Effective Nutrition of the Preterm Infants in NICU.

Dr. Mahmoud Elhalik
Consultant Neonatologist
Head of Neonatal Intensive Care Unit
Director of Neonatology Fellowship Program - DHA
Latifa Women & Children Hospital
Dubai, October 2019
References

• Nutritional Support Strategies for the Preterm Infant in the NICU. PGHN 2018 October 21(4):234-247
• Fanaroff and Martin's Neonatal-Perinatal Medicine, 10th Ed 2015
• Beyond the NICU: Comprehensive Care of the High-Risk Infant 2015
• Human Milk Composition: Nutrients and Bioactive Factors, Pediatr Clin North Am. Author manuscript; available in PMC 2014 February 01.
• Adamkin DH. Mother’s milk, feeding strategies, and lactoferrin to prevent necrotizing enterocolitis. JPEN. 2012:36.
• De Curtis M, Rigo J. The nutrition of preterm infants. Early Hum Dev. 2012
• Collins CT, Chua MC, Rajadurai VS, et al. Higher protein and energy intake is associated with increased weight gain in pre-term infants. J Paediatr Child Health. 2010;
• Low energy intake during the first 4 weeks of life increases the risk for severe retinopathy of prematurity in extremely preterm infants, Stoltz Sjöström E, et al. Arch Dis Child Fetal Neonatal Ed 2016
• Maggio M, De Vita F, Lauretani F, et al. IG-1, the cross road of the nutritional, inflammatory and hormonal pathways to frailty. Nutrients 2013
Outline

Introduction – Prematurity & the NICU

Optimal Nutrition & Premature Infant Nutrition
Early Postnatal Nutrition

Aggressive Parenteral Nutrition \ Enteral Nutrition – The Evidence

Breast Milk & Preterm Infants \ Fortification of HM

Postdischarge Nutrition. \ Take Home Message
Critical need to address Newborn & Preterm Births

- Worldwide, 15 million babies are born preterm / Yr.
- > 1.1 Million Die

Preterm Complications 35%

Intrapartum–related events 24%

Estimates for child causes of death 2000-2016
Prematurity & the NICU

- Prematurity is one of the leading causes of infant death & major disabilities such as CP & MR.

- Advances in neonatal care (antenatal steroids & PN surfactant) $\rightarrow$ ↑ survival rates among preterm infants through the 1990s.

- ↑ in survival rate was accompanied by an ↑ in number of preterm infants with major medical complication and poor neurodevelopmental outcomes.

- Premature nutrition is one of the major factors which affects outcome.
  - We still know very little about optimal nutrition of VLBW infants
Nutrition - Definition

- Process of nourishing the body, *supplying what is necessary to sustain life.*

- Achievement of satisfactory growth and avoidance of deficiency states.

*(Nelson's Textbook of Paediatrics)*

For Neonatologists; ultimate goal of feeding preterm infants is to *improve the outcome* of these infants to a level that is comparable to healthy term born infants.

- *i.e.* a Postnatal Growth Rate that comes close to *Fetal Growth Rate* with comparable tissue composition & functional outcome similar to that of Healthy Term-born Infants

*(ESPGHAN Committee on Nutrition & AAP Committee on Nutrition).*
Fetal Nutrition

- Parenteral (mostly!)
  - Continuous supply of glucose.
  - Protein taken up at about 4 grams/Kg/day.
  - Lipids at 3 grams/kg/day.

- Stores are laid late in gestation
  - At 28 weeks, a Foetus has ~:
    - 20% of term calcium and phosphorus stores
    - 20% of term fat stores
    - 25% of term glycogen stores
Premature Infant Initial Nutrition After birth
Common Practice !!!!!!!!!!!!!

- Interrupted flow of placenta-provided nutrients.

- **Partial replacement !!!!**
  - Dextrose only
  - Delay in total parenteral nutrition
  - Amino acids and lipids frequently delayed or interrupted.

- **Impaired growth → ↑ M & M**
Nutritional Status and Key Outcomes.

Past history
- IUGR
- Poor growth and nutrition
- Gestation

Current status
- Increased needs or losses
- Postnatal age
- Gut function

Nutritional status

Key outcomes

Short-term
- Weight gain
- NEC
- Respiratory function

Medium-term
- Infant growth
- Neuro-development

Long-term
- Cognition
- Cardiovascular health
- Type II diabetes
Growth Failure

IUGR (Intrauterine Growth Restriction)
- Maternal nutrient stores & intake
- Maternal illness
- Placental insufficiency

EUGR (Extrauterine Growth Restriction)
- Neonatal status at birth
- Neonatal illnesses
- Energy/Protein expenditure vs. intake /Malnutrition
## Risk of General Malnutrition in Preterms

<table>
<thead>
<tr>
<th>Gestational age at birth</th>
<th>Birth weight</th>
<th>Risk of malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 28 wk</td>
<td>&lt; 1000 g</td>
<td>Extremely high</td>
</tr>
<tr>
<td>28-32 wk</td>
<td>1000-1500 g</td>
<td>Very high</td>
</tr>
<tr>
<td>33-36 wk</td>
<td>1500-2500 g</td>
<td>Moderate/low</td>
</tr>
</tbody>
</table>
Why do extremely preterm infants have high risk of malnutrition?

- Lack of nutrient stores
- Expected increase weight 4-5-fold during 3-4 months in NICU
- Prematurity (including morbidity) leads to poor tolerance of parenteral and enteral nutrition
- Lack of knowledge and adequate clinical routines & guidelines.

Consequences of Poor Nutrition

- Serious metabolic disturbances
- Sepsis
- NEC
- Osteopenia
- BPD / CLD
- ROP
- Poor Neurodevelopmental Outcome
# Adverse Developmental Sequelae in Adults Born Preterm

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adverse Sequelae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>• Significant decrease in brain volume</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of neurological disabilities</td>
</tr>
<tr>
<td>Cardiovascular &amp; Metabolic</td>
<td>• Low insulin sensitivity and high blood pressure</td>
</tr>
<tr>
<td></td>
<td>• Increased intra-abdominal fat and higher risk of metabolic complications</td>
</tr>
<tr>
<td></td>
<td>• Increased arterial stiffness</td>
</tr>
<tr>
<td></td>
<td>• Reduced ventricular size and volume; impaired systolic function</td>
</tr>
<tr>
<td>Bone Health</td>
<td>• Significantly lower bone mineral density</td>
</tr>
<tr>
<td>Others</td>
<td>• Increased risk of social disabilities in adulthood (in terms of educational</td>
</tr>
<tr>
<td></td>
<td>level attained, income, and establishment of family)</td>
</tr>
</tbody>
</table>
# Nutrient Requirements

## Macronutrients

- Water (mL)
- Energy (kcal)
- Protein (g)
- Fat (g)
- Carbohydrate (g)

## Micronutrients

### Vitamins

- Vitamin A (int. unit)
- Vitamin D (int. unit)
- Vitamin E (int. unit)
- Vitamin K (mcg)
- Folic acid (mcg)
- Niacin (mg)
- Pyridoxine (mcg)
- Riboflavin (mcg)
- Thiamine (mcg)
- Vitamin B12 (mcg)
- Vitamin C (mg)

### Electrolytes, minerals, and trace elements

- Sodium (mEq)
- Potassium (mEq)
- Chloride (mEq)
- Calcium (mg)
- Phosphorus (mg)
- Magnesium (mg)
- Zinc (mcg)
- Copper (mcg)
- Chromium (mcg)
- Manganese (mcg)
- Iron

---

- **Enterally fed infants**
- **Parenteral Nutrition (PN)**
Three Stages of Nutrition Support in Preterm Infants

- Early aggressive nutrition
- HMF or Preterm formula (Growing Care Stage)
- Post-discharge nutrition

Early Nutrition Mediates the Influence of Severity of Illness on ELBW Infants

- **↑ Total energy intake** during first 7 days of life in critically ill infants
  - **↓ Odds Ratio** of adverse outcomes as NEC, LOS, BPD and NDI by ~ 2% for each 1kcal/kg/d of total energy intake.

**In summary,** Early, aggressive parenteral and enteral nutritional support was associated with lower rates of death and short-term morbidities and improved growth and neurodevelopmental outcomes.

### Calorie needs (kcal/kg/day) for preterm infants to achieve normal growth rates

<table>
<thead>
<tr>
<th>Study</th>
<th>Calorie needs, kcal/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AAP Committee on Nutrition</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Enterally fed infants</strong></td>
<td></td>
</tr>
<tr>
<td>• Resting Energy Expenditure (REE)</td>
<td>50</td>
</tr>
<tr>
<td>• Activity (0–30% above REE)</td>
<td>0-15</td>
</tr>
<tr>
<td>• Thermoregulation</td>
<td>5-10</td>
</tr>
<tr>
<td>• Thermic effect of feeding (synthesis)</td>
<td>10</td>
</tr>
<tr>
<td>• Fecal loss of energy</td>
<td>10</td>
</tr>
<tr>
<td>• Energy storage (growth)</td>
<td>25-35</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100-130</strong></td>
</tr>
<tr>
<td><strong>Parenteral Nutrition (PN) (Intravenously fed infants)</strong></td>
<td></td>
</tr>
<tr>
<td>• Resting energy expenditure</td>
<td>50</td>
</tr>
<tr>
<td>• Activity</td>
<td>0-5</td>
</tr>
<tr>
<td>• Thermoregulation</td>
<td>0-5</td>
</tr>
<tr>
<td>• Thermic effect of feeding (synthesis)</td>
<td>10</td>
</tr>
<tr>
<td>• Energy storage (growth)</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>85-95</strong></td>
</tr>
</tbody>
</table>

**ESPGHAN Committee on Nutrition**

Normal Growth Rates **115–130**
Energy and Carbohydrates: Nutritional Recommendations

- Both energy and protein are necessary to produce normal rates of growth.
  - **110–130 kcal/kg/day for enterally fed preterm infants**
  - **85–95 kcal/kg/day for parenterally fed infants**

- Carbohydrates (primarily glucose); principle sources of energy for brain & heart
  - **High energy intakes in preterm infants results in greater fat accumulation**
  - Glucose to be administered to maintain a GIR of 5–8 mg/kg/min: up to 12–15 mg/kg/min as tolerated.

- High infusion rates of glucose → hyperglycemia and may contribute to inflammatory injuries and fatty infiltration of liver & heart & other organs.
  - Routine use of insulin to prevent hyperglycemia or promote growth may be harmful
Practical Tips For Energy

- **Dextrose** Calories **not to exceed 50%** of total calories on TPN.
- **Lipids** Calories **not to exceed 40%** of total calories on TPN.
- **Protein** Calories **not to exceed 12%** of total calories in TPN.

- Excessive energy administration TPN of carbohydrate & lipid → metabolic intolerance including hypertriglyceridemia, acidosis & excessive fat deposition, especially in the liver.

- SGA or IUGR and BPD infants may need as much as 25–45% more energy.

- **Begin IV infusions of Protein (3-4 grams/kg/d) & Lipid (3 grams/kg/day) right after birth to prevent protein and energy insufficiency**
Low Energy Intake During the First 4 Weeks of Life Increases the Risk for Severe ROP

Amino Acids (AA) / Proteins

- Major driving force for growth.
- Inadequate AA or protein intakes during their first several days → Catabolic State.
- Immediate commencement to preterm infants following birth:
  - TPN; Initial safe intake; 2.0–2.5 g/kg/d
    - Gradual ↑ to 3.5-4.0 g/kg/d
  - Full Enteral nutrition, 3.5–4.5 g/kg/d (ELBW); gradually ↓ 2–2.5 g/kg/d (term)
    - Either with Fortified human (donor) milk or PTF.
  - Catch-up growth is needed, intakes up to 4.5 g/kg/d

- With these recommendations, risk of Growth Retardation becomes rare.
Rationale for Providing Lipids Early

- **EFA status in early infancy is low and is rapidly exacerbated with lipid free PN.**

- **Lipid emulsions that are not purely soybean-based - preferred**
  - ↓ risk of sepsis and promote more favorable LC-PUFA profile.
  - Lipid emulsions containing fish oil are potentially useful → better DHA status

- Important in brain and retinal development.

- Availability of Lipid in PN → Prevention of catabolism and protein sparing.

- **When To Start Lipids ; ASAP—D1 - No studies show problems starting at 3.0 gm/kg/d.**
DHA Levels and Chronic Lung Disease

Mean DHA levels for all infants

Postnatal week (birth = week 0)

C. Martin, J Peds. 2011
<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Current regimen based upon pediatric multivitamin formulation* (unit/kg/day)</th>
<th>Estimate based upon the needs of premature infants (unit/kg/day)</th>
<th>Maximum not to exceed term infant (unit/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat-soluble vitamins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A (microg)</td>
<td>280</td>
<td>500</td>
<td>700</td>
</tr>
<tr>
<td>E (mg)</td>
<td>2.8</td>
<td>2.8</td>
<td>7</td>
</tr>
<tr>
<td>K (microg)</td>
<td>80</td>
<td>80</td>
<td>200</td>
</tr>
<tr>
<td>D (microg)</td>
<td>4</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td><strong>Water-soluble vitamins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C, Ascorbic acid (mg)</td>
<td>32</td>
<td>25</td>
<td>80</td>
</tr>
<tr>
<td>B1, Thiamin (mg)</td>
<td>0.48</td>
<td>0.35</td>
<td>1.2</td>
</tr>
<tr>
<td>B2, Riboflavin (mg)</td>
<td>0.56</td>
<td>0.15</td>
<td>1.4</td>
</tr>
<tr>
<td>B6, Pyridoxine (mg)</td>
<td>0.4</td>
<td>0.18</td>
<td>1</td>
</tr>
<tr>
<td>Niacin (mg)</td>
<td>6.8</td>
<td>6.8</td>
<td>17</td>
</tr>
<tr>
<td>Pantothenate (mg)</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Biotin (microg)</td>
<td>8</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Folate (microg)</td>
<td>56</td>
<td>56</td>
<td>140</td>
</tr>
<tr>
<td>Vitamin B12 (microg)</td>
<td>0.4</td>
<td>0.3</td>
<td>1</td>
</tr>
</tbody>
</table>
### Suggested Monitoring Strategy For PN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Timing &amp; Frequency of Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sodium, potassium, chloride, bicarbonate and glucose</td>
<td>• Daily over at least first 3–4 days</td>
</tr>
<tr>
<td>• Calcium and phosphate (± magnesium)</td>
<td>• Twice weekly until stable</td>
</tr>
<tr>
<td>• Plasma triglycerides</td>
<td>• Twice weekly (or if lipidmic serum)</td>
</tr>
<tr>
<td>• Liver function tests</td>
<td>• Weekly</td>
</tr>
<tr>
<td>• Weight</td>
<td>• Daily or alternate days</td>
</tr>
<tr>
<td>• Length and head circumference</td>
<td>• Weekly</td>
</tr>
</tbody>
</table>

Monitoring Triglycerides

Different norms are recommended by different authors

(e.g. 100-150, <200 mg/dl, etc.)

Eight week old Infants Triglyceride Concentration (mg/dL)

- Formula fed median = 158.50 (min to max= 81.00 to 327.00)
- Human milk fed median = 164.50 (min to max= 59.00 to 418.00)
Standard PN solutions should generally be used over individualized PN solutions (strong consensus).

Individually tailored PN solution should generally be used when the nutritional requirements cannot be met by the available range of standard PN formulations (i.e. in very sick and metabolically unstable patients such as those with abnormal fluid and electrolyte losses; and in infants and children requiring PN for prolonged periods such as those with short bowel syndrome (strong consensus).

Computerized prescription, whether standardized or individualized, should be used in the ordering process of PN when possible (strong consensus).
Enteral Nutrition

Early Feeding With Human Milk (first weeks-months) has a profound impact on later functional outcome

Breast Milk is the Best
Enteral Nutrition - Route of Feeding

Infants who do not have a coordinated suck must be tube fed.

- **Nasogastric tubes** — relatively simple to place and secure. May ↑ airway resistance (50%).

- **Orogastric tubes** — useful with nasal CPAP. Difficult to secure and keep down. Common.

- **Transpyloric tubes** — More difficult to pass, not frequently used due to:
  - Possible ↑ of NEC and risk of gut perforation,
  - ↓ gastric acid and gastrin secretion
  - ↓ fat absorption, as lingual and gastric lipase are bypassed

- **Gastrostomy:** Rarely used; GORD (with fundoplication), Esophageal anomalies, Neurological problems
Enteral nutrition: Frequency of feeding

Feeding practices vary greatly between NICUs.

**Intermittent bolus feeds**: Most units use 2–4 hr. bolus feeds. More physiological, associated with cyclical hormone release.

**Continuous feeding** by infusion:
- Smaller gastric volumes at any time
- Possibly better absorption in SBS & in infants with protracted diarrhea
- NG tube may become displaced — risk of aspiration

**Continuous versus intermittent feeds** — an ongoing debate! —
- No Difference in reaching full oral.
## Stages of Breast Milk

<table>
<thead>
<tr>
<th>Stage</th>
<th>Time Frame</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st - Colostrum</td>
<td>First 3-5 days following birth.</td>
<td>- Creamy, yellow, thick milk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- <strong>High in protein, vitamins, minerals and antibodies.</strong></td>
</tr>
<tr>
<td>2nd – Transitional Milk</td>
<td>Lasts about 2 weeks</td>
<td>- Thinner, whiter milk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- <strong>High in fat, Lactose and vitamins.</strong></td>
</tr>
<tr>
<td>3rd – Mature Milk</td>
<td>Until baby is weaned</td>
<td>- <strong>90% water for hydration</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Carbohydrate, protein and fat needed for growth and energy.</td>
</tr>
</tbody>
</table>
### Compounds with Immunological Properties in Human Milk (Field J Nutr 2005)

#### Anti-microbial compounds

1. Immunoglobulins: sIgA, sIgG, sIgM
2. Lactoferrin, lactoferricin B and H
3. Lysozyme
4. Lactoperoxidase
5. Nucleotide-hydrolyzing antibodies
6. κ-Casein and α-lactalbumin
7. Haptocorrin
8. Mucins
9. Lactadherin
10. Free secretory component
11. **Oligosaccharides and prebiotics**
12. Fatty acids
13. Maternal leukocytes and cytokines
14. sCD14
15. Complement and complement receptors
16. β-Defensin-1
17. Toll-like receptors
18. Bifidus factor

#### Immune development compounds

1. Macrophages
2. Neutrophils
3. Lymphocytes
4. Cytokines
5. Growth factors
6. Hormones
7. Milk peptides
8. Long-chain polyunsaturated fatty acids
9. Nucleotides
10. Adhesion molecules

#### Anti-inflammatory compounds

1) Cytokines: IL-10 and TGFβ
2) IL-1 receptor antagonist
3) TNFα and IL-6 receptors
4) sCD14
5) Adhesion molecules
6) Long-chain polyunsaturated fatty acids
7) Hormones and growth factors
8) Osteoprotegerin
9) Lactoferrin
10) Long-chain polyunsaturated fatty acids
11) Hormones and growth factors fatty acids

#### Tolerance/priming compounds

1. Cytokines: IL-10 and TGFβ
2. Anti-idiotypic antibodies
### Host Defense Benefits

- **Lower incidence of infections**
- ↓ NEC
- ↓ diarrhea & UTI
- ↓ L. O. Sepsis
- ↓ Otitis Media

  ▪ slgA, lactoferrin, lysozyme, oligosaccharides, nucleotides, cytokines, growth factors, enzymes, antioxidants

  ▪ Specific A.A. may all contribute to the improved host defense

### Neurodevelopment

- **Improved long-term cognitive development**
- 'Intention' to breastfeed may also influence outcome by positive health behaviors in the mothers
- **Improved visual function, Decreased ROP**

Factors that influence ND outcome may include LC-PUFA, cholesterol, antioxidants, taurine, growth factors....

### Gastrointestinal Effects

- **More rapid gastric emptying**
- **Improved lactase activity**
Comparison of the spectra representing metabolite profiling identified that lactose and oligosaccharides levels, especially those fucosylated were significantly higher in preterm milk samples compared with full-term milk.

Conclusions

➢ To promote proper growth, it is desirable that preterm infants receive their OMM or at least DHM from lactating mothers who delivered at the same gestational age.
Probiotics - Prebiotic

- Debated, no conclusive evidence to recommend the routine use

- Available trials – **NO** optimal probiotic strain or prebiotic, dosing regimen, or protocol has been identified.

- Safety and efficacy of each probiotic strain must be tested separately.
  - Data generated with one probiotic strain do not necessarily apply to another strain.

- Precautions to minimize negative alterations in the intestinal microbiota with current medical practices (e.g. antibiotics) and the use of bioactive agents such as pro- & prebiotics are warranted in the neonate.
Fortification of HM

- **HM** is the best nutrient uniquely suited not only to term but also to preterm infants → health benefits at short and long-term including protection against NICU challenges such as NEC, ROP, BPD, sepsis and neurocognitive improvement.

- Therefore, it is the first choice in preterm feeding.

- Unfortified HM doesn’t provide sufficient amounts of nutrients to tiny preterm infants.

To prevent EUGR which is associated with poor neurocognitive outcome and to avoid specific nutrient deficiencies, Nutrient Fortification of HM is necessary.
European Milk Bank Association (EMBA) Working Group (WG) on HM Fortification Recommendations

- Human milk fortification can be started safely with multi-nutrient fortifiers when the milk volume reaches 50–80 ml/kg/d.

- Optimization of HM fortification is required.

- Individualized fortification (Adjustable or Targeted) is the recommended method for HM fortification.

- Quality improvement of the fortifiers is an ongoing process. It is too early to draw conclusions about the use of HM-based fortifiers.
### Nutrient Composition of Selected Fortifiers

#### Bovine-Based Products (Per Gram of Powder)

<table>
<thead>
<tr>
<th>Fortifier</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml)</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>4.4 (L)</td>
<td>3.5</td>
<td>3.6</td>
<td>4.9 (L)</td>
<td>3.9 (L)</td>
<td>3.4</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>0.36&lt;sup&gt;PH&lt;/sup&gt;</td>
<td>0.25&lt;sup&gt;EH&lt;/sup&gt;</td>
<td>0.2&lt;sup&gt;EH&lt;/sup&gt;</td>
<td>0.4</td>
<td>0.3</td>
<td>0.82&lt;sup&gt;EH&lt;/sup&gt;</td>
</tr>
<tr>
<td>Na (mg)</td>
<td>9.2</td>
<td>8.0</td>
<td>5.4</td>
<td>5.6</td>
<td>4.2</td>
<td>7.8</td>
</tr>
<tr>
<td>Ca (mg)</td>
<td>18.9</td>
<td>14.9</td>
<td>10</td>
<td>32</td>
<td>33</td>
<td>5.2</td>
</tr>
<tr>
<td>P (mg)</td>
<td>11</td>
<td>8.7</td>
<td>7</td>
<td>18</td>
<td>19</td>
<td>5.2</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>0.1</td>
<td>0</td>
</tr>
</tbody>
</table>

#### Human Milk-Based Fortifier (Per Volume)

<table>
<thead>
<tr>
<th>K</th>
<th>L</th>
<th>M</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>28</td>
<td>42</td>
<td>56</td>
<td>71</td>
</tr>
<tr>
<td>1.2</td>
<td>1.8</td>
<td>2.4</td>
<td>3</td>
</tr>
<tr>
<td>20</td>
<td>40</td>
<td>42</td>
<td>45</td>
</tr>
<tr>
<td>103</td>
<td>106</td>
<td>108</td>
<td>111</td>
</tr>
<tr>
<td>53.8</td>
<td>54.9</td>
<td>56</td>
<td>57.5</td>
</tr>
<tr>
<td>0.1</td>
<td>0.15</td>
<td>0.2</td>
<td>0.25</td>
</tr>
</tbody>
</table>
## Reasonable Strategy to Optimize Enteral Feeding Practices in ELBW (<1,000 g) & VLBW (1,000–1,499 g) infants

<table>
<thead>
<tr>
<th>Preferred Milk</th>
<th>ELBW</th>
<th>VLBW</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First feeding</strong></td>
<td>Between 6 and 48 h of life</td>
<td>Between 6 and 48 h of life</td>
</tr>
<tr>
<td><strong>Initial feeding (MEF)</strong></td>
<td>0.5 ml/kg/h or 1 ml/kg q2h</td>
<td>1 ml/kg/h or 2 ml/kg q2h</td>
</tr>
<tr>
<td><strong>Duration of MEF</strong></td>
<td>1–4 days</td>
<td>1–4 days</td>
</tr>
<tr>
<td><strong>Feeding advancement</strong></td>
<td>15–25 ml/kg/day</td>
<td>20–30 ml/kg/day</td>
</tr>
<tr>
<td><strong>If continuous feeding</strong></td>
<td>+0.5 ml/kg/h q12h</td>
<td>+1 ml/kg q8h</td>
</tr>
<tr>
<td><strong>If q2h intermittent feeding</strong></td>
<td>+1 ml/kg q12h</td>
<td>+1 ml/kg q8h</td>
</tr>
<tr>
<td><strong>HM fortification</strong></td>
<td>Before 100 ml/kg/day</td>
<td>Before 100 ml/kg/day</td>
</tr>
<tr>
<td><strong>Target energy intakes</strong></td>
<td>110–130 kcal/kg/day</td>
<td>110–130 kcal/kg/day</td>
</tr>
<tr>
<td><strong>Target protein intakes</strong></td>
<td>4–4.5 g/kg/day</td>
<td>3.5–4.0 g/kg/day</td>
</tr>
</tbody>
</table>

*Own mother’s breast milk or donor HM, OR preterm infant formula if there is no access to HM.

Feeding Intolerance in Preterm Infants

**Gastric residual:**
- **Low volume**
- **Nonbile stained**
- **Not bloody**
- **Benign abdominal examination**

- **Continue feeding**
- **Monitor and follow-up**

**Gastric residual:**
- **Moderate volume** (30%–50% of feeds)
- **Nonbile or blood stained**
- **Benign abdominal examination**

- **Reduce feed volume**
- **Monitor and follow-up**

**Gastric residual:**
- **Large** (more than 50% of feeds)
- **Nonbile or blood stained**
- **Benign abdominal examination**

- **Stop 2–4 feeds**
- **Assess clinically and investigate if indicated**
- **Monitor and follow-up**

**Gastric residual:**
- **Bilious or blood stained**

- **Stop feeds**
- **Assess clinically**
- **Request laboratory investigation and abdominal X-ray**
- **Manage accordingly**
- **Follow-up**
Iron Supplements Reduced Iron Deficiency At 6 Months

<table>
<thead>
<tr>
<th></th>
<th>0 mg</th>
<th>1 mg</th>
<th>2 mg</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency</td>
<td>36%</td>
<td>8%</td>
<td>4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>10%</td>
<td>3%</td>
<td>0%</td>
<td>0.002</td>
</tr>
</tbody>
</table>


Iron supplements reduced Behavioral Problems at 3 Years


- **Dietary iron intake of:**
  - 2 mg/kg/day for infants with BW 1,500–2,500 g
  - 2–3 mg/kg/day for infants with BW of <1,500 g
  - Prophylactic iron (iron drops, PTF or fortified HM) at 2–6 wks of age (at 2 wks in VLBWI).
  - Preterms with prolonged TPN → 0.2–0.25 mg/kg/d of parenteral iron (Monit..)
Nutritional Assessment - Appropriate charts relating body weight with infant’s age.

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Chart</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>To assess intrauterine growth</td>
<td>Fenton 2013</td>
<td>Reference sex specific, cross-sectional charts. Range: 22 to 50 weeks postmenstrual age.</td>
</tr>
<tr>
<td>To monitor intra-hospital growth</td>
<td>Growth calculator: <a href="https://www.growthcalculator.org">https://www.growthcalculator.org</a></td>
<td>Reference specific for sex, gestational age and percentile, longitudinal curves.</td>
</tr>
<tr>
<td>To monitor growth after discharge</td>
<td>Intergrowth-21st standards</td>
<td>Standard longitudinal curves. Range: 37 to 64 postmenstrual age.</td>
</tr>
</tbody>
</table>

*Nutritional Assessment in Preterm Infants: A Practical Approach in the NICU. Nutrients - August 2019*
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight</strong></td>
<td>Simple and reproducible.</td>
<td>Does not give any information on body composition.</td>
</tr>
<tr>
<td><strong>Body length</strong></td>
<td>Reflects skeletal growth and predicts fat-free mass.</td>
<td>Accurate measurement is difficult.</td>
</tr>
<tr>
<td><strong>Head circumference (HC)</strong></td>
<td>Reflects brain growth.</td>
<td>It may be affected by causes other than nutrient intake.</td>
</tr>
<tr>
<td><strong>Mid-upper arm circumference (MUAC)</strong></td>
<td>Reflects the combined arm muscle and fat.</td>
<td>Measurement is technically difficult in extremely preterm infants.</td>
</tr>
<tr>
<td></td>
<td>It may estimate body adiposity.</td>
<td></td>
</tr>
<tr>
<td><strong>Skinfolds</strong></td>
<td>Estimates body fat.</td>
<td>Do not reflect intra-abdominal fat.</td>
</tr>
<tr>
<td></td>
<td>Convenient for bedside assessment.</td>
<td></td>
</tr>
</tbody>
</table>
**Nutritional Assessment** - Biochemical markers of protein and bone status in preterm infants - ex

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood urea nitrogen (BUN)</strong></td>
<td>Low BUN is a good marker of low protein intake in enterally fed, clinically stable infants.</td>
<td>High BUN is not easy to interpret, since it may represent appropriate amino acid intake, low energy intake relative to protein intake, or amino acid intolerance.</td>
</tr>
<tr>
<td><strong>Serum phosphate</strong></td>
<td>High specificity and positive predictive value as a marker of MBD.</td>
<td>Low sensitivity and negative predictive value as a marker of MBD. Insufficient evidence as a reliable marker of MBD.</td>
</tr>
<tr>
<td><strong>Serum alkaline phosphatase</strong></td>
<td>Levels &gt;900 U/L yield a specificity of 71% and a sensitivity of 88% as a marker of MBD</td>
<td>Insufficient evidence as a reliable marker of MBD.</td>
</tr>
</tbody>
</table>
## Nutritional assessment of infants <1500 grams birthweight - Laboratory monitoring

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, hematocrit</td>
<td>After the infant is receiving enteral iron supplementation, measure every 2 weeks until results are stable. Recheck prior to hospital discharge.</td>
</tr>
<tr>
<td>Calcium, phosphorus, alkaline phosphatase</td>
<td>In infants &lt;1500 g birth weight, measure starting at 5 to 6 weeks of age. Measure weekly until alkaline phosphatase is &lt;600 IU/L and serum phosphorus is &gt;4.5 mg/dL. Once stable beyond these thresholds, no need to repeat.</td>
</tr>
<tr>
<td>Blood urea nitrogen (BUN)</td>
<td>Measure in infants with poor growth. BUN &lt;10 mg/dL may suggest the need for more protein intake.</td>
</tr>
<tr>
<td>Serum electrolytes</td>
<td>In selected infants (those receiving diuretics, or feeds of unfortified human milk, or limited intake, or slow growth).</td>
</tr>
</tbody>
</table>
Consensus Recommandations on Postdischarge Nutrition.

1. Ideal discharge wt. of preterm infants may be dependent on several factors; (1.8kg)

2. Sucking/swallowing ability of infants should be good at discharge.

3. Counseling should be provided for resuscitation prior to discharge.

4. Scheduled for follow Up - for up to a minimum of 2 years.

5. In preterm infants who are **on formula milk**, switching to a standard formula is recommended after they have reached their birth centile (i.e., after catch-up has been completed). There is not much evidence on the benefits of switching after an increase in weight beyond this.

6. Complementary feeding may be initiated at the corrected age of 4 months.

Ultimate Goal of Preterm Nutrition

- Mimic intrauterine growth rates & later to imitate growth rates of term breastfed infants
- Limit the degree and duration of initial weight loss in preterm infants, to support their nutritional needs, and to facilitate regain of birth weight within 7–14 days of life.
- Approximate target weight gain considered is 10–20 g/kg/day.

- Judicious nutritional support to maintain lean body mass and bone density, prevention of complications (e.g., CLD, NEC, LOS, ROP), optimization of neurodevelopment growth.
Final Comment

1. Preterm birth is a nutritional emergency.

2. Start parenteral nutrition, including amino acids and lipids, within the first 24 h after birth, less amino acids/protein could lead to neurological deficits.

3. Start enteral feeding early as it promotes tolerance.

4. Breastmilk is the optimal food for all infants but requires supplementation to produce and sustain growth in very preterm infants, if not available, fortified donor milk or PTF may serve as alternatives, both being safe.

5. Rapid early growth is associated with improved cognitive outcomes in infants born preterm.

6. The objective of neonatal nutritional strategies should be to optimize neurodevelopmental outcomes rather than growth alone.
