>.03 (.03)</td>
<td>NS (NS)</td>
<td>.06 (NS)</td>
<td>.01 (.02)</td>
<td>NS (NS)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Human milk dose and IQ

Correlation coefficients, adjusted for maternal education and social class

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</thead>
<tbody>
<tr>
<td>Whole group; n = 50</td>
<td>Boys; n = 26</td>
<td>Girls; n = 24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIQ</td>
<td>0.274 (p = 0.054)</td>
<td>0.424 (p = 0.011)</td>
<td>0.366 (p = 0.043)</td>
<td></td>
</tr>
<tr>
<td>PIQ</td>
<td>0.365 (p = 0.273)</td>
<td>0.444 (p = 0.023)</td>
<td>0.006 (p = 0.968)</td>
<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>0.249 (p = 0.081)</td>
<td>0.570 (p = 0.014)</td>
<td>0.084 (p = 0.800)</td>
<td></td>
</tr>
</tbody>
</table>

• Human milk intake is correlated with brain white matter development
• Effects are only seen for males
• No significant relationships were seen in girls or with grey matter
• Gender differences for brain development are present in both animal and humans

Isaacs et al, Pediatr Res, 2009

Preterm infants are at risk of later cardiovascular disease

- Decreases vascular pliability, a surrogate marker of later cardiovascular disease

Singhal et al., Circulation 2004;109(9):1108-11.

Are preterm infants at risk of insulin resistance?

- Hofman et al.: preterm infants both AGA and SGA had reduced insulin sensitivity at prepubertal age
- Hovi et al.:  
  - a 6.7% increase in the 2-hour glucose concentration  
  - a 16.7% increase in the fasting insulin concentration  
  - a 40.0% increase in the 2-hour insulin concentration  
  - an 18.9% increase in the insulin-resistance index determined by homeostatic model assessment  
  - an increase of 4.8 mm Hg in systolic blood pressure


11/4/10
Are preterm infants at risk of insulin resistance?

- No relationship found between prematurity and later insulin sensitivity.
- Largest determinant was adult trunk fat and oral contraceptive use.
- SO, still not clear.

Willemsen et al., J Clin Endocrinol Metab 2009;94(5):1695-700.

GROWTH

Body Composition of the Fetus

- Initiation
- Advancement
- Fortification
- Stable Growth
- Postdischarge

Ziegler (1976)

Feeding Progression

Initiation

- Very Early (DOL 1)

- Early Trophic (DOL 3-5)
  - Tyson JE, Kennedy RA. Trophic feedings for parenterally fed infants. Cochrane Database Syst Rev. 2005

Feeding Intolerance

- Metoclopramide

- Erythromycin
  - Body temperature is best

- Body Position
  - Right side down

- Temperature
  - Body temperature in fever


Tyson JE, Kennedy KA. Trophic feedings for parenterally fed infants. Cochrane Database Syst Rev. 2005
Gastric residuals

- Volume
  - Definitions
  - absolute volume
  - % of feed
  - mL/kg
- Color
  - Blood, Bile, Undigested milk, Clear

Effect of Preterm Birth on Lactogenesis in Women


Vitamin D effects: the modern panacea

- Vit D deficiency
- 5-50% pregnant women
- 10-56% in breastfed infants
- Prevention of certain disease states
  - Infection
  - Cardiovascular disease
  - Autoimmune diseases (multiple sclerosis, rheumatoid arthritis)
  - Cancer (breast, ovarian, colorectal, prostate)
  - Type 2 diabetes mellitus

Vitamin D and bones

- Essential for the normal development of bones
- Vit D deficiency leads to demineralization of bone and rickets
- Premature infant at high risk for osteopenia, compounded if Vit D deficient
Vit D is inversely proportional to skin pigmentation

Vitamin D Insufficiency Is Prevalent among Pregnant African American Adolescents
- serum 25-OH vit D levels in 80 pregnant African American teens (<19yrs)
- vit D levels were 16.5 +/- 1.1y
- vit D insufficiency (<20ng/mL) evident in 46.25% of mothers
- vit D deficiency (<15ng/mL) in 21.25% of mothers


AAP Statement on Vitamin D
- It is now recommended that all infants and children, including adolescents, have a minimum daily intake of 400 IU of vitamin D beginning soon after birth.

Section on Breastfeeding and Committee on Nutrition

Human milk and optimal growth
- Human milk alone does not provide adequate nutrients for the rapidly growing preterm infant
- Deficiencies include:
  - Energy
  - Protein
  - Minerals
  - Vitamins
  - Trace elements
- There is a need to standardize human milk nutrition

Summary
- The preterm infant faces a serious nutritional emergency
- Adequate nutrition is essential for normal growth and brain development
- The impact of early nutrition affects later health
- Vitamin D has unique roles in the health of the mother-infant dyad