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Post Discharge Preterm Formula: Neonates **Draft June 19, 2009**				1 of 11

PURPOSE

To enhance the nutritional intake, and improve growth and bone mineral accretion, of preterm infants with a birth weight of less than or equal to 1800 grams[Oconnor 2008 picaud cooke 1998, bishop 1993, wheeler 1996, carver 2001];and/or preterm infants that are small for gestational age at discharge (less than the 10th percentile for weight at a given gestational age). [Dusick 2003 esphgan]

GOALS

1. To promote catch-up growth and accretion of lean body mass. [Lucas, Wheeler, AAP Cooke, o'coonor 2004 adamkin]

2. To optimize somatic (weight, length, and head circumference) and brain growth associated with delays in the neurodevelopment of preterm infants. [Lucas 1998. 1990 Hack Coooke 2001, morley 1996, 1994]

3. To normalize body stores for specific nutrients (calcium, phosphorous, zinc, iron, and sodium).

4. To optimize bone growth and mineralization during periods of rapid skeletal development. [Bishop, brunton, occonoor 2004, chan1993, bishop 1993, cooke 1998, carver 2001, lucas 2001AAP Hall 1993]

5. To decrease the potential risk factors (hypertension, insulin resistance, obesity) for cardiovascular disease which are associated with poor nutritional intake, growth restriction, late catch-up growth, and poor lean body mass.

STANDARD OF PRACTICE GUIDELINES

1. Discontinue human milk fortifier (HMF) once the intake of HMF exceeds 16 packets per day (to avoid high intakes of vitamins and minerals) or one to two weeks prior to discharge home. Refer to Clinical Practice Guidelines 2-H-3 Human Milk Fortifier: Guidelines for use in very-low-birth weight and extremely-low-birth weight infants.

2. Discontinue preterm nutrient enriched formula one to two weeks prior to discharge home.

3. Once HMF or preterm nutrient enriched formula has been discontinued, consider initiating human milk fortified with postdischarge formula (PDF) and/or PDF if human milk is not available.
    a. Preterm infants with a birth weight of less than or equal to 1500 grams should be discharged home on human milk fortified with PDF as either a supplement to breastfeeding and/or PDF if human milk is not available.
    b. Preterm infants with a birth weight between 1500 and 1800 grams with a discharge weight of less than the tenth percentile or who required nutrient enriched breast milk

and/or formula should be discharged home on human milk fortified with PDF as either a supplement to breastfeeding and/or PDF if human milk is not available.

4. Preterm infants with a birth weight between 1500 and 1800 grams and an appropriate weight for postconceptional age at discharge should be discharged home on human milk or iron fortified term infant formula with long chain polyunsaturated fatty acids.

5. Gradually increase the caloric density and protein content of expressed breast milk (EBM) or formula if EBM is not available by:
    a. Fortifying EBM with PDF,
    b. Concentrating formula,
    c. Increasing the frequency of EBM fortified feeds until appropriate growth is achieved.
        i. Sustain growth greater than 15 grams/kg/day (<37 weeks) or **10 to 30 grams/day** (≥ 37 weeks gestation age) with appropriate head circumference and length growth.
            1. Quality of weight gain is an important consideration as excessive fat deposition can put an infant at risk for long-term adverse health outcomes. [adamki, hales 2003]
            2. Cardiovascular disease and its risk factors are influenced by growth acceleration across centiles. Early growth acceleration programs the vascular biology associated with early atherosclerosis. More moderate growth is more beneficial to infants [singhal 2004].
            3. Measuring actual body composition of very preterm infants is not practical in a clinical setting.
        ii. Early head circumference growth of > 0.9 cm per week is associated with better neurodevelopmental and growth outcomes.
6. If weight gain is suboptimal and the baby is on a set total fluid intake consider increasing the total fluid intake to increase both energy and protein intake.
7. Additional protein may be considered in those infants that experience growth failure and do not respond to feedings with increased caloric density. [Adamkin]
    a. Inadequate protein intake may be partially responsible for the poor growth of very low birth weight infants as the protein content of human milk decreases with the duration of lactation. [adamkin Carson 1998]
    b. A higher energy intake may promote better protein utilization, but may also result in higher rates of fat accretion. [adamki hales 2003]

Discontinuation of Preterm Postdischarge Formula

1. Continue EBM fortified with PDF or PDF only until 9 to 12 months corrected age if:
    a. Growth is stable
    b. Weight gain velocity is suboptimal
    c. Weight has dropped by 2 percentile curves on the growth charts developed by the National Centre for Health Statistics [centre of disease]
    d. Weight is below the 3rd percentile, or
    e. Chronic disease is present.

2. If weight gain exceeds recommendations **(> 30 grams/day)** and infant is crossing percentiles in an upward trend
    a. Gradually increase the number of breastfeeds and monitor growth closely to ensure that weight gain is maintained.

b. Continue PDF (0.75 kcal/mL) if infant is being formula fed until 3 months corrected age and then reassess growth.

Frequent monitoring of growth (weight, length, head circumference) should be routine practice postdischarge to identify those preterm infants that require additional nutrition support.

VITAMINS AND MINERALS [Tsang, Nutrition committee, health Canada CPS]

	Trivisol (≤ 3.5 kg)	D-Vi-Sol (> 3.5 kg)	Elemental Iron
Breastfed preterm infant	1 mL/day	1 mL/day	3 to 4 mg/kg/day (birth weight less than 1000 grams) 2 to 3 mg/kg/day (birth weight greater than 1000 grams)
Post-discharge formula (22 Kcal/oz)	Tri-visol or D-Vi-sol (0.5 mL/day) if daily volume <600 mL/day	Tri-visol or D-Vi-Sol (0.5 mL/day) if daily volume <600 mL/day	3 to 4 mg/kg/day (birth weight less than 1000 grams) 2 to 3 mg/kg/day (birth weight greater than 1000 grams)
Breastfed and Post-discharge Formula	0.5mL/day if 50% feeds are post-discharge formula and volume is <600mL/day	0.5mL/day if 50% feeds are post-discharge formula and volume is <600mL/day	3 to 4 mg/kg/day (birth weight less than 1000 grams) 2 to 3 mg/kg/day (birth weight greater than 1000 grams)

SUGGESTIONS FOR MONITORING BONE MINERALISATION POSTDISCHARGE

1. Biochemical markers (proposed for the screening of metabolic bone disease but are not considered diagnostic).
   a. Serum alkaline phosphatase and serum phosphate are associated with growth therefore it is important to differentiate between associations with growth parameters and bone mineral content. [faerk 00]
      i. Serum alkaline phosphatase every 4 weeks if serum levels are greater than 900 iu/L[backstorm] and liver disease is not present.
      ii. Serum alkaline phosphatase reference range 150 – 600 iu/L
      iii. Serum phosphate [rigo 00] if serum level is less than 1.8 mmol/mL [(backstrom)]
2. Urinary bone resorption markers (if available and appropriate as an outpatient)
   a. Urinary excretion of calcium
   b. Urinary excretion of phosphorous
3. Aim for 10 to 30 gram/day weight gain
   - Weight, length, head circumference, and bone area are significantly associated with bone mineral content. Weight gain may be a good indicator of bone mineralization; however, both weight and length are likely more reliable as weight gain can be caused by fluid accumulation or excessive fat deposition [Faerk 2000]. Bone mineral content is significantly associated with body weight and to a lesser extent with dietary mineral or Vitamin D intake [Rigo 2000]; however, results of randomized trials conflict. Promotion of adequate growth should be the focus of preventing metabolic bone disease [faerk 2002].
4. Calcium and phosphate

    a. To provide calcium and phosphorous in amounts that meet the demands of rapid bone formation that normally occurs in the last trimester [(miller 2003].
        i. Calcium accretion rate: approximately 150 mg/kg/day
        ii. Phosphorous accretion rate: approximately 75 mg/kg/day

5. Vitamin D [rigo 07 faerk 2000]
    a. 400 - 800 IU per day (1 to 2 mL D-vi-sol)
    b. In preterm infants, vitamin D requirements are influenced by body stores at birth, length of gestation, and maternal stores [rigo 2000]. A relative malabsorption of vitamin D from a low secretion of bile acids may increase the needs of vitamin D of preterm infants [rigo 2000]. Bone formation and mineralization are related to mineral supply (calcium, phosphorous), hormonal factors (PTH, rPTH, and Vitamin D), genetics, and physical activity [Rigo 2000].
6. IUGR infants should be monitored closely. Holland et al. found IUGR infants had a higher incidence of postnatal rickets, suggesting chronic damage to the placenta may alter phosphate transport [Harrison article].
7. Infants who received ventilation for a prolonged period are at increased risk for poor bone mineralization [boweden].

SUMMARY

At discharge from hospital, each infant's medical condition and nutritional status needs to be considered when prescribing the appropriate diet and nutrient supplements [AAp]. Continued growth monitoring is required so feeding plans can be developed and changed to meet the needs of individual infants and to prevent underfeeding and overfeeding. Health care professionals must consider an infant's medical condition and ongoing therapies required, that may further impede the requirements and delivery of adequate nutrition. Currently the optimum duration for feeding enriched formula after discharge remains unknown and likely varies with birth weight, clinical course during hospitalization, and postdischarge catch-up growth.

BACKGROUND

Extremely low birth weight infants accumulate protein, energy, mineral, and nutrient deficits during their hospitalization in the neonatal intensive care unit. [Dusick 2003 embleton] The National Institute for Child and Human Development Neonatal Research Network reported that intrauterine growth restriction was present in 22% of the study cohort at birth (4438 infants). By 36 weeks corrected age, 97% of the very low birth weight infant population had growth failure with weight less than the 10th percentile. [Lemons] At 18 to 22 months, forty percent have weights, lengths, and head circumferences less than the 10th percentile. [Dusick]

In utero growth restriction for infants born weighing less than 1000 grams is associated with a greater incidence of postnatal growth failure, including head circumference, compared to infants who are appropriate for gestation age [Dusick 2003]. Dusick (2003) et al. concluded that postnatal growth failure is inversely related to birth weight. Nutritional deficiency and growth restriction in utero and in early infancy may have consequences for cardiovascular risk factors such as hypertension, insulin resistance, and obesity, and for long term cardiovascular health [barker 2002 hales2003]. Growth and body composition in preterm infants during the neonatal period is influenced by diet [Pieltain] and the degree of growth restriction in utero. [atkinson2000 lucas 2001, 1996]

Infants who fail to achieve their growth potential during the first weeks of postnatal life tend to have less favorable outcomes with respect to growth and neurodevelopment (Brandt et al., 2003, Latal-Hajnal et al., 2003, Luo et al., 1998 as cited in ESPGHAN 2006). Early postnatal nutrition has permanent effects on the components of metabolic syndrome (hypertension, dyslipidaemia, obesity, and insulin resistance) affecting one's susceptibility to cardiovascular disease. [singhal 2004 singhal 2004] Aggressive nutritional management during hospitalization promotes earlier onset of and more rapid rates of postnatal growth of preterm infants [locus 84,carver] which may be associated with later developmental advantages [1ucas 98 lucase 1990].

Human milk fed infants often accrue the greatest nutritional deficits [occonor 2003 embleton 2001] by discharge. Protein content of human milk declines with the duration of lactation; therefore, fortification of human milk is required to meet the preterm infant's protein requirements [adamkin]. The nutritional status of preterm infants at hospital discharge determines their need for enriched milks and/or specific nutrient supplements.

Recent studies have shown that improving the nutrition of preterm infants postdischarge will have effects on their developmental outcomes and susceptibility to chronic diseases in adulthood [Adamkin]. Fetal growth restriction relative to genetic growth potential could result in deleterious growth acceleration postnatally, having long term consequences on an infants' long term health outcome (Karlberg 1995 as cited in Singhal et al., 2004). In review of these findings though, one must balance slower growth and possibly under-nutrition with the adverse effects that this may have on the brain. The first year of life provides an important opportunity for human somatic and brain growth to compensate for earlier deprivation [Hack]. Evidence suggests that either low birth weight and/or rapid postnatal weight gain, or nutrient-enriched diet in infancy [Singhal 2004] or any combination may predispose infants to adverse long-term outcomes, such as cardiovascular disease, type 2 diabetes, hypertension, obesity and osteoporosis in adulthood [Hales 2003 Fagerberg 2004 tu 2005 barker 2002 eriksonn 2002, cole 2004 hales Metcalf2001 toschke2004].

At term, preterm infants born prior to 32 weeks of gestation age have a bone mineral content 25 to 70% lower than in term infants [horsman]. The lowest bone mineral content was associated with prolonged ventilation. The duration of preterm formula was correlated with higher bone mineral content. [Bowden]

Bone mineralization of preterm infants reach values, adjusted for anthropometric parameters appropriate for skeletal and body size (between 6 and 12 months of age), similar to that of healthy term infants [fewtrell 1999 Bowden rigo 2000], with little difference between preterm and term bone mineralization by age two [schanle].

Biochemical indicators of bone mineralization (serum calcium, serum phosphate, serum alkaline phosphatase), photon absorptiometry, and x-ray can be used to identify premature infants with metabolic bone disease, [rigo2007]. However, Faerk et al. (02) found no association exists between serum alkaline phosphatase or phosphate and whole body bone mineral content at term. It is recognized that all of the above noted biochemical indicators have their limitations [Faerk 00]. Dual energy x-ray absorptiometry (DEXA) is currently the "gold standard" however is currently not available at Foothills Medical Centre, Peter Lougheed Centre and Rockyview General Hospital NICU's in Calgary Alberta. [Rigo 2007] At this time, there is no universal consensus as to how to monitor postnatal changes in bone metabolism.

Current research does not advocate that nutrition should be restricted in infancy but allows health care professionals to focus on the type of weight gain (i.e. lean body mass vs. adiposity). Replicating intrauterine body composition changes appears to be a more physiologic approach to growth in the very preterm infant. [Adamkin] After discharge from hospital, all premature infants need to be monitored for somatic growth (weight, length, and head circumference), osteopenia of prematurity, and iron deficiency anemia. [Yeun] Early detection and intervention will prevent short term morbidity and may potentially affect an individual's long term health.

APPENDIX A

150 mL/kg/day	Mature Preterm Human Milk (Zenk)	4 packets Similac Advance HMF/100 mL EBM Abbott	Neosure 22 kcal/oz	P-RNI CPS	Institute of Medicine Dietary Reference Intakes for term-born infants
Energy Intake kcal/kg/day	101	119	113	100 - 120	
Protein Intake g/kg	2.1	3.5	3.0	2.2	
Vitamin A mcg/day	176	443	156	450 (birth wt < 1000 grams) 200-450 (birth wt ≥ 1000 grams)	6000 preformed Vitamin A
Vitamin D IU/kg	3.0	180	80	400 – 800 IU per day	1800
Calcium mmol/kg	1.9	5.2	3.0	6.3 mmol/d (breast fed) 9.4 mmol/d	

				(formula fed)	
Phosphorous mmol/kg	0.6	3.8	2.3	3.4 mmol/d (breast fed) 8.8 mmol/d (formula fed)	
Zinc micromol/kg	8.0	30	20	15.0 micromol/kg Estimate	
Iron Mg/kg	0.2	0.7	2.1	3.0 – 4.0 (birth wt < 1000 grams) 2.0 – 3.0 (birth weight ≥ 1000 grams)	

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