Growth and Macronutrients for the Premature Infant

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NAC
NUTRITION ADVISORY COMMITTEE

Objectives

- Review the unique nutritional needs of preterm infants
- Review the incidence and causes of extrauterine growth restriction (EUGR) in very low birthweight (VLBW) infants
- Summarize the evidence regarding the impact of nutrition on neurodevelopmental outcomes
- Define the protein and energy requirements
- Discuss a variety of nutritional strategies for meeting protein and energy

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Why is Nutrition Important for the Preterm Infant, particularly the Very Low and Extremely Low Birthweight Preterm Infant?

What Is Fetal Nutrition and Growth?

- Calories: 120 kcal/kg/d
- Protein: 3 g/kg/d
- Weight Velocity: 14-16 g/kg/d

Review of Preterm Energy Needs

- Glucose provides 80-90% fetal energy consumption in utero
- Glycogen storage does not occur before 27 weeks, gradually increases until 36 weeks
- A glucose infusion rate (GIR) of 4-7 mg/kg/d is required to meet basal metabolic rate (BMR)

Taylor SN et al 2010; Cowett RM et al 2004; Mitanchez D 2007

Review of Preterm Energy Needs

- Natural growth period during third trimester is disrupted including formation of adipose tissue
- Infants born 24-25 weeks require large quantities of essential fatty acids to achieve growth similar to in utero growth
- Main source of energy for fetus is glucose with ~70% of fetal glucose converted to fat
- At birth, fat becomes the main source of energy

Review of Preterm Protein Needs

- Require at least 1 g/kg/day to avoid negative nitrogen balance in preterm infants
- At least 3 g/kg/day promotes positive nitrogen balance and protein accretion
- ~ 4 g/kg/day is needed to match fetal protein accretion rate
- Providing <4 g/kg/d in VLBW infants results in protein deficiency that contributes to extrauterine growth restriction (EUGR)

Denne SC 2007;Taylor SN et al 2010

The Goals

- To aim for postnatal growth rate that approximates fetal growth rate and mimics fetal body composition
- To strive for a functional outcome similar to that of infants born at term

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Extrauterine Growth Restriction

- What is it?
  - Falling below the 10th percentile post-birth
  - Inadequate growth compared to fetal growth
  - Born AGA and becoming SGA
- Difficulties
  - What is expected fetal growth?
  - Should a preterm infant be expected to grow exactly as a fetus?

AGA: Appropriate for gestational age   SGA: Small for gestational age

Example of EUGR

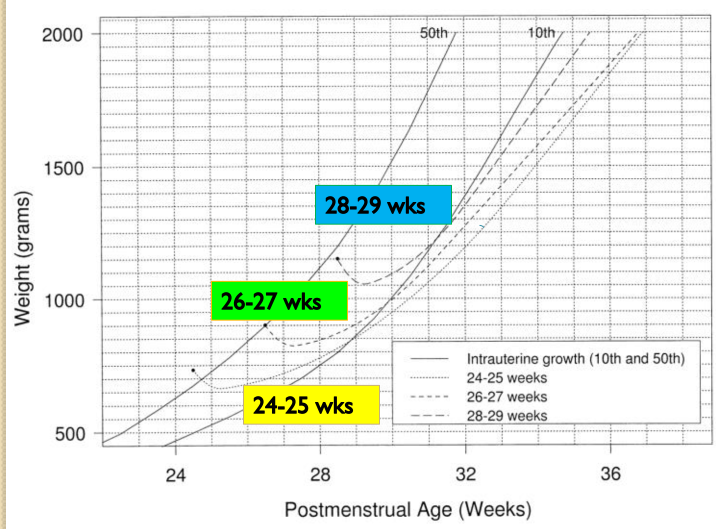
Age	Gestational Age, week	Weight, kg	Weight Percentile*
Birth	26	0.95	>50th
2 wk	28	0.98	>10th
4 wk	30	1.1	~10th
10 wk	36	2.0	3rd
14 wk	40	2.55	<3rd

*Based on Fenton growth chart.

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

NICHD Growth Observational Study:

Average body weight vs. post menstrual age in weeks



PEDIATRICS

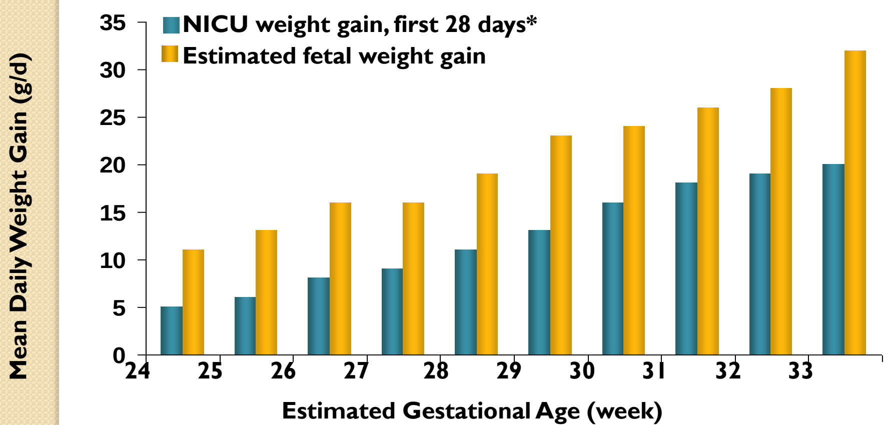
Ehrenkranz R A et al. Pediatrics 1999;104:280-289

EUGR in Preterm Infants

- N=24,371 premature infants discharged from 124 NICUs
- At discharge
  - 28% had EUGR for weight
  - 34% had EUGR for length
  - 16% had EUGR for head circumference

Clark RH, et al. *Pediatrics* 2003;111:986-90.

Weight Gain in NICU vs Fetal Development

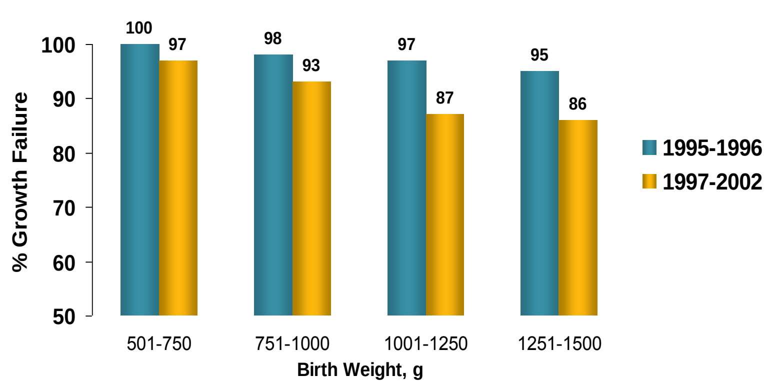


* Includes postnatal weight loss

Clark RH, et al. *J Perinatol* 2003;23:337-44.

Incidence of Growth Failure* in VLBW Infants at 36 Weeks

NICHD Neonatal Research Network Centers



*Growth failure defined as weight <10th percentile at 36 weeks post menstrual age

Lemons JA, et al. *Pediatrics* 2001;107;e1; Fanaroff AA, et al. *Am J Obstet Gynecol* 2007;196:147. e1-8.

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To Match Fetal Growth

- **Relies heavily on time to regain birthweight**
- Growth catch-up requirement
  - 27 week, 1,000 gram infant (50th percentile)
  - 14 days to return to birthweight
  - To average a velocity of 15 g/kg/d from birth to 36 weeks, must gain an additional 4.3 g/d

Embleton ND 2007

Optimal Growth Velocity

- 20-30 g/kg/d associated with ≥ z-score
- To recover days lost while regaining birthweight
- **18-21 g/kg/d—improved neurodevelopment**

26 wks	818 g	38th percentile	
27 2/7 wks	818 g	18th percentile	
32 3/7 wks	1800 g	36th percentile	20.8 g/kg/d
40 weeks	3400 g	37th percentile	30.4 g/d

  - Goal >18 g/d once birthweight has been regained through discharge

- Goal for Head Circumference > 0.9 cm/wk

Ehrenkranz RA et al 2006; Martin CR et al 2009

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Catch-Up Growth in Preterm Infants

- Babies in utero grow rapidly during the last trimester
- Preterm infants need to grow at a faster rate if they are expected to catch up to the growth of their full term counterparts

Avoiding Growth Deficits

- The two macronutrients that are limiting for growth of lean body mass are protein and carbohydrates
- Growth failure is caused by inadequate intake of either one—intakes of both must be adequate.

Early Protein and Energy

- Association with improved 18-month neurodevelopment
- Critical deficits accrued
  - Protein 12-14 g/kg in first week
  - Energy 335-406 kcal/kg in first week
  - 45% of variation in growth explained by energy deficit
- Comparison of growth velocity in the first 28 days
  - Day 7-28 growth velocity was associated with fat, carbohydrate, and protein intake at Day 7, but not at Day 14

Stephens BE et al 2009; Embleton NE et al 2001; Martin CR et al 2009

Early Energy

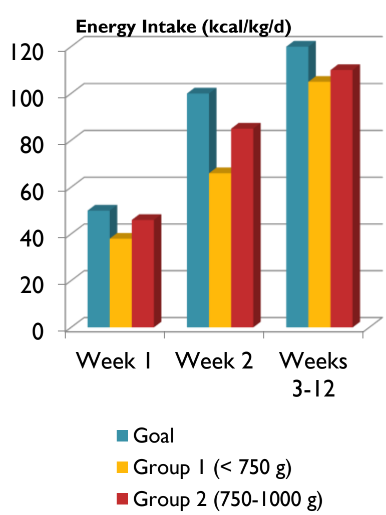
- Energy to grow
  - Early energy is more critical than protein
  - Evidence supports a relationship between nutrient supply in the 1st week of life and later cognitive development in ELBW infants
- Energy to maximize protein accretion
- Carbohydrates
- Lipids Goal—Infusion by 24 hours of life

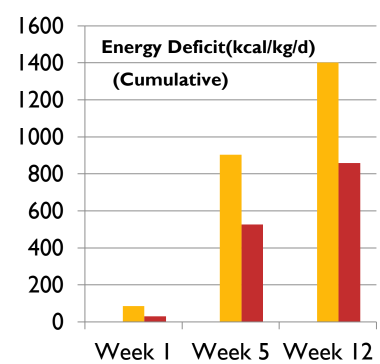
Martin CR 2009; Embleton NE 2001

Inadequate Non-Protein Energy

- Degradation of protein for energy vs. accrual of lean mass (resulting in negative N balance)
- Lipolysis and fatty acid oxidation for energy rather than providing membrane deposition in the brain
  - Altering critical development of the brain may lead to abnormal neurologic function and poor long-term outcomes
  - IV Lipids are crucial for providing essential fatty acids and high-density energy

Significant Energy Deficit from Inadequate Energy Intakes





Ernst KD et al. *J Perinatol* 2003; 23:477-82.

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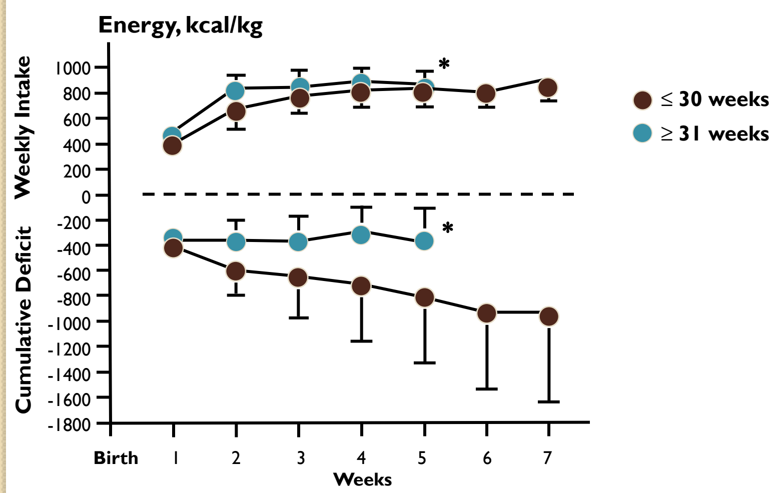
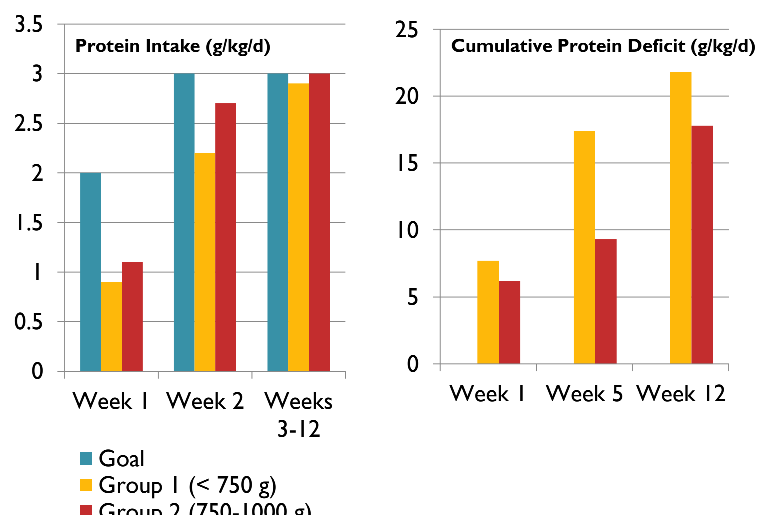
Weekly Energy Intake and Cumulative Deficit



*P<0.01 for overall intakes and deficits vs infants ≤30 weeks.

Embleton NE, et al. *Pediatrics* 2001;107:270-3.

Significant Protein Deficit from Inadequate Protein Intakes



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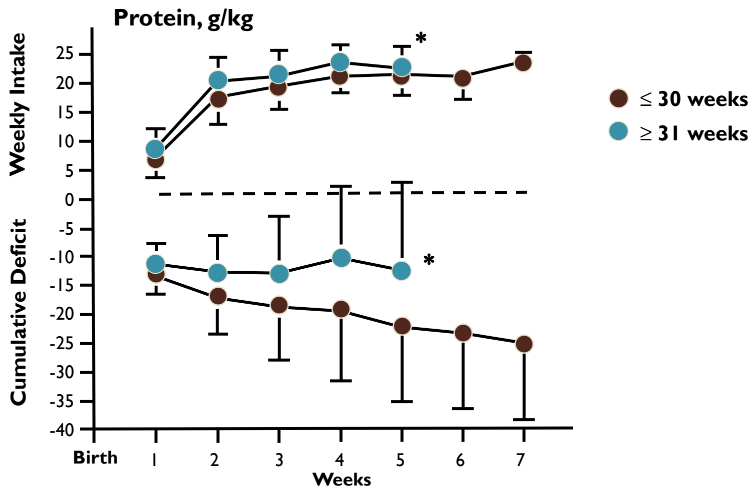

*P<0.01 for overall intakes and deficits vs infants ≤30 weeks.

Embleton NE, et al. *Pediatrics* 2001;107:270-3.

Impact of Growth on Neurodevelopmental Outcomes and Morbidity

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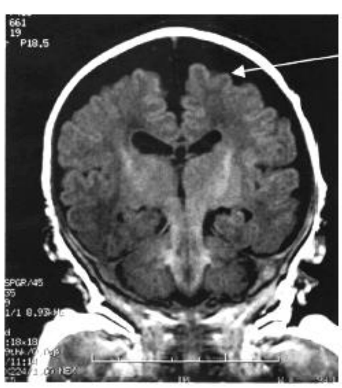
The Long-term Effect on Neurodevelopment

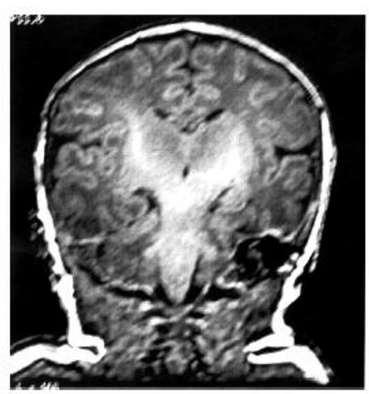
- In-hospital
  - Weight gain of 18-21 g/kg/day
  - Head circumference growth of 0.9-1.1 cm/week
  - Better neurodevelopment and growth outcomes at 18-22 months
- Postnatal growth lag associated with
  - Neurologic and sensory handicaps
  - Poor school performance
  - Head circumference <10th at 8 months = cognitive, educational, and psychosocial delays at 8 years

MRI of VLBW Infants at 40 Weeks GA

Born at 23 weeks GA



Born at 30 weeks GA

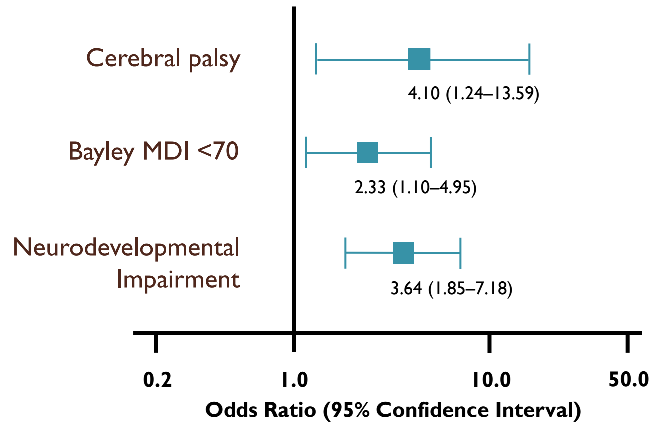


- At 40 weeks GA, significant cerebral abnormalities in infant born at 23 weeks GA (left)
- 10 of 11 infants with gestation <26 weeks had this pattern of cerebral abnormality

Inder et al. *J Pediatr* 2003;143:171-179

Decreased Head Growth Associated with Poor Outcomes

ELBW infants, in-hospital HC growth: **0.67** vs **1.17** cm/wk



HC=Head circumference

MDI=Mental Development Index

Ehrenkranz RA, et al. *Pediatrics* 2006;117:1253-61.

Inadequate Weight Gain Associated with Morbidity

- ELBW infants who experienced the slowest rate of in-hospital weight gain had the highest morbidity
- Weight gain, **12.0** vs **21.2** g/day
  - NEC: 20% vs 4%
  - Late-onset sepsis: 83% vs 55%
  - BPD: 56% vs 31%
  - Postnatal steroid therapy: 64% vs 30%

Ehrenkranz RA, et al. *Pediatrics* 2006;117:1253-61.

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Provision of Optimal Nutrition

Early Parenteral Nutrition for VLBW and ELBW Infants

- Trophamine can begin upon admission at 2.5-3 g/kg/d
- Begin TPN to include dextrose, Trophamine, and lipids by 24 hours of life
- Advance GIR to 6-8 mg/kg/min; protein to 3-4 g/kg and lipids to 2 g/kg by DOL 2
- Goal GIR of 6-8 mg/kg/min, 3.5-4 g Protein/kg, and 85-95 kcal/kg by DOL 3-4

Randomized Controlled Trials of Early Protein Efficacy and Safety

Trial	Population	Comparison	Efficacy Outcomes	Safety Outcomes
Thureen et al 2003	28 ELBW infants	1 g/kg/d versus 3 g/kg/d with glucose and lipid	Higher positive protein balance with 3g/kg/day	No difference in acidosis or BUN
Ibrahim et al 2004	32 VLBW infants	2 g/kg/d initiated 48 hours of age versus 3.5 g/kg/d initiated Day 1 with glucose and lipid	Greater nitrogen balance with early 3.5 g/kg/d	No difference in BUN, creatinine, and pH
te Brakke et al 2005	135 VLBW infants	1.2 g/kg/d on Day 2 and increased to 2.4 g/kg/d Day 3 versus 2.4 g/kg/d within 2 hours of delivery	Positive nitrogen balance achieved earlier with early 2.4 g/kg/d	BUN, acid/base balance all within normal reference range
Clark et al 2007	122 infants <30 weeks gestation	1 g/kg/d and increased by 0.5 g/kg/d to 2.5 g/kg/d versus 1.5 g/kg/d and increased by 1 g/kg/d to 3.5 g/kg/d	No difference in growth	BUN and amino acid higher in higher amino acid group

ELBW: Extremely low birth weight (≤ 1000 g)
VLBW: Very low birth weight (≤ 1500 g)

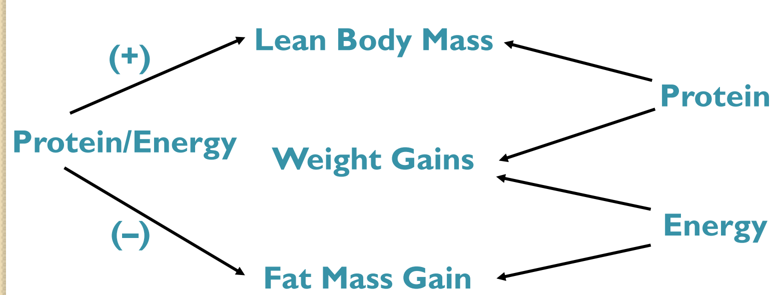
Initiating Enteral Feeds

- Trophic feeds to begin as soon as clinically appropriate
- Standardized feeding guidelines are important for advancement of feeds
- Adjust the TPN as feeds are advanced to maintain overall nutrition at goal

Protein-to-Energy (P/E) Ratio (g/100 kcal)

- Relationship between protein and energy consumption
  - Affects body composition
- Increased P/E ratio desirable
  - Maximizes lean body mass accrual
  - Limits fat mass deposition
- As preterm infant grows, required P/E ratio decreases

P/E Ratio on Body Composition

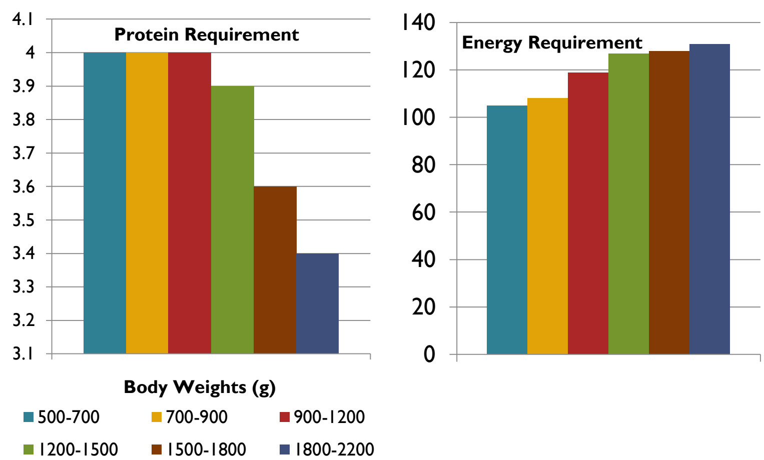


To increase lean body mass accretion and limit fat mass deposition, an increase in protein/energy ratio is mandatory

Adapted from Rigo J, Senterre J. *J Pediatr* 2006;149:S80-8.

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Protein and Energy Requirements Change



Ziegler EE. *J Pediatr Gastroenterol Nutr* 2007;45(suppl):S170-S174.

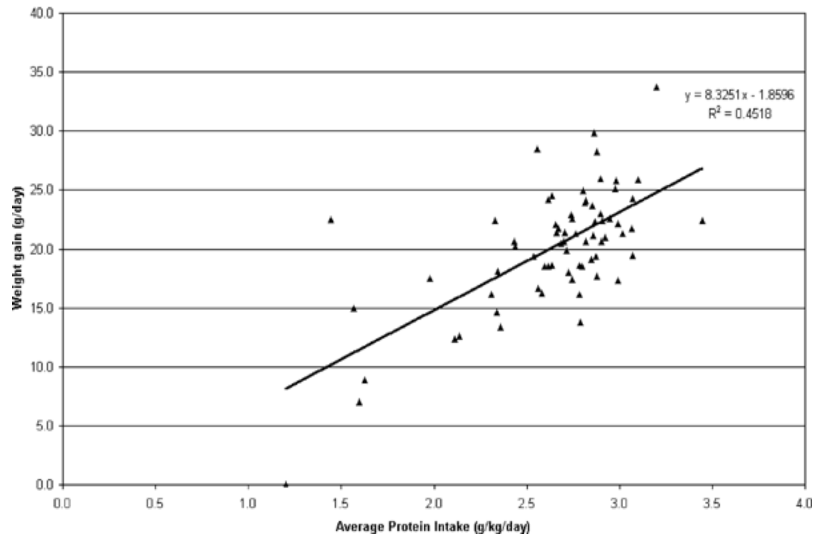
Growth Rates Vary Based on Composition of Feeds

	Group 1 n=14	Group 2 n=15	Group 3 n=15
Formula			
Protein, g/kg/d	2.8	3.8	3.9
Energy, kcal/kg/d	119	120	142
Protein/Energy, g/100 kcal	2.4	3.2	2.7
Outcomes			
Δ Weight, g/kg/d	16.0 (1.8)*	19.1 (3.2)	21.5 (2.2)
Δ Length, cm/wk	1.04 (0.18)	1.21 (0.34)	1.28 (0.47)
Δ HC, cm/wk	0.98 (0.11)	1.15 (0.25)	1.24 (0.26)
Δ Skinfold thickness†, mm/wk	0.69 (0.21)	0.77 (0.28)	1.22 (0.31)*

Significantly different from other 2 groups; †triceps and subscapular skinfolds.

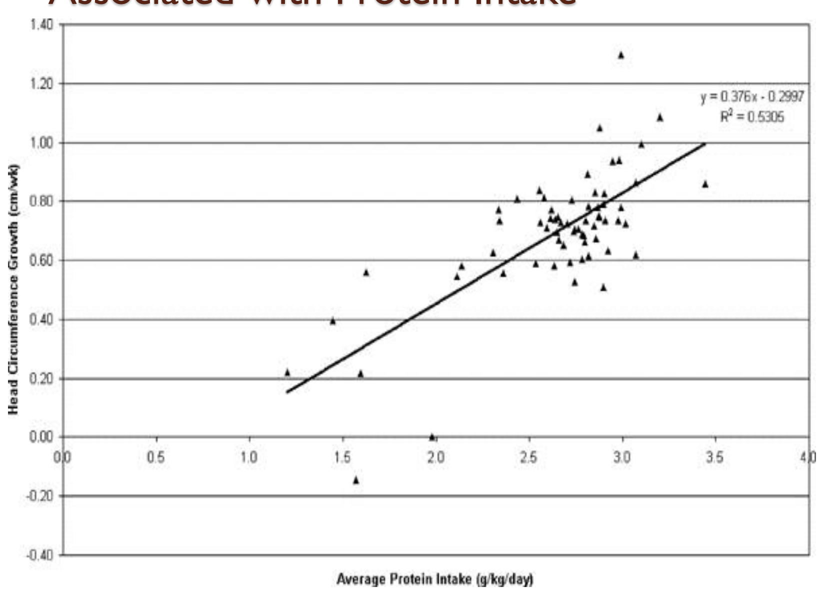
Kashyap S, et al. *J Pediatr* 1988;113:713-721.

Increased Weight Gain is Associated with Protein Intake in ELBW infants



Ernst KD et al. *J Perinatol* 2003; 23:477-82.

Increase in Head Circumference is Associated with Protein Intake



Ernst KD et al. *J Perinatol* 2003; 23:477-82.

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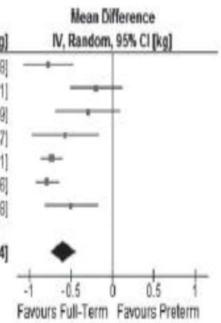
Body Composition at Term Equivalent: Systematic Review & Meta-analysis

A Weight

Study or Subgroup	Preterm Mean [kg]	Preterm SD [kg]	Preterm Total	Term Mean [kg]	Term SD [kg]	Term Total	Weight	Mean Difference IV, Random, 95% CI [kg]
Ahmad 2010	2.679	0.572	20	3.453	0.5	39	13.2%	-0.77 [-1.07, -0.48]
Fusch 1999	3.2	0.7	52	3.4	0.8	41	12.7%	-0.20 [-0.51, 0.11]
Mcleod 2009	2.91	0.71	20	3.206	0.445	14	9.9%	-0.30 [-0.68, 0.09]
Olhager 2006	3.319	0.25	8	3.889	0.555	9	9.5%	-0.57 [-0.97, -0.17]
Roggero 2009	2.46	0.45	159	3.192	0.486	87	21.4%	-0.73 [-0.86, -0.61]
Uthaya 2005	2.68	0.26	38	3.47	0.29	29	20.9%	-0.79 [-0.92, -0.66]
Vasu 2009	2.88	0.7	22	3.38	0.4	39	12.3%	-0.50 [-0.82, -0.18]
Total (95% CI)			**319**			**258**	**100.0%**	**-0.59 [-0.75, -0.44]**

Heterogeneity: I² = 87%
Test for overall effect: Z = 7.35 (P < 0.00001)



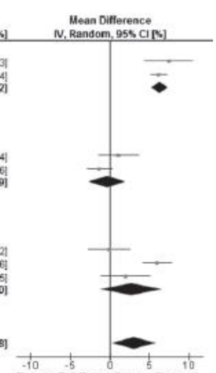
(Johnson MJ et al 2012)

Body Composition at Term Equivalent: Systematic Review & Meta-analysis

A %TBF

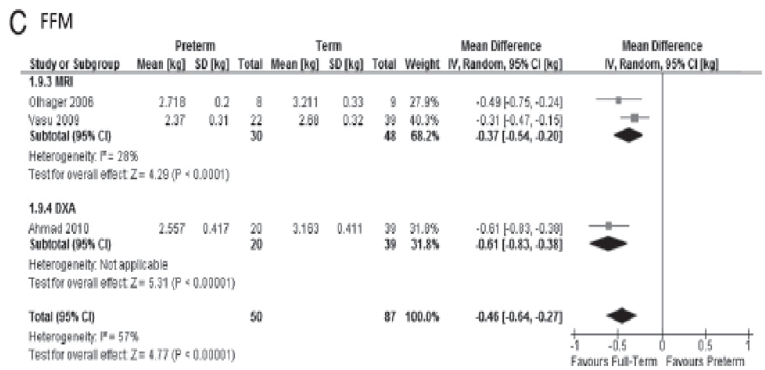
Study or Subgroup	Preterm Mean [%]	Preterm SD [%]	Preterm Total	Term Mean [%]	Term SD [%]	Term Total	Weight	Mean Difference IV, Random, 95% CI [%]
ADP								
Mcleod 2009	17	2.5	20	9.5	5.4	14	13.4%	7.50 [4.47, 10.53]
Roggero 2009	14.8	4.4	159	8.6	3.7	87	15.5%	6.20 [5.16, 7.24]
Subtotal (95% CI)			**179**			**101**	**28.8%**	**6.34 [5.36, 7.32]**
Heterogeneity: I² = 0%								
Test for overall effect: Z = 12.67 (P < 0.00001)								
MRI								
Olhager 2003	18.1	1.4	8	17	3.6	9	14.0%	1.10 [-1.44, 3.64]
Uthaya 2005	17	4	38	18.3	2.5	29	15.1%	-1.30 [-2.86, 0.26]
Subtotal (95% CI)			**46**			**38**	**29.1%**	**-0.32 [-2.63, 1.99]**
Heterogeneity: I² = 60%								
Test for overall effect: Z = 0.27 (P = 0.79)								
DXA								
Ahmad 2010	11.1	5.2	20	11.2	4.1	39	13.9%	-0.10 [-2.72, 2.52]
Atkinson 1994	22	6	69	16	5	87	14.9%	6.00 [4.24, 7.76]
Fusch 1999	18	8	52	16	7	41	13.3%	2.00 [-1.05, 5.05]
Subtotal (95% CI)			**141**			**167**	**42.1%**	**2.74 [-1.23, 6.70]**
Heterogeneity: I² = 87%								
Test for overall effect: Z = 1.35 (P = 0.18)								
Total (95% CI)			**366**			**306**	**100.0%**	**3.06 [0.25, 5.88]**

Heterogeneity: I² = 93%
Test for overall effect: Z = 2.13 (P = 0.03)



(Johnson MJ et al 2012)

Body Composition at Term Equivalent: Systematic Review & Meta-analysis

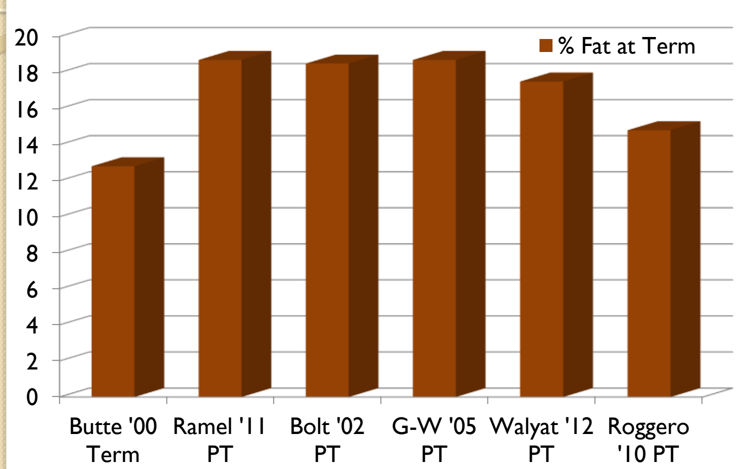


C FFM

Study or Subgroup	Preterm Mean [kg]	Preterm SD [kg]	Preterm Total	Term Mean [kg]	Term SD [kg]	Term Total	Weight	Mean Difference IV, Random, 95% CI [kg]
1.9.3 MRI								
Olhager 2006	2.718	0.2	8	3.211	0.33	9	27.9%	-0.49 [-0.75, -0.24]
Vasu 2009	2.37	0.31	22	2.68	0.32	39	40.3%	-0.31 [-0.47, -0.15]
Subtotal (95% CI)			**30**			**48**	**68.2%**	**-0.37 [-0.54, -0.20]**
Heterogeneity: I² = 28%								
Test for overall effect: Z = 4.29 (P < 0.0001)								
1.9.4 DXA								
Ahmad 2010	2.557	0.417	20	3.163	0.411	39	31.8%	-0.61 [-0.83, -0.38]
Subtotal (95% CI)			**20**			**39**	**31.8%**	**-0.61 [-0.83, -0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.31 (P < 0.00001)								
Total (95% CI)			**50**			**87**	**100.0%**	**-0.46 [-0.64, -0.27]**
Heterogeneity: I² = 57%								
Test for overall effect: Z = 4.77 (P < 0.00001)								

(Johnson MJ et al 2012)

% Fat Mass: Preterm Infants at or near Term vs. Term Newborns



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Parenteral Protein and Energy Requirements of Preterm Infants

Body weight, g	Protein, g/kg/d	Energy, kcal/kg/d	P/E, g/100 kcal
500-700	3.5	89	3.9
700-900	3.5	92	3.8
900-1200	3.5	101	3.5
1200-1500	3.4	108	3.1
1500-1800	3.2	109	2.9
1800-2200	3.0	111	2.7

P/E = Ratio of protein to energy, expressed as grams of protein per 100 kcal.

Ziegler E. *J Pediatr Gastroenterol Nutr* 2007;45:S170-4.

Enteral Protein and Energy Requirements of Preterm Infants

Body weight, g	Protein, g/kg/d	Energy, kcal/kg/d	P/E, g/100 kcal
500-700	4.0	105	3.8
700-900	4.0	108	3.7
900-1200	4.0	119	3.4
1200-1500	3.9	127	3.1
1500-1800	3.6	128	2.8
1800-2200	3.4	131	2.6

P/E = Ratio of protein to energy, expressed as grams of protein per 100 kcal.
Ziegler E. *J Pediatr Gastroenterol Nutr* 2007;45:S170-4.

Enteral Nutrition Recommendations

	Kcal/kg per day	Pro g/kg per day	G Pro/ 100 kcal
Micropreterm ≤29 wks	120-140	3.5-4.5	3-3.6
Preterm ≥29 & ≤34 wks	110-130	3.5-4.2	---
Late preterm 34-37 wks	110-130	3-3.6	---
Post-discharge VLBW*	105-125	2.8-3.2	---
Term Infant (IOM, DRI)	90 (72-108)	1.5	---

*34-38 weeks; assuming no accumulated nutritional deficits

(Uauy R 2013)

Daily Protein and Energy Needs Including Need for Catch-Up

	26-30 weeks	30-36 weeks	36-40 weeks
Protein g/kg	**3.8-4.2** (4.4)	**3.4-3.6** (3.6-4)	**2.8-3.2** (3-3.4)
Energy kcal/kg	**126-140** (134)	**121-128** (120-130)	**116-123** (115-121)
PE Ratio g:100 kcal	**3** (3.3)	**2.8** (3)	**2.4-2.6** (2.6-2.8)

(Rigo and Senterre, J Peds 2006)

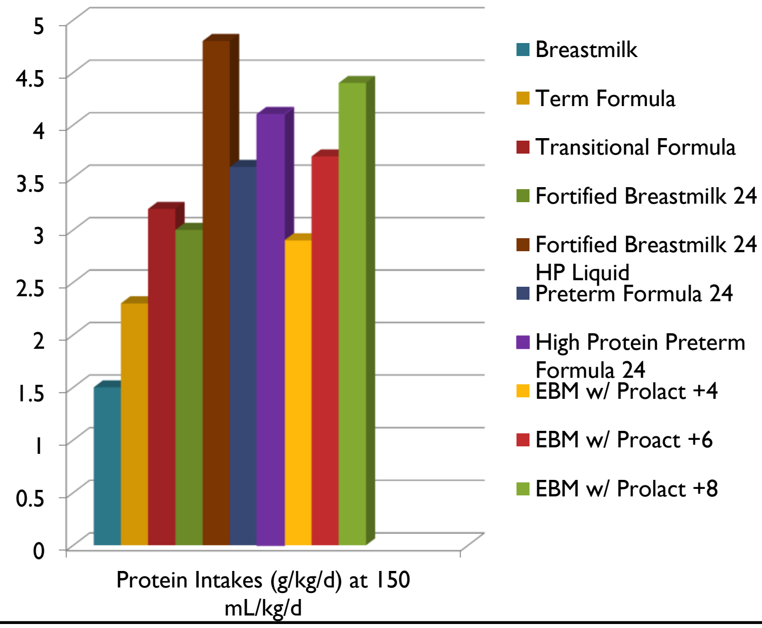
For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Sources of Recommended Intakes for Newborns

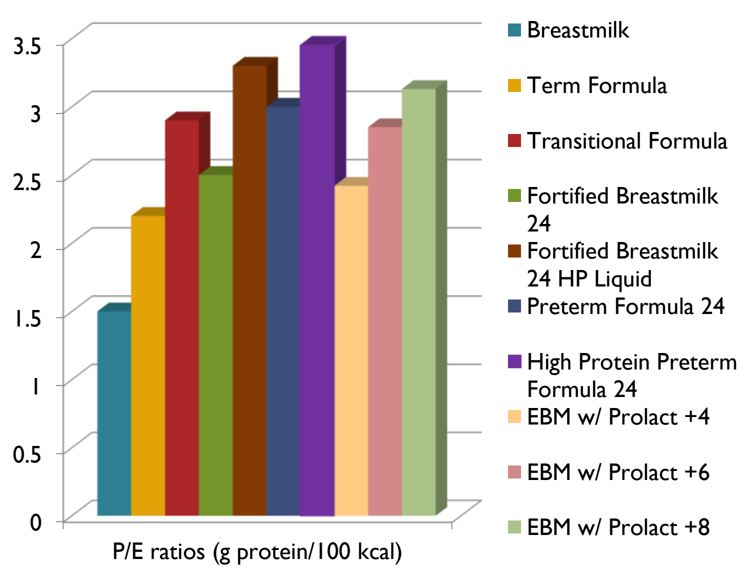
- Koletzko B, Poindexter B, Uauy R, eds. Nutritional Care of Preterm Infants, Karger, 2014
- Uauy R (Ed). Global Neonatal Consensus Symposium: Feeding the Preterm Infant. Journal of Pediatrics 162(3); Supplement 1. March, 2013.
- ESPGHAN. Agostoni C et al, JPGN. 2010;50:85-91
- Rigo J and Senterre J. Nutritional needs of premature infants: Current issues. Journal of Pediatrics 149:S80-S88, 2006.
- American Academy of Pediatrics. Kleinman RE (ed). Nutritional needs of the preterm infant. In, Pediatric Nutrition Handbook, 7th Ed. Elk Grove Village, IL: AAP, 2014. p 83-122.
- Dietary Reference Intakes (term infants) (IOM) http://iom.edu/Home/Global/News%20Announcements/DRI

Feeding Strategies

Enteral Feeding Options



P/E ratio of Various Feeding Types

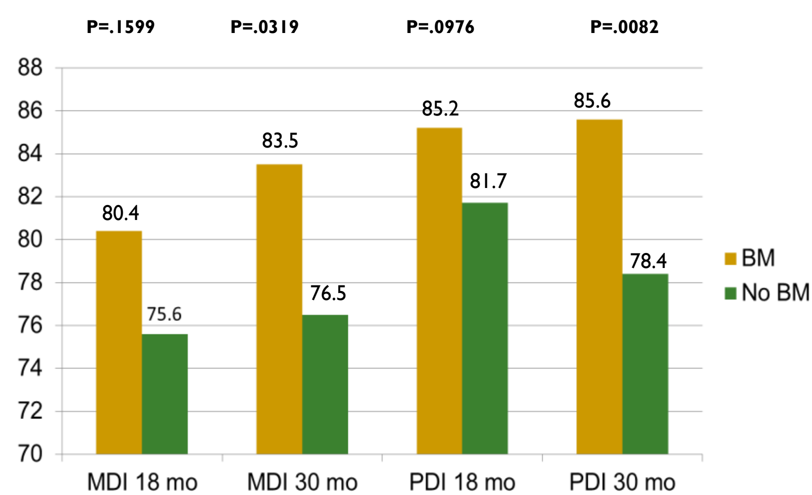


Benefits of Breastmilk

- Reduced Risk of Sepsis Due to Immune Properties
- Decreased Risk of NEC
- Feeding HM is associated with improved neurocognitive outcomes

(O'Connor DL 2003, Lucas A 2001)

Long Term Benefits of Human Milk



Vohr, B. R. et al. *Pediatrics* 2007;120:e953-e959

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Breastmilk Protein Supplementation

- Term Breastmilk has less protein than Preterm Breastmilk
- Additional protein is recommended for preterm infants receiving maternal (term) or banked milk or for a prolonged period of time

(Hay WW 2009)

Strategies to Increase Protein Content of Breastmilk Feeds

- Fortification of Human Milk with Bovine based fortifier
- Advancement of Prolacta supplementation
- Whey protein supplement available
- Hydrolyzed casein liquid supplement available

Protein Levels in Fortified Preterm Human Milk

	Preterm Human Milk, Postnatal Days		
	6–10 days	22–30 days	≥30 days
Protein in **unfortified** milk,[1] g/100 mL	1.9	1.5	1.2
Protein in **fortified** milk,* g/100 mL	2.84	2.44	2.14
Protein/energy ratio, g/100 kcal	3.6	2.9	2.7
Protein intake, g/kg/d @ 120 kcal/kg/d	4.3	3.5	3.3

*Fortification of 100 mL human milk with 4 packets of human milk fortifier adds 0.94 grams of protein and 14 kcal.

1. Schanler RJ, Atkinson SA. In: Tsang RC, et al, eds. *Nutrition of the Preterm Infant*. 2nd ed. Digital Educational Publishing; 2005.

Prolacta's Human Milk Fortifiers

Prolact +4 with Term Breastmilk	1.92 g Protein/100mL	2.9 g Protein and 120 kcal per150 mL
Prolact +6 with Term Breastmilk	2.43 g Protein/100 mL	3.7 g Protein and 130 kcal per150 mL
Prolact +8 with Term Breastmilk	2.94 g Protein/100 mL	4.41 g Protein and 140 kcal per150 mL

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Strategies for Increasing Protein Content in Formula Feeds

- Use of 24 kcal/oz High Protein preterm formula for VLBW infants not receiving human milk
- Additional protein supplementation if needed for specialized feeds
- "Adjustable" fortification concept
  - Protein intake adjusted based on metabolic response (BUN < 9)
  - Provides infants with adequate protein intakes and appropriate growth
  - Daily attention to nutritional intake and growth velocity

Arslanoglu et al 2010

Protein Levels in Preterm Formulas

	Preterm Formula (s) 24 kcal	High-Protein Preterm Formula (s) 24 kcal
Protein/energy ratio, g/100 kcal	3.0	3.3 / 3.5
Protein intake, g/kg/d, @ 120 kcal/kg/day	3.6	4.0 / 4.2

Considerations Regarding Energy Intake in Relation to Fat in Feeds

- Potential fat losses with certain diagnoses
- Potential fat losses in donor milk feeds
- Increased fat losses with continuous drip feeds of breastmilk, particularly within the first hour of feeding
- If providing exclusively breastmilk feeds, two options for increasing the fat content include hindmilk and Prolact CR™

When to Feed >24 kcal/oz Feeds

- Concentrated feeds should be considered for infants who cannot meet their needs for growth with standard preterm formula or standard fortified breast milk
- For example, fluid restricted infants will need concentrated feeds
  - **Careful attention should be placed on achieving proportional growth**
- Engineered Breastmilk, such as Hindmilk with additional protein supplementation is an option
- Prolacta's fortifiers come in +4, +6, +8, and +10 concentrations, in addition to Prolact CR™ (Human Milk Cream)
- 30 kcal/oz Preterm Formulas are available

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Concerns for Feeds at Discharge

- Continued "catch-up" growth
  - Critical period for weight: 1st 6 months of life
  - Head Circumference: 1st year of life
  - Opportunity for somatic and brain growth to compensate for earlier deprivation
  - In VLBW infants, failure to catch up in weight by 8 months was associated with
    - Lower Bayley development quotients*
    - Smaller head circumferences*
    - Higher rate of neurosensory impairment*

Concerns for Feeds at Discharge

- Preterm infants often discharged home before term age
- Late preterm period continues to require increased kcals and protein
- Delayed growth at time of discharge common (nearly 100% of infants <1kg at birth plot <10%ile at time of discharge)

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Infants at Highest Risk

- ELBW and/or SGA
- Breast-fed or Specialized Term Formula
- Parenteral Nutrition; Gastrostomy Feeding
- Poor Weight Gain (<20g/d) prior to D/C
- BPD; SBS; Neurological/Developmental Impairment; Cardiac Disease
- Low Socioeconomic Status

Options for Feeds at Discharge

- Fortified Breastmilk
- Transitional (Discharge) formulas
  - Nutrient-enriched to meet preterm needs
- Breastmilk alternating with a more concentrated formula or use of SSC 30 as a "booster"
- Concentrated Breastmilk using transitional formula powder
- Specialized term formula when necessary (possibly with addition protein supplementation)

Groh-Wargo, S et al. ICAN, Jun 2014

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Intake for 2 kg infant @ ~120 kcal/kg

Nutrient	Human Milk (HM)	HM enriched w/ PTDF*	HM: PTDF 1:1	HM:HMF 1:50	HM:PF 24 HP 1:1	HM:HMF 1:25
Volume, mL/kg	180	150	170	165	165	150
Protein, g/kg	**1.6**	**1.9**	2.6	3.2	3.1	3.9
Ca, mg/kg	40	55	91	132	132	185
P, mg/kg	23	32	52	72	70	102
Zn, mcg/kg	360	513	910	1110	1129	1700
Vit D, IU/d	4	36	95	108	102	178

*PTDF: preterm discharge formula; Term HM; Estimated needs at D/C: Protein (2.5-3.1 g/kg); S Groh-Wargo, ICAN

Fortified Breastmilk at Discharge

- Feeding fortified HM improves nutrient intake, bone mineralization, and length and head growth compared to feeding HM without fortification (O'Connor DL 2008, Aimone A 2009)
- Feeding fortified HM may not improve overall growth compared to feeding preterm formula (Zachariassen G 2011)
- Fortification of HM following discharge does not interfere with breastfeeding success (O'Connor DL 2008; Zachariassen G 2011)

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Discharge Growth Outcomes Significantly Improved with Fortified Human Milk

- Fed fortified human milk for up to 12 weeks post-d/c
- Sustained improvements of all growth parameters through the 1st year of life

—Fortified human milk (n=19)
---Human Milk (unfortified) (n=20)

Aimone A et al. *J Pediat Gastroenterol & Nutr.* 49(4):456-466, October 2009.

Pediatric Nutrition AAP, 7th Ed, 2014, p109-110

- Breastmilk alone may not be sufficient to provide adequate nutrition without additional supplementation
- **"Strong consideration should be given to fortification of human milk for a minimum of 12 weeks for those infants who weigh less than 1250g at birth** and/or have incurred intrauterine or extrauterine growth restriction…"

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Transitional Formulas at Discharge

- Higher P/E ratio due to increased protein content
  - 49% more protein than term formula (per 100 mL)
  - 10% increase in kcal
- 48% more calcium, 62% more phosphorus, and 75% more zinc
- Additional vitamins and trace elements
- Increased weight, length and head circumference growth
- Improved bone mineral content (BMC)
- Enhanced lean body mass accretion
- Normalization of biochemical indices of nutritional status

Roggero P et al, Growth and Fat-Free Mass Gain in Preterm Infants After Discharge. Pediatrics 2012

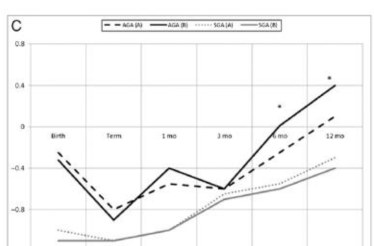

FIGURE 2
A, Mean weight *z* scores at term, 3, 6, and 12 months of corrected age according to randomization. B, Mean length *z* scores at term, 3, 6, and 12 months of corrected age according to randomization. C, Mean head circumference *z* scores at term, 3, 6, and 12 months of corrected age according to randomization. A, treatment A (term formula); B, treatment B (nutrient-enriched formula). *AGA (B) versus AGA (A) $P = .04$.

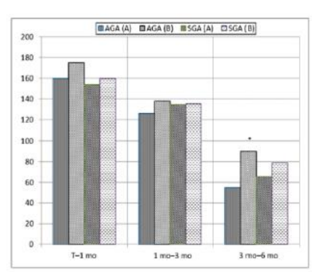

FIGURE 4
Fat-free mass gain (g) at each study point. T, term. A, treatment A (term formula); B, treatment B (nutrient-enriched formula). *AGA (B) versus AGA (A) $P = .01$.

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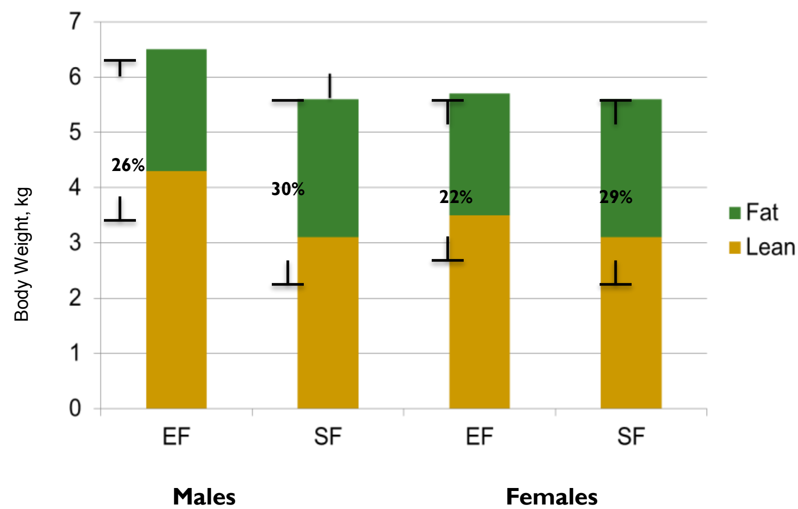
Transitional Formulas and Body Composition



Brunton JA et al 1998

Conclusions from PTDF Studies

- Results: Compared to standard formulas or unfortified human milk, PTDF formulas provide increased protein and mineral intake and may support improved growth and body composition following hospital discharge
- Infants <1250 g BW and exclusive breast feeders are at greatest nutritional risk
- Potential for catch-up is greatest in the first 1-2 months following discharge from the NICU
- More studies with ELBW infants are needed

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Length of Use of PTDF

- Guidelines for Perinatal Care, 6th Edition, 2007
- AAP, Pediatric Nutrition, 7th Ed, 2014, p110.
- Cochrane Reviews

Suggested Schedule for Length of Use of PTDF with Follow-Up

Birthweight	Length of use (CA*)
<750 g	12 months
750 - 1000 g	9 - 12 months
1000 - 1500 g	6 - 9 months
1500 - 2000 g	3 - 6 months
2000 – 2500 g	1 - 3 months
> 2500 g	term – 1month

*CA=corrected age

#MetroHealth Medical Center, Cleveland, OH

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

Discharge Collaboration

- Communication between NICU and PCP
  - Summary of nutritional goals
  - Updated growth chart
  - Emphasize importance of routine growth monitoring
- Communication with WIC

In Conclusion…

- Preterm infants, particularly VLBW and ELBW infants, are at risk for poor growth
- Poor growth leads to poor outcomes
- Improved nutrition improves outcomes
  - In hospital
  - Post discharge

For the video presentation replay visit http://www.prolacta.com/webinars/growth-for-premature-infants

About Prolacta Bioscience®

Prolacta develops clinically proven, high-value products derived from human milk that are designed to meet the needs of extremely premature infants in the Neonatal Intensive Care Unit.

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Advancing the Science of Human Milk

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