Preterm Dietary Supplements

Dr Umesh Vaidya

IAP Neocon, Mumbai 2015
Preterm VLBW Nutrition: Ideal practice

Minimal enteral feeds (10 ml / kg / day)

Human breast milk

Feed advancement @ 20 ml / kg / day

Human milk fortification 100 ml / kg / day

Parenteral nutrition (ELBW < 1000 g)

Aminoacids 1 – 1.5 g / kg / day Day 1

Lipids 1 – 2 g / kg / day Day 1-3

## Case, Baby of MI 28 wks, BW 1280 gms

<table>
<thead>
<tr>
<th>DAYS</th>
<th>NUTRITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAY 1</td>
<td>TPN (1.5 g amino acids; 1.5 g lipids)</td>
</tr>
<tr>
<td>DAY 2</td>
<td>Minimal Enteral Feeding</td>
</tr>
<tr>
<td>DAY 2-8</td>
<td>Grading up of feeds</td>
</tr>
<tr>
<td></td>
<td>HMF started</td>
</tr>
<tr>
<td>DAY 9-30</td>
<td>Fortified milk- full feeds</td>
</tr>
<tr>
<td>DAY 33-34</td>
<td>Sodium supplementation</td>
</tr>
<tr>
<td>DAY 30-35</td>
<td>Transition to oral feeds- discharge</td>
</tr>
</tbody>
</table>

**Weight gain: Day 9 –30  -  10 gms / day**
Initial birth weight: 1280 gms
Birth weight regained on day 34
Birth centile: 30th (Fenton)
Discharge centile: 3rd
Extrauterine growth retardation – EUGR

Wt at 1 month 720 gm

Born at 28 wks, BW 1020 gm

RDS / Pulmonary morbidity

Wt at 1 month 720 gm
EUGR - A serious problem in preterms

Preterms 23 – 34 weeks, 24371 Preterms

Growth < 10th percentile at 40 weeks

WT 28 %
LNTH 34 %
HC 16 %

Possible neurologic and sensory handicaps

CONSEQUENCES OF INADEQUATE EARLY NUTRITION

Post-natal Growth Restriction - a global concern

Vulnerable periods

Nutritional insults – impaired somatic growth
Impaired neuro-cognitive development

Ehrenkranz et al Pediatrics 2006
In-hospital Growth Velocity and Neurodevelopmental Outcomes

Mental developmental index (MDI) <70 (p<0.01)

Pediatric quality indicators (PDI) <70 (p<0.001)

Cerebral palsy (p<0.01)

Neurodevelopmental impairment (p<0.001)
DEFINING GROWTH TARGETS

Weight gain 10-15 gm/kg/day
Length gain 0.75-1 cm/wk
HC gain 0.75 cm/wk
NUTRITIONAL CARE PLAN

Early

INTERIM NUTRITION

INTERMEDIATE NUTRITION

ENTERAL NUTRITION

FORTIFICATION OF ENTERAL FEEDS

POST DISCHARGE NUTRITION
GLUCOSE ALONE AS NUTRITION
(26 weeks, 1000g)

Denne SC, J Clin Invest 1996
First Week Protein and Energy Intake and Neurodevelopmental Outcomes

- Retrospective study of 124 ELBW infants at 18 months CA
- AA intake 1\textsuperscript{st} week: 1.8 ± 0.4 g/kg/day
- Energy intake 1\textsuperscript{st} week: 60 ± 8 kcal/kg/day
Current recommendation

Day 1 Min AA 1.5 g/kg (3 g / kg preferred)
Started within 1 hr of birth
Increase to 4 g / kg within few days
LIPIDS 1 – 2 g / kg Day 1

Several studies (AA 3.5 g / kg , Lipids 3 g / kg)
No increase in BUN, lipids, acidosis

_Uhing MR Clin Perinatol 2009_
MINIMAL ENTERAL FEEDING

- EBM 8-12 ml/kg, 3-6 hrly, starting 1-3 hrs after birth
- Preferably with EBM / Donor Human milk

GRADING UP FEEDS

Increments of at least 20 ml/kg/day (Full feeds Day 7)
Caution in babies < 750 g and SGA infants as data limited

(Cochrane Systematic Review 2011)
Human Milk Banking
A National mission

Network of Human Milk Banking
### Effect of human milk feeding on morbidity & hospital stay

<table>
<thead>
<tr>
<th></th>
<th>Human Milk &gt; 50 ml/kg/d</th>
<th>Human milk and formula</th>
<th>Preterm formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.infants</td>
<td>62</td>
<td>63</td>
<td>42</td>
</tr>
<tr>
<td>Human milk intake</td>
<td>96 ± 23</td>
<td>20 ± 15</td>
<td>0</td>
</tr>
<tr>
<td>NEC n(%)</td>
<td>1(2%)</td>
<td>16(25%)</td>
<td>6(13%)</td>
</tr>
<tr>
<td>Late onset sepsis (LOS) n (%) **</td>
<td>19(31%)</td>
<td>29(45%)</td>
<td>22(48%)</td>
</tr>
<tr>
<td>LOS &amp; NEC n(%)</td>
<td>19(31%)</td>
<td>35(56%)</td>
<td>25(54%)</td>
</tr>
<tr>
<td>Hosp stay days ***</td>
<td>73 ± 19</td>
<td>87 ± 43</td>
<td>88 ± 47</td>
</tr>
</tbody>
</table>


B. Wt. 1000 g GA < 30 wks, *p < 0.01, ** p < 0.07, ***p < 0.05
Mean MDI and PDI scores for ELBW infants at 18 & 30 months age

* p = .03, ** p = .008
Enteral nutrient supply for preterm Infants:
Commentary ESPGHAN Committee on Nutrition

- Fluid: 110-200 ml/kg/d
- Energy intake 110-135 kcal/kg/d
- Protein intake 3.5 –4.5 g/kg/d (much higher)
- Fat intake 4.4 – 6.6 g/kg/d
- CHO intake 11.5 - 16 g/kg/d
# PRETERM: ADEQUACY OF BREAST MILK?

<table>
<thead>
<tr>
<th>NUTRIENT</th>
<th>PRETERM MILK (PER 100ML)</th>
<th>EBM 200 ml / kg</th>
<th>Requirement</th>
<th>DEFICIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (g)</td>
<td>1.1 – 1.5</td>
<td>2.2 - 3.0</td>
<td>3.5 – 4</td>
<td>1.3 – 1</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>20</td>
<td>40</td>
<td>120 – 140</td>
<td>80 – 100</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>15</td>
<td>30</td>
<td>60 – 90</td>
<td>30 – 60</td>
</tr>
<tr>
<td>Zinc (mcg)</td>
<td>295</td>
<td>590</td>
<td>800 – 1200</td>
<td>500 – 700</td>
</tr>
<tr>
<td>Vitamin A (IU)</td>
<td>250</td>
<td>500</td>
<td>1400 – 2500</td>
<td>1000 – 2000</td>
</tr>
<tr>
<td>Vitamin D(IU)</td>
<td>2.2</td>
<td>4.4</td>
<td>800 – 1000</td>
<td>800 – 1000</td>
</tr>
</tbody>
</table>
Types of Fortification

**Mono-component Fortification**
- Carbohydrates
- Proteins
- Fats
- Calcium PO4
- Iron
- Vitamins

**Multi-component Fortification**
Combination of 2 or more nutrients
## MONO- COMPONENT FORTIFICATION

<table>
<thead>
<tr>
<th>Component</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>no evidence available</td>
</tr>
<tr>
<td>Fats (MCT oil)</td>
<td>Little evidence (1 RCT) showed no effect</td>
</tr>
<tr>
<td>Proteins</td>
<td>4 studies 90 babies, Better short term growth, Long term effects ?</td>
</tr>
</tbody>
</table>
MULTI-COMPONENT FORTIFICATION: The Evidence

13 studies, > 600 patients

**Short term outcome**

- Increased wt gain 3.6 g/kg/d
- Increased LNTH increment 0.12 cm/week
- Increased HC 0.12 cm/week

**Long term outcome**

- No difference in WT./LNTH/HC at 12 & 18 mths
- No effects on neurodevelopmental outcome
- No effects on bone mineral content

*Cochrane database 2009*
Problems with Standard Fortification

58 % VLBW infants receiving fortified EBM have extra – uterine growth retardation at discharge

Henrikson C et al 2009

Standard Fortification – Protein deficits
Proteins is the issue!!

LOW PROTEIN INTAKE IS THE PRIMARY LIMITING FACTOR FOR GROWTH FAILURE

• Assumed higher protein content of human milk
• Low protein content of fortifiers
• Transition from high protein PN solutions to lower protein enteral feeds
Variable Protein Content of EBM
Variable Protein content of EBM

Baby G
EBM protein 1.9 g / 100 ml

Baby S
EBM protein 0.8 g / 100 ml
Human milk analysis is essential to the health and growth of preterm babies.

Miris Human Milk Analyser helps clinicians manage preterm nutrition quickly and simply.
# Protein content of Fortifiers (per gm)

<table>
<thead>
<tr>
<th>Fortifier</th>
<th>Protein Content (gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactodex HMF (Raptakos)</td>
<td>0.1</td>
</tr>
<tr>
<td>Hijam (Endocura)</td>
<td>0.25</td>
</tr>
<tr>
<td>Enfamil HMF (MJ)</td>
<td>0.27</td>
</tr>
<tr>
<td>Similac HMF (Abbott)</td>
<td>0.25</td>
</tr>
<tr>
<td>Aptamil BMF (Milupa)</td>
<td>0.2</td>
</tr>
<tr>
<td>FM 85 (Nestle)</td>
<td>0.2</td>
</tr>
</tbody>
</table>
## Novel Methods of Fortification

### Focus on more protein

<table>
<thead>
<tr>
<th>Fortification Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard Fortification</strong></td>
<td>Pre-determined amount of fortifier added to EBM</td>
</tr>
<tr>
<td><strong>Targeted Fortification</strong></td>
<td>Analyse EBM for proteins and add desired amount of fortifier to reach 3.5 g / kg /day</td>
</tr>
<tr>
<td><strong>Adjustable Fortification</strong></td>
<td>Assess protein intake by evaluation of infant’s metabolic response by checking BUN (Increase dose of fortifier if BUN &lt; 9 mg %, maintain between 9 - 14)</td>
</tr>
</tbody>
</table>

*Recommendation & Guidelines for perinatal practice*
Arslanoglou S, Moro GE, Ziegler E, J. Perinatal Med 2010
Adjustable Fortification : Turkey study

58 preterm VLBWs (<32 weeks,<1500 g)

Adjustable Fortification based on Blood urea levels

<table>
<thead>
<tr>
<th>BUN</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 9 mg %</td>
<td>Increase Protein by 0.55 g</td>
</tr>
<tr>
<td>14-20 mg %</td>
<td>Decrease Protein by 0.55 g</td>
</tr>
<tr>
<td>&gt; 20 mg %</td>
<td>Stop Protein supplement</td>
</tr>
</tbody>
</table>

Study group 4g/kg/day versus Control group 2.78 g/kg/day

Result : Significant improvements in WT,LNTH,HC

Alan S et al, Early Human Dev 2013
Is there an alternative Protein supplement?

**Skimmed Milk Powder (SMP)**

Each 100 g contains

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>360 kcal</td>
</tr>
<tr>
<td>Proteins</td>
<td>34.5 g</td>
</tr>
<tr>
<td>Fats</td>
<td>1 g</td>
</tr>
<tr>
<td>CHO</td>
<td>52 g</td>
</tr>
<tr>
<td>Calcium</td>
<td>1250 mg</td>
</tr>
<tr>
<td>PO4</td>
<td>970 mg</td>
</tr>
<tr>
<td>Sodium</td>
<td>500 mg</td>
</tr>
</tbody>
</table>
SMP FORTIFICATION
(2 gm / 100 ml @ 170 ml / kg / day)

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy kcal</td>
<td>126</td>
<td>(110 – 135)</td>
</tr>
<tr>
<td>Proteins (g)</td>
<td>3</td>
<td>(3.5 – 4)</td>
</tr>
<tr>
<td>CHO (g)</td>
<td>13.7</td>
<td>(11.6 – 13.2)</td>
</tr>
<tr>
<td>Fats (g)</td>
<td>7.2</td>
<td>(4.8 – 8.8)</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>102</td>
<td>(120 – 140)</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>58.5</td>
<td>(60 – 90)</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>25.5</td>
<td>(69 – 115)</td>
</tr>
</tbody>
</table>
WHAT WE DO ???

NUTRITIONIST-GUIDED ENTERAL FEEDING

• Early TPN for all < 1500 g

• Minimal Enteral Nutrition with Colostrum

• Use of Expressed Breast milk /Donor milk

• Rapid grading up in stable prems (20-30 ml/kg/day)

• Fortification at 100 ml/kg/day with HMF/SMP

• Optimal calories , proteins, Vitamin D, Calcium PO4, Iron
Bedside Nutrition Management Tool

Kimaya NICU Nutrition Software

- Bedside nutrition plan
- Individualized calculations for Enteral & Parenteral Nutrition
- Linkage between EN & PN
- Helps in optimizing calorie & protein intake
- Growth chart interface
## TPN Calculation

<table>
<thead>
<tr>
<th>Day of TPN</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Weight (Kg)</td>
<td>1</td>
</tr>
<tr>
<td>Dextrose Concentration (%)</td>
<td>10</td>
</tr>
<tr>
<td>Fluid Intake (ml/kg/day)</td>
<td>80</td>
</tr>
<tr>
<td>Fat Requirement (gm/kg/day)</td>
<td>1</td>
</tr>
<tr>
<td>Lipid Concentration (%)</td>
<td>20</td>
</tr>
<tr>
<td>Overfill Factor</td>
<td>1.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amino Acid (gm/kg)</th>
<th>Na (meq/kg)</th>
<th>K (meq/ml)</th>
<th>Ca (meq/kg)</th>
<th>Mg (meq/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.0 %</td>
<td>3.3 meq/ml</td>
<td>2.0 meq/ml</td>
<td>0.45 meq/ml</td>
<td>4.0 meq/ml</td>
</tr>
</tbody>
</table>

**Other Infusions/Enteral Feeds**

**You are currently on 3 month trial plan**
Enteral Calculation

Day Of Life: 9
Current Weight (Kg): 12
Intake (ml): 17
Intake Frequency (per hour): 2 h

Type of Intake: EBM

Additives
- HMF
- MCT Oil
- SMP

Intake
- 0.5gm (1/4)
- MCT intak
- SMP intake

Values

Day of life

Enteral Feeding

Total Fluid: 204 ml/day
Total Calories: 165.21 kcal
Total Proteins: 3.66 gm

Calories

Total Fluid: 170 ml/kg/day
Total Calories: 137.68 kcal/kg
Total Proteins: 3.05 gm/kg
Growth chart
## Daily Nutrition Plan

<table>
<thead>
<tr>
<th>Date</th>
<th>Fluid (ml/kg/day)</th>
<th>Proteins (gm/kg/day)</th>
<th>Calories (kcal/kg/day)</th>
<th>Total Fluid (ml/kg/day)</th>
<th>Total Proteins (gm/kg/day)</th>
<th>Total Calories (kcal/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-10-10</td>
<td>Enteral TPN</td>
<td>175</td>
<td>2.86</td>
<td>128.50</td>
<td>175</td>
<td>2.86</td>
</tr>
<tr>
<td>2015-10-06</td>
<td>Enteral TPN</td>
<td>177</td>
<td>2.89</td>
<td>129.85</td>
<td>177</td>
<td>2.89</td>
</tr>
<tr>
<td>2015-10-02</td>
<td>Enteral TPN</td>
<td>177</td>
<td>2.89</td>
<td>129.85</td>
<td>177</td>
<td>2.89</td>
</tr>
<tr>
<td>2015-09-30</td>
<td>Enteral TPN</td>
<td>175</td>
<td>2.90</td>
<td>129.02</td>
<td>175</td>
<td>2.90</td>
</tr>
<tr>
<td>2015-09-29</td>
<td>Enteral TPN</td>
<td>175</td>
<td>2.94</td>
<td>129.57</td>
<td>175</td>
<td>2.94</td>
</tr>
<tr>
<td>2015-09-23</td>
<td>Enteral TPN</td>
<td>163</td>
<td>2.90</td>
<td>122.52</td>
<td>163</td>
<td>2.90</td>
</tr>
<tr>
<td>2015-09-13</td>
<td>Enteral TPN</td>
<td>175</td>
<td>3.17</td>
<td>132.25</td>
<td>175</td>
<td>3.17</td>
</tr>
<tr>
<td>2015-09-04</td>
<td>Enteral TPN</td>
<td>173</td>
<td>3.10</td>
<td>130.18</td>
<td>173</td>
<td>3.10</td>
</tr>
<tr>
<td>2015-09-02</td>
<td>Enteral TPN</td>
<td>179</td>
<td>3.37</td>
<td>137.05</td>
<td>179</td>
<td>3.37</td>
</tr>
<tr>
<td>2015-08-23</td>
<td>Enteral TPN</td>
<td>140</td>
<td>3.46</td>
<td>117.06</td>
<td>140</td>
<td>3.46</td>
</tr>
<tr>
<td>2015-08-18</td>
<td>Enteral</td>
<td>174</td>
<td>3.49</td>
<td>135.32</td>
<td>174</td>
<td>3.49</td>
</tr>
</tbody>
</table>
Tailor-made Nutrition

- Optimal fortification of human milk
- Growth and metabolic monitoring (Proteins, Hb, Ferritin, Ca PO4, alk PO4)
Baby K, GA 25 weeks Triplet, Weight 710 gms
What could be the reasons for poor growth?

- Inadequate feeding due to poor suck and swallow
- Inadequate breast milk
- Cold stress
- Exaggerated anaemia of prematurity
- Inadequate calorie / protein intake due to discontinuation of fortification
- Sepsis/sickness in the baby
- Electrolyte imbalance (Late onset Hyponatraemia)
3. Human milk fortification after Discharge

Powdered Human Milk Fortifier (HMF)

Proper training of mother important
Estimate approx milk intake and calculate dose of HMF
Express milk to mix HMF and then can breastfeed
2 gm in 50 ml EBM (1 gm HMF in 25 ml EBM)

Fortification with MCT oil – not recommended due to lack of scientific evidence *(Cochrane Review 2009)*

Special post – discharge formulae (72–80 kcal/dl)
4. Post-Discharge Nutritional Supplementation

Stable, full feeds

- Multivitamin with Zinc (? Continue till 1 year)
- Calcium : Phosphorus (continue till term / 3 kg)
- Vitamin D 800 IU per day (ESPGHAN 2010)
  (continue till 1 year)

4 - 6 weeks

- Start Iron supplementation
- Continue till one year
Nutritional supplementation for preterms

- **Vitamin A** - 1500 IU per day
  
  (Dose of multivitamin drops to be titrated accordingly)

- **Zinc** - 2.5 mg - 3 mg / d

- **Vitamin D**: 800-1000 IU /day *(ESPGHAN 2010)*

- **Calcium** - 150 mg /kg

- **Phosphorus** - 75 mg /kg
<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Brand A</th>
<th>Brand B</th>
<th>Brand C</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2500 IU</td>
<td>1000 IU</td>
<td>2750 IU</td>
</tr>
<tr>
<td>D3</td>
<td>200 IU</td>
<td>400 IU</td>
<td>250 IU</td>
</tr>
<tr>
<td>E</td>
<td>2.5 mg</td>
<td>1.5 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>C</td>
<td>40 mg</td>
<td>40 mg</td>
<td>40 mg</td>
</tr>
<tr>
<td>B₁</td>
<td>1 mg</td>
<td>2 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>B₆</td>
<td>---</td>
<td>1 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>K</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

**DOSE:**
- 0.5 ml
- 1 ml
- 0.5 ml
Iron supplementation

- < 1000g: 4 mg / kg / d
- 1000-1500g: 3-4 mg / kg / d
- 1500-1800g: 2-3 mg / kg / d
- >1800g: 2 mg / kg / d

- Start at 4-6 weeks, Continue till 12-15 months
- For babies <1500 gm early supplementation (2 weeks) may be considered
# IRON DROPS (per ml)

<table>
<thead>
<tr>
<th></th>
<th>Brand T</th>
<th>Brand F</th>
<th>Brand R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elemental iron</td>
<td>25 mg</td>
<td>20 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>$B_{12}$</td>
<td>12.5 ug</td>
<td>4 ug</td>
<td>NIL</td>
</tr>
<tr>
<td>Folic acid</td>
<td>200 ug</td>
<td>200 ug</td>
<td>100 ug</td>
</tr>
<tr>
<td>Lysine</td>
<td>200 mg</td>
<td>5 mg</td>
<td>NIL</td>
</tr>
</tbody>
</table>

mg Fe / drop: 1, 1, 0.3
6. When to start complementary foods?

• Complementary food should be started about at corrected age of 4-6 months for preterm infants

Deborah L, Unger S. Seminars in fetal and neonatal medicine, (2013)

• Generally, most babies would be around 5 kg, would have some neck support and tongue-thrust reflex would have diminished

• Complementary foods are chosen as per recommendation for term infants
SUMMARY

- Postnatal growth retardation common in preterm LBWs
- Optimal growth targets unclear, but prevention of EUGR is mandatory
- Current trends favour aggressive nutrition strategies to improve neurologic outcome
- Early PN, use of human milk, fortification of enteral feeds to achieve adequate calories and proteins
SUMMARY (Contd)

Human Milk Banking now a national mission

Donor Human milk has both short and long-term benefits

Protein deficits are contributing to growth failure

Recent guidelines suggest higher protein intakes for babies < 1500 g

Novel methods for protein fortification are being studied
SUMMARY (Contd)

Essential to drive and achieve optimal growth amongst all odds

Bedside management tool facilitates better nutrition by providing the interface between nutrition delivery and growth outcome
LET US PROVIDE THE BEST NUTRITION !!!

OPTIMAL GROWTH IS

TOMORROW’S OUTCOME!