"I'M NOT SURE BUT I THINK THE FOUR BASIC FOOD GROUPS ARE FROZEN, CANNED, JUNK, AND TAKE-OUT."
Macronutrient Caloric Content

- Protein
- Lipid
- Carbohydrate
Energy Content of Foods

Calculated from the heat released by the total combustion of food in a calorimeter. Can be expressed as kcal or joules (1 kcal=4.13 kJ).
AGA 27 week : How do we Nourish this Baby?
Parenteral Nutrition: Common Practice

- Amino acids started in first week of life and advanced slowly in increments.
- Lipid infusions started in first week of life and advanced incrementally.
- Amino acids and lipids frequently delayed or interrupted.
Excuses To Withhold ENTERAL “Feedings”

- Low APGAR scores.
- Umbilical catheters.
- Apnea and Bradycardia.
- Mechanical ventilation.
- CPAP.
- Vasoactive drugs.
- TPN is available.
NICU vs. Fetal Weight Gain

Ehrenkranz et al Pediatrics 1999
Calorie intake and cumulative deficit over the first 10 days: 50 British NICUs

Grover A et al. JPEN J Parenter Enteral Nutr 2008;32:140-144
Protein intake and cumulative deficit over the first 10 days: 50 British NICUs

Grover A et al. JPEN J Parenter Enteral Nutr 2008;32:140-144
# 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>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>690</td>
<td>86.6</td>
<td>8.8</td>
<td>0.1</td>
<td>19.5</td>
</tr>
<tr>
<td>26</td>
<td>880</td>
<td>86.8</td>
<td>9.2</td>
<td>1.5</td>
<td>123.6</td>
</tr>
<tr>
<td>28</td>
<td>1160</td>
<td>84.6</td>
<td>9.6</td>
<td>5</td>
<td>326.2</td>
</tr>
<tr>
<td>40</td>
<td>3450</td>
<td>74.0</td>
<td>12</td>
<td>15.3</td>
<td>3152.4</td>
</tr>
<tr>
<td>2 months</td>
<td>5450</td>
<td>71.4</td>
<td>11.4</td>
<td>25</td>
<td>9866</td>
</tr>
</tbody>
</table>

Ziegler, E. Growth, 1976
Intravenous Nutrition (IVN): General Principles and Why it is Necessary to Use

1. Metabolic and thus nutritional requirements in the infant do not stop with birth.

2. Preterm infants have insufficient nutrient stores to support metabolic needs for very long.

3. The metabolic and nutrient requirements of the newborn are equal to or greater than those of the fetus of the same gestational age.

4. Intravenous feeding is always indicated when normal metabolic and nutritional needs in newborn infants are not met by normal enteral feeding.
As Total energy intake during the first 7 days of life increased in critically ill infants, the Odds Ratio of such adverse outcomes as NEC, late onset sepsis, BPD and NDI decreased by approximately 2% for each 1kcal/kg/d of total energy intake.

25 wk

term
First week protein and energy intake and neurodevelopmental outcome @18 months

- Retrospective study of 124 ELBW infants at 18 months CA

In-hospital growth velocity and neurodevelopmental outcome

- Cohort study, 600 infants with birth weight 501 to 1000g

**MDI < 70**

(P<0.01)

<table>
<thead>
<tr>
<th>Weight gain quartiles (g/(kg·d))</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0</td>
<td>30</td>
</tr>
<tr>
<td>15.6</td>
<td>25</td>
</tr>
<tr>
<td>17.8</td>
<td>20</td>
</tr>
<tr>
<td>21.2</td>
<td>10</td>
</tr>
</tbody>
</table>

**Neurodevelopmental impairment**

(P<0.001)

<table>
<thead>
<tr>
<th>Weight gain quartiles (g/(kg·d))</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>15.6</td>
<td>40</td>
</tr>
<tr>
<td>17.8</td>
<td>30</td>
</tr>
<tr>
<td>21.2</td>
<td>10</td>
</tr>
</tbody>
</table>

**Cerebral palsy**

(P<0.01)

<table>
<thead>
<tr>
<th>Weight gain quartiles (g/(kg·d))</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0</td>
<td>25</td>
</tr>
<tr>
<td>15.6</td>
<td>20</td>
</tr>
<tr>
<td>17.8</td>
<td>15</td>
</tr>
<tr>
<td>21.2</td>
<td>10</td>
</tr>
</tbody>
</table>

**PDI < 70**

(P<0.001)

<table>
<thead>
<tr>
<th>Weight gain quartiles (g/(kg·d))</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0</td>
<td>60</td>
</tr>
<tr>
<td>15.6</td>
<td>40</td>
</tr>
<tr>
<td>17.8</td>
<td>30</td>
</tr>
<tr>
<td>21.2</td>
<td>10</td>
</tr>
</tbody>
</table>
ENERGY REQUIREMENTS

- **120 CAL/KG/D FOR GROWTH IF FED ENTERALLY.**
- **IF ON TPN, POSITIVE NITROGEN BALANCE CAN BE ATTAINED WITH 60 CAL/KG/D WITH ABOUT 2.5 G/KG/D OF PROTEIN.**
- **MINIMAL CALORIC INTAKE FOR WEIGHT GAIN IS ABOUT 80 CAL/KG/D IF ON TPN.**
Energy Requirements in Preterm Infant

Energy Expenditure = 83 kcal

Resting Metabolic Rate = 50
Activity = 15
Cold Stress = 10
Synthesis / Thermic effect of food = 8

Energy Stored = 25 kcal
Energy Excreted = 12 kcal
TOTAL = 120 Kcal (if enterally fed).
Glucose

- 6-8 mg/min/kg beginning at birth,
- increasing to 10-14 mg/min/kg for full IVN (~60-80 Kcal/kg/day),
- done sort of reflexively, without considering the degree of illness or other pathophysiology in the infant.

Unfortunately, this all too often leads to HYPERGLYCEMIA

Why?
- Maximum Oxidation of Glucose is about 12 mg/kg/min.
- Infusion rates of glucose greater than 12 mg/kg/min may exceed capacity for infants with lung disease to eliminate CO\(_2\).
Carbon dioxide production almost doubled from 4.7 to 7.9 mL/kg/min when the glucose intake increased from 10 to 24 g/kg/day. 

Van Aerde, 2003
Why hyperglycemia?

Persistent glucose production (gluconeogenesis and glycogenolysis), despite high rates of glucose infusion and insulin production.

Chacko S, Sunehag A. Arch Dis Child Fetal Neonatal Ed 2010;95:F413-F418
Furthermore, in sicker infants, increased counter-regulatory hormones that produce glycogenolysis and gluconeogenesis.

- Hypoxia-ischemia → Increased catecholamines
  - Increased glycogenolysis
  - Decreased insulin secretion
  - Decreased insulin action
  - Increased protein breakdown

- Hypoxia-ischemia → Increased cortisol
  - Increased gluconeogenesis
  - Increased protein breakdown
  - Decreased insulin secretion
  - Increased protein breakdown

Rozance, et al., 2008
And infused catecholamines, to support cardiac output and blood pressure do the same thing as those produced endogenously.

Inhibit insulin secretion.
Other complications of Hyperglycemia—when maximal glucose oxidative capacity (>11-14 mg/kg/min) is exceeded.

Established adverse effects---

- ↑ energy expenditure (glucose-to-fat synthesis is energy expensive)
- ↑ oxygen consumption (and hypoxia)
- ↑ carbon dioxide production (and tachypnea)
- ↑ Fat deposition in excess of lean mass
- ↑ Fatty infiltration of heart and liver
Benefits of **tight** Insulin-glucose control? (noted primarily in adults)

1. Reduced morbidity and mortality
2. Improved metabolic status (improved EE)
3. Improved cardiovascular status (CO)
4. Improved systemic and regional $\text{DO}_2$
5. Improved immunity, reduced infection, better wound healing, improved nitrogen balance.

**But—highly controversial!**

Subsequent trials (42 hospitals, 4 countries) failed to demonstrate benefits from **tight** glucose control and actually demonstrated significant excess mortality using the tight glucose range vs. the conventional range.
Insulin infusion vs. reduced glucose infusion to treat hyperglycemia in 500-750 g infants

No difference in all age/weight groups on:
Death, Sepsis, ROP, NEC, ICH, CLD, NICU days, or Growth.

Perhaps safer, therefore, to just lower the glucose infusion rate.

Done because studies in adults suggested that tight control of hyperglycemia in adults decreased mortality.

International Randomized trial: **0.06** U per Kg insulin per hour versus standard neonatal care.

Early Insulin group had lower glucose levels.

Intention to treat insulin group showed higher mortality at 28 days.

Essential Fatty Acid Deficiency

Fig. 4. Flaky skin on the foot of patient SW who had received prolonged fat-free intravenous alimentation.

Paulsrud JR
Triglyceride Structure

3 Fatty Acids + Glycerol
Fatty Acids

CHAIN LENGTH
- Short-chain fatty acids (≤6 carbons)
- Medium-chain fatty acids (8-12 carbons)
- Long-chain fatty acids (≥14 carbons)

NUMBER OF DOUBLE BONDS
- Saturated fatty acids (none)
- Monounsaturated fatty acids (1)
- Polyunsaturated fatty acids (2 or more)
Fatty Acid Nomenclature

Number of Carbons \( \rightarrow \) Number of Double Bonds

18:1\(\omega\)9

Position of First Double Bond From Noncarboxyl (\(\omega\) or n-) Terminus
Linoleic acid, a polyunsaturated fatty acid. Both double bonds are cis.
## Nomenclature of Fatty Acids

<table>
<thead>
<tr>
<th>Names</th>
<th>IUPAC</th>
<th>carboxyl-reference</th>
<th>ω-reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>palmitic acid</td>
<td>hexadecanoic acid</td>
<td>16:0</td>
<td>16:0</td>
</tr>
<tr>
<td>stearic acid</td>
<td>octadecanoic acid</td>
<td>18:0</td>
<td>18:0</td>
</tr>
<tr>
<td>oleic acid</td>
<td>9-octadecenoic acid</td>
<td>18:1 $\Delta^9$</td>
<td>18:1 ($\omega$-9)</td>
</tr>
<tr>
<td>linoleic acid</td>
<td>9,12-octadecenoic acid</td>
<td>18:2 $\Delta^9,12$</td>
<td>18:2 ($\omega$-6)</td>
</tr>
<tr>
<td>linolenic acid</td>
<td>9, 12, 15-octadecenoic acid</td>
<td>18:3 $\Delta^9,12,15$</td>
<td>18:3 ($\omega$-3)</td>
</tr>
</tbody>
</table>
Essential Fatty Acids and their Derivatives

- Linoleic Acid-$C_{18:2\omega-6}$: 2-series Prostaglandins (PGE$_2$).
- Linolenic Acid-$C_{18:3\omega-3}$: DHA, EPA and 2-series prostaglandins (PGE$_3$)--less inflammatory and strongly inhibit platelet aggregation.
LCPUFA Synthesis

Haggarty P. EJCN 55:1563, 2004
**Triene: Tetraene Ratio**

**Trienes:** Derived from Non Essentials (C18:1n9)
- Palmitic → Oleic → Eicosatrienoic

**Tetraenes:** Derived from Essentials (C18:2n6, C18:3n3)

Desaturase enzymes prefer the Essentials, but if essentials are not present, Desaturases will act on the non-essentials and increase the ratio.

If **Triene/Tetraene** is > 0.2, this is considered EFA deficiency.
## Biochemical EFA Deficiency in Prematures: Holman Index

<table>
<thead>
<tr>
<th>Linoleic acid intake (g/kg/d)</th>
<th>NO IV Lipid</th>
<th>NO IV Lipid</th>
<th>IV Lipid +</th>
<th>NO IV Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS + NO Feed</td>
<td>0</td>
<td>0.02</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>RDS + Feed +</td>
<td>0</td>
<td>0.20</td>
<td>0.80</td>
<td>1.0</td>
</tr>
<tr>
<td>NO Feed</td>
<td>0</td>
<td>0.50</td>
<td>1.1</td>
<td>1.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Triene:Tetraene Ratio &gt; 0.2</th>
<th>NO IV Lipid</th>
<th>NO IV Lipid</th>
<th>IV Lipid +</th>
<th>NO IV Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS + NO Feed</td>
<td>1 (5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RDS + Feed +</td>
<td>3 (15%)</td>
<td>1 (3%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NO Feed</td>
<td>16 (80%)</td>
<td>4 (13%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Birth weight 1.35 kg, gestational age 31 wk; IV Lipid + = 1 - 3 g/kg/d

Gutcher, AJCN 1991; 54:1024
What do You Do? What do Others Do?

Nutritional practices in the neonatal intensive care unit:
analysis of a 2006 neonatal nutrition survey.
In utero lipid supply is approximately 2.5-3.0 grams/kg/d.

Essential Fatty Acid (EFA) status in early infancy is low and is rapidly exacerbated with lipid free nutrition.

Long Chain Polyunsaturated Fatty Acid (LCPUFA) derivatives from EFAs are important in brain and retinal development.

Prevention of catabolism and protein sparing.
## Biochemical EFA Deficiency in Prematures: Holman Index

<table>
<thead>
<tr>
<th>Linoleic acid intake (g/kg/d)</th>
<th>NO IV Lipid</th>
<th>NO IV Lipid</th>
<th>IV Lipid +</th>
<th>NO IV Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RDS +</td>
<td>RDS +</td>
<td>RDS +</td>
<td>NO RDS</td>
</tr>
<tr>
<td></td>
<td>NO Feed</td>
<td>Feed +</td>
<td>NO Feed</td>
<td>Feed +</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0.02</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0.20</td>
<td>0.80</td>
<td>1.0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0.50</td>
<td>1.1</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Triene: Tetraene Ratio > 0.2**

<table>
<thead>
<tr>
<th></th>
<th>NO IV Lipid</th>
<th>NO IV Lipid</th>
<th>IV Lipid +</th>
<th>NO IV Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RDS +</td>
<td>RDS +</td>
<td>RDS +</td>
<td>NO RDS</td>
</tr>
<tr>
<td></td>
<td>NO Feed</td>
<td>Feed +</td>
<td>NO Feed</td>
<td>Feed +</td>
</tr>
<tr>
<td>1</td>
<td>1 (5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>3 (15%)</td>
<td>1 (3%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>16 (80%)</td>
<td>4 (13%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Birth weight 1.35 kg, gestational age 31 wk; **IV Lipid + = 1 - 3 g/kg/d**

Gutcher, AJCN 1991; 54:1024
Dogmas to Withhold Lipids

- Hyperbilirubinemia
- Sepsis
- PPHN
- Lung Disease
- Liver Disease
- Thrombocytopenia
Fat Requirements

- Endogenous lipid stores are about 20 g in a 1000g ELBW infant at birth.
- How long will this last?
Calculation (assume 1 kg baby)

- Need total of 80 Kcal/Kg/d for growth
- Glucose:
  - 8mg/kg/min ~ 39 Kcal
- Amino Acids:
  - 3 gm/Kg/d = 12 Kcal
- Lipids:
  - Still need ~30 Kcal for 80 total
  - 30 kcal X cc/2.2 Kcal X 0.2 gm/cc = 2.7 gm/d
Safety and Efficacy of Early Parenteral Lipid and High-Dose Amino Acid Administration to Very Low Birth Weight Infants

Hester Vlaardingerbroek, MD, PhD¹, Marijn J. Vermeulen, MD, PhD¹, Denise Rook, MD, PhD¹, Chris H. P. van den Akker, MD, PhD¹, Kristien Dorst¹, Josias L. Wattimena², Andras Vermes, PharmD, PhD³, Henk Schierbeek, PhD¹,⁴,⁵, and Johannes B. van Goudoever, MD, PhD¹,⁴,⁵

**Objective** To assess the efficacy and safety of early parenteral lipid and high-dose amino acid (AA) administration from birth onwards in very low birth weight (VLBW, birth weight <1500 g) infants.

**Study design** VLBW infants (n = 144; birth weight 862 ± 218 g; gestational age 27.4 ± 2.2 weeks) were randomized to receive 2.4 g of AA kg⁻¹·d⁻¹ (control group), or 2.4 g AA kg⁻¹·d⁻¹ plus 2-3 g lipids kg⁻¹·d⁻¹ (AA + lipid group), or 3.6 g AA kg⁻¹·d⁻¹ plus 2-3 g lipids kg⁻¹·d⁻¹ (high AA + lipid group) from birth onwards. The primary outcome was nitrogen balance. The secondary outcomes were biochemical variables, urea rate of appearance, growth rates, and clinical outcome.

**Results** The nitrogen balance on day 2 was significantly greater in both intervention groups compared with the control group. Greater amounts of AA administration did not further improve nitrogen balance compared with standard AA dose plus lipids and was associated with high plasma urea concentrations and high rates of urea appearance. No differences in other biochemical variables, growth, or clinical outcomes were observed.

**Conclusions** In VLBW infants, the administration of parenteral AA combined with lipids from birth onwards improved conditions for anabolism and growth, as shown by improved nitrogen balance. Greater levels of AA administration did not further improve the nitrogen balance but led to increased AA oxidation. Early lipid initiation and high-dose AA were well tolerated. *(J Pediatr 2013;163:638-44)*.
WHEN TO START LIPIDS

ASAP—As Soon As Possible. No studies that show problems starting at 3.0 gm/kg/d.
USUALLY NOT MORE THAN 3.0 GM/KG/D NEED PROVIDED.
HYPERLIPIDEMIA TOUGH TO MONITOR PROLONGED INFUSIONS USUALLY SAFE (<0.2 GM/KG/HR).
Monitoring Triglycerides

- Different norms are recommended by different authors (e.g. 100-150, <200 mg/dl, etc.)
- Is this efficacious and /or realistic?
1. What happens to DHA levels after premature birth?
2. If low, do they cause disease?
Even if mothers are receiving fish oil or omega 3 supplements, ELBW babies do not receive much milk because of lack of enteral feedings.
Metabolizable DHA Intake During the 1st 4 weeks in 40 Preterms

In utero accretion = 45 mg/kg/day

Lapillone, Neonatology 2010; 98:397-403
AGA 27 Week Preterm: How do we Nourish this Baby?

This baby would have a DHA deficit of 661 mg/kg by 28 days after birth.
DHA Levels and Chronic Lung Disease

C. Martin, J Peds. 2011;159:743-9
Fish oil emulsion vs. historical controls: improved (shorter time to) reversal of cholestasis.
Perhaps Improved DHA intake with Newer Parenteral Lipid Emulsions Containing Fish Oil

<table>
<thead>
<tr>
<th>Oil</th>
<th>Intralipid</th>
<th>Omegaven</th>
<th>SMOF-lipid</th>
<th>Lipoplus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>soybean</td>
<td>Fish 100%</td>
<td>Soy 30</td>
<td>Soy 40%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td></td>
<td>Olive 25%</td>
<td>Coconut 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Coconut 30%</td>
<td></td>
</tr>
<tr>
<td>Linoleic</td>
<td>44 – 62</td>
<td>0.1 - 0.7</td>
<td>22</td>
<td>24.5</td>
</tr>
<tr>
<td>Linolenic</td>
<td>4 – 11</td>
<td>0.2</td>
<td>2</td>
<td>3.5</td>
</tr>
<tr>
<td>Palmitic</td>
<td>7 – 14</td>
<td>0.25 - 1.0</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Oleic</td>
<td>19 – 30</td>
<td>0.6 - 1.3</td>
<td>31</td>
<td>8</td>
</tr>
<tr>
<td>DHA</td>
<td>0</td>
<td>1.4 - 3.1</td>
<td>2</td>
<td>2.5</td>
</tr>
</tbody>
</table>
| Alpha-
Tocopherol | 38 mg/dL   | 150-296 mg/dL | ?   | ?       |
| Phytosterols| 348 mg/L   | 0        | ?          | ?        |

Original Communication

Short-Term Use of Parenteral Nutrition With a Lipid Emulsion Containing a Mixture of Soybean Oil, Olive Oil, Medium-Chain Triglycerides, and Fish Oil: A Randomized Double-Blind Study in Preterm Infants

Maissa Rayyan, MD1; Hugo Devlieger, MD, PhD1; Frank Jochum, MD, PhD2; and Karel Allegaert, MD, PhD1

Financial disclosure: The clinical research of Karel Allegaert is supported by the Fund for Scientific Research, Flanders (Belgium) by a Fundamental Clinical Investigatorship (1800209 N) and a research grant (1506409 N). The study was conducted for registration purposes and therefore was sponsored by Fresenius Kabi, Bad Homburg, Germany. Hugo Devlieger and Frank Jochum have received speaking honoraria and consulting fees from Fresenius Kabi. The publication of the supplement in which this article appears is sponsored by Nestlé Nutrition Institute.

Background: For premature neonates needing parenteral nutrition (PN), a balanced lipid supply is crucial. The authors hypothesized that a lipid emulsion containing medium-chain triglycerides (MCTs) and soybean, olive, and fish oils would be as safe and well tolerated as a soybean emulsion while beneficially influencing the fatty acid profile. Methods: Double-blind, controlled study in 53 neonates (<34 weeks’ gestation) randomized to receive at least 7 days of PN containing either an emulsion of MCTs and soybean, olive, and fish oils or a soybean oil emulsion. Target lipid dosage was 1.0 g fat/kg body weight [BW]/d on days 1–3, 2 g/kg BW/d on day 4, 3 g/kg BW/d on day 5, and 3.5 g/kg BW/d on days 6–14. Results: Test emulsion vs control, mean ± SD: baseline triglyceride concentrations were 0.52 ± 0.16 vs 0.54 ± 0.19 mmol/L and increased similarly in both groups to 0.69 ± 0.38 vs 0.67 ± 0.36 on day 8 of treatment (P = .781 for change). A significantly higher decrease in total and direct bilirubin vs baseline was seen in the test group compared with the control group (P < .05 between groups). In plasma and red blood cell phospholipids, eicosapentaenoic acid and docosahexaenoic acid were higher, and the n-6/n-3 fatty acid ratio was lower in the test group (P < .05 vs control). Conclusions: The lipid emulsion, based on a mixture of MCTs and soybean, olive, and fish oils, was safe and well tolerated by preterm infants while beneficially modulating the fatty acid profile. (JPN J Parenter Enteral Nutr. 2012;36:81S-94S)

Keywords: parenteral nutrition; premature infant; fish oils; triglycerides; liver function; fatty acids
Amino Acids

- What day do you start?
- How much do you start with?
Essential Amino Acids
Biologic value of proteins

The ability to provide the essential amino acids required for tissue maintenance.

- Egg albumin=100%
- Milk=85%
- whole wheat bread=30%
Getting All Essential Amino Acids on Vegetarian Diet

![Graph showing the amount of essential amino acids in different diets]

- **Beans**
  - Lysine
  - Methionine + Cystine

- **Wheat**
  - Need more

- **Beans + Wheat (1:1)**
  - Lysine
  - Methionine + Cystine

The graph compares the amount of essential amino acids in beans, wheat, and a mixture of beans and wheat in a 1:1 ratio. Lysine and Methionine + Cystine are indicated separately.
Amino Acids

Protein turnover rate is high in the fetus, requiring large amino acid uptake rates.

**Fetal animal growth data**, when scaled to human fetal growth rate, predict fetal amino acid requirements = \(3.6-4.8\) g//kg/day

**Factorial Method** (Ziegler)—
predict human fetal amino acid requirements = 4 g/kg/day

**Fetal AA delivery rates**

- 24 - 28 weeks 3.75 - 4.0 g/kg/d
- 28 - 32 weeks 3.5 g/kg/d
- >32 weeks 3.2 g/kg/d
- Term 2.8 – 3.0 g/kg/d

Meier, Peterson, Kennaugh, Battaglia, et al.
Preterm nutrition - actual recommendation

- Very low birth weight (VLBW) preterms have a different nutrient distribution
- Preterms with lower birth weight need more proteins

**Protein Requirement (g/100 kcal) in Relation to birth weight**

<table>
<thead>
<tr>
<th>Birth Weight (g)</th>
<th>10-20% of Preterms</th>
<th>80-90% of Preterms</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-700 g</td>
<td>3.6-4.1 g/100 kcal (ESPGHAN)</td>
<td>3.2-3.6 g/100 kcal (ESPGHAN)</td>
</tr>
<tr>
<td>700-900 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>900-1200 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1200-1500 g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1500-1800 g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ziegler EE, Carlson SJ, 2009
Body Protein over the First week of Postnatal life: Glucose vs. Protein Accretion in the Fetus vs. Different Amino Acid Intakes

Denne, SC. *Seminars in Perinatology* Volume 31, Issue 2, April 2007
Above 80 non-protein kcal/kg/d, there is no further increase in protein gain for an increase in energy intake (protein gain is primarily dependent on protein intake!).
Many NICUs delay TPN amino acids, then begin at 0.5 g/kg/d and advance slowly. Using this approach, may infants do not attain the intrauterine accretion (3.5-4.0 g/kg/d) until they are 7-14 days of age. This leads to a significant early protein deficit.
# High vs. Low Amino Acid Intake and Glucose/Insulin

<table>
<thead>
<tr>
<th></th>
<th>Low amino acids</th>
<th>High amino acids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucose, mmol/L (mg/dL)</strong></td>
<td>6.2 ± 0.7 (113 ± 13)</td>
<td>6.9 ± 0.8 (125 ± 14)</td>
</tr>
<tr>
<td><strong>Insulin, pmol/L (µU/mL)</strong></td>
<td>75 ± 13 (10.5 ± 1.9)</td>
<td>139 ± 23 (19.3 ± 3.1)*</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SEM.

* Significant difference between groups, *p* < 0.05.
Delayed TPN, Hyperglycemia and Hyperkalemia

Delayed TPN

Low Leucine, arginine
Other amino acids

Insulin

Glucose

K+
Serum BUN

Thureen, et al.  
Peds Research, 2003

$p=0.232$
But--there have been exceptions---

Standard vs. Early-High AA infusions using Aminosyn PF during first week of life in <1000 g, >24 wks GA infants.


Thureen et al. 3 g/kg/d Trophamine

highest BUN mean plasma Total AA concentrations.

Very high AA concentrations—Why?
Individual Amino Acids – even at 3 g/kg/d there still is room for improvement!

Even at high amino acid infusion rates, current IV Amino Acid solutions may not produce normal (fetal) concentrations of all essential amino acids, which “will” limit growth.

(Thureen and Hay)
Early nutrition in premature babies can be safe and efficacious and may prevent significant morbidity.

Many of the dogmas that have prevented rapid incorporation of early nutrition have either been disproved, not based on fact or weak.

Begin IV infusions of protein (3-4 grams/kg/d) and lipid (3 grams/kg/day) right after birth to prevent protein and energy insufficiency and to keep the baby within normal limits.