Post Discharge Nutrition in the VLBW Infant
Current Concepts in Neonatal Care
Hilton Head, South Carolina

David H Adamkin
Professor Of Pediatrics
Director of Division of Neonatology
Director of Nutritional Research
Rounsavall Chair of Neonatal Medicine
Co-Director of Neonatal Fellowship
University of Louisville
September 2014

Post Discharge Nutrition in the NICU
Graduate Baptist Hospital 14th Annual Pediatric Symposium
May 2015

David H Adamkin
Professor Of Pediatrics
Director of Division of Neonatology
Director of Nutritional Research
Rounsavall Chair of Neonatal Medicine
Co-Director of Neonatal Fellowship
University of Louisville

Disclosures

Investor in Medolac Laboratories

• I will not discuss any off-label use and/or investigational use in my presentation
Asymmetric EUGR with head sparing, POSTNATAL GROWTH FAILURE,
The Cumulative Protein Deficit*

Protein Deficit

Typical Protein Intake

Infants <750 gm

Infants 750-1000 gm

Reference Requirement*

Protein Intake gm/kg/day

Weeks after preterm birth

Weeks 1

Weeks 2

Weeks 3-12

*Graphic adapted from Ernst 2003 with reference requirement based on intrauterine protein accretion rate from Ziegler 1994

TOO FAT? TOO THIN?

Birth Weight / Preterm Birth/ Postnatal Growth Rate/ Body Composition / Fat-Lean

ADULT

Hypertension

Heart Disease

Obesity

Diabetes
Preterm Birth and Body Composition
@Term Equivalent Age (TEA): A Systematic Review and Meta Analysis

8 studies N=733 30wks gest, 1180gms BW. Term Controls 39.6wks 3410gms

<table>
<thead>
<tr>
<th>Preterm@TEA vs Term</th>
<th>Mean Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Increase % body fat</td>
<td>3%</td>
</tr>
<tr>
<td>2) Less Fat Mass</td>
<td>50g</td>
</tr>
<tr>
<td>3) Much less Fat Free Mass</td>
<td>460g</td>
</tr>
<tr>
<td>4) HC</td>
<td>-1.03cm</td>
</tr>
</tbody>
</table>

Less Lean with more similar Fat. Significant constraint on acquisition of lean tissue

Johnson et al Peds 2012

Altered Adiposity After Extremely Preterm Birth (Uthaya et al Ped Res 2005)

n = 38 <32weeks whole body MR adipose tissue
n = 29 Term

HYPOTHESIS:
• Quantity and distribution of adipose tissue are markers of morbidity risk
• Third trimester is a period of rapid adipose tissue deposition
• Preterm infants may be at risk of altered adiposity

Available energy stores in the fetus and newborn

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Wt (g)</th>
<th>Water (%)</th>
<th>Protein (%)</th>
<th>Lipid (%)</th>
<th>Glycogen (g)</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>690</td>
<td>86.6</td>
<td>8.8</td>
<td>0.1 (mg)</td>
<td>3.5</td>
<td>19.5</td>
</tr>
<tr>
<td>26</td>
<td>880</td>
<td>86.8</td>
<td>9.2</td>
<td>1.5 (mg)</td>
<td>4.5</td>
<td>123.8</td>
</tr>
<tr>
<td>28</td>
<td>1160</td>
<td>84.6</td>
<td>9.6</td>
<td>3.3 (mg)</td>
<td>5</td>
<td>356.2</td>
</tr>
<tr>
<td>40</td>
<td>3450</td>
<td>74</td>
<td>12</td>
<td>11.2 (mg)</td>
<td>15.3</td>
<td>3152.4</td>
</tr>
<tr>
<td>2 mo.</td>
<td>5450</td>
<td>63.7</td>
<td>11.4</td>
<td>22.4</td>
<td>25</td>
<td>9666</td>
</tr>
</tbody>
</table>


RESULTS
1) PT infants at term were significantly lighter and shorter, but no difference in HC vs Term born infants
2) PT had highly significant decrease in subcutaneous adipose tissue and significantly increased intraabdominal adipose tissue
3) Illness severity (days of level 1 and 2 ICU days, British Perinatal Med. criteria) was the principal determinant of increased intraabdominal adiposity.

Growth restriction with head sparing and preferential visceral fat deposition

Predominant Fat Mass Deposition in ELBW

- Imbalances in P/E
- Recovery from early malnutrition
- Stress/Illness
Growth Failure in VLBW Infants Is Associated With:

- Cumulative losses by hospital discharge of protein and energy
- Reduced body stores of nutrients (e.g., Fe, DHA, ARA)
- Reduced bone density
- Altered Adiposity

Embleton Ped 2001

Post Discharge Period Programming Growth and Improving Outcomes

- First year of life provides an important opportunity for human somatic and brain growth to compensate for earlier deprivation
- Opportunity to promote lean body mass
- Catch up growth to enhance neurodevelopment

Total Energy Expenditure per Kilogram and Total Energy Expenditure per Kilogram of Fat-free Mass in ELBW and Term Infants

N=24  Study at ~36 weeks  PCA  "p ≤ .01

Double labeled water  Guilfoyl et al.  J of Peds Nov 2008

Range of Protein Intakes  "g protein/kg/d at150 mL/kg/d"

Human milk provides ~1.5 g/kg/d of protein

- Term formula
- Nutrient-enriched formula
- Preterm formula 24
- High-protein preterm formula 24
- Requirement 2.8-3.2 g/kg/d

Postdischarge Formula Is Nutrient Enriched

- Protein
  - Postdischarge formula (22 cal/oz)
  - Term formula (30 cal/oz)

- Other Nutrients
  - Calcium
  - Phosphorus
  - Potassium
  - Iron
  - Zinc
  - Magnesium

Note: All data under 0.0 calorie.
Nutrient-Enriched Formula or Post-Discharge Formula (PDF) Contains

- Predominantly an increase in protein with extra energy
- Extra calcium, phosphorus, and zinc
- Additional vitamins and trace elements

Post-Discharge Strategy

- Replenish accumulated nutrient deficiencies
- Catch-up growth
- Promote lean body mass
- Bone Mineralization
- Enhance Neurodevelopment

---

Nutrient Intake Recommendations for VLBW Infants at NICU Discharge (per kg/d)

<table>
<thead>
<tr>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>PE Ratio [g/100]</th>
<th>Calcium (mg)</th>
<th>Phosphorus (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigo and Senterre (2006)</td>
<td>116 – 123</td>
<td>2.8 - 3.2</td>
<td>2.4 – 3.2</td>
<td></td>
</tr>
<tr>
<td>Rigo and Senterre (with need of catch up growth) (2006)</td>
<td>115 – 121</td>
<td>3 – 3.4</td>
<td>2.6 – 2.8</td>
<td></td>
</tr>
<tr>
<td>Ziegler</td>
<td>131</td>
<td>3.4</td>
<td>2.6</td>
<td></td>
</tr>
</tbody>
</table>

---

Evidence for Nutrient-Enriched Formulas for Premature Infants
Nutrient Enriched Formula leads to Increased Growth From 3\textsuperscript{rd} and 25\textsuperscript{th} Centiles to 25\textsuperscript{th} and 50\textsuperscript{th} over 9 Mos

Nutrient Enriched Formulas
Increased Bone Mineral Content to 9 mo CA

Preterm Infants Gained More Weight and Length When Fed Post Discharge Formula the First Year
Nutrient-Enriched Formula to 12 Months Corrected Age (CA) Improved Proportional Growth

- Gained more weight through 1 and 2 mo CA  
- Longer at 3 mo CA  
- <1250 g at birth  
  - Weighed more at 6 and 12 mo CA  
  - Longer at 6 mo CA  
  - Larger HC at term and 1, 3, 6, 12 mo CA  
- Appeared to be of particular benefit for growth of infants <1250 g and male infants  
- Compared with the infants fed term formula, those fed the nutrient-enriched formula consumed  
  - Less formula  
  - More protein  
  - Similar kcal  

Critical Growth Epochs
Differences in mean weight between male infants assigned to a preterm formula and male infants assigned to a standard term formula from discharge to 6 months of age

<table>
<thead>
<tr>
<th>Age</th>
<th>Difference in Weight, g</th>
<th>40 to 48 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>-9</td>
<td></td>
</tr>
<tr>
<td>Enrollment</td>
<td>118</td>
<td></td>
</tr>
<tr>
<td>4 weeks</td>
<td>700</td>
<td></td>
</tr>
<tr>
<td>8 weeks</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>880</td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>700</td>
<td>Increased Lean Body Mass</td>
</tr>
<tr>
<td>5 months</td>
<td>700</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>14 months</td>
<td>1500</td>
<td></td>
</tr>
</tbody>
</table>

Growth and Fat Free Mass Gain in Infants After Discharge

- RCT n=270 @TEA Term Formula (TF) vs Post Discharge Formula (PDF)
- Human milk < 20% of diet
- Protein 2.0g/dl vs 1.4 ; P/E 2.6 vs 2.0
- Diets through 6 mos Corrected age (CA)
- Body Composition Air Displacement Plethysmography
- Anthropometrics Term,1,3,6,12 mos CA

**RESULTS**

Protein Intakes greater but less volume consumed with PDF.

No Differences in weight or length gain despite more protein

All AGA demonstrated Catch Up growth

Mean HC larger for AGAPDF fed @ 6/12 mos

Fat Free Mass lower @ 6 mos for AGA fed

**Potential Benefits of Nutrient Enriched Formula Post Discharge for AGA Preterm Infants**

- HEAD CIRCUMERENCE GROWTH
- INCREASED FAT FREE MASS GAIN

1) Growth restriction with increased adiposity = Inadequate P/E ratio during hospitalization
2) Higher protein intake first 6 mos CA promotes recovery of FFM without any detriment to ponderal growth.
Michelangelo's famous statue, David, has returned to Italy this week after an amazingly successful 12 week, 20 city, U.S. tour which was sponsored by McDonald's.
How Important Is Head Circumference?

Brain Growth and Neurodevelopment
Neuro/Intellectual Function at School Age With Subnormal Head Circumference at 8 Months

Subnormal HC in VLBW Infants at 8 Months of Age Predicted Poorer Outcomes at 8 Years of Age  
N=249

- Neurological Impairment
- Lower IQ
- Limited Academic Skills
<table>
<thead>
<tr>
<th>Neurodevelopmental Outcomes in subgroups of VLBW premature infants</th>
<th>Adequate catch-up growth</th>
<th>Delayed extrauterine growth (EUGR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA (28wks/1050g)</td>
<td>good neurodevelopmental outcome</td>
<td>decreased mental and motor function</td>
</tr>
<tr>
<td>SGA (31wks/950g)</td>
<td>good neurodevelopmental outcome (similar to AGA with adequate catch-up growth)</td>
<td>decreased motor function</td>
</tr>
</tbody>
</table>

VLBW, very low birthweight; predominantly SGA; *9 and 24 months