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Feeding the Premature Infant

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Nutritional management of the premature infant has become an integral part of the medical care provided to these infants. With the ever increasing survival of low-birth-weight and very-low-birth-weight infants, understanding the principles of nutritional therapy becomes all the more important. It is estimated that there are four million births in the United States every year; with an estimated prematurity rate of 9%, the number of infants requiring such management is enormous. This section focuses on nutritional goals, nutrient requirements, and enteral and parenteral routes of nutritional therapy.

Nutritional Goals for the Premature Infant

Prematurity is defined as an infant with a gestational age of less than 38 weeks born before completion of 37 weeks gestation. A post-term infant is one whose birth occurs from the beginning of the first day of week 43 (>42 weeks). Classifying infants as preterm, term, or post-term assists in establishing the level of risk for neonatal morbidity, nutritional needs, and long-term sequelae. Assessment of gestational age is based on maternal dates, obstetric dating by ultrasonography, and physical examination.[1] Ultrasonography has improved the ability to estimate gestational age. Estimation by physical exam relies on the predictable changes in the pattern of physical and neurological changes that occur with advancing gestation and form the basis of the examinations for the estimation of gestational age. The Ballard exam may overestimate the age of premature infants and, on the other hand, may underestimate that of post-term infants.[2] Because of the error in gestational age assessment, particularly in very-low-birth-weight infants, a New Ballard Score is currently used.[3] This modified examination is particularly suited for the very small premature infant, and the estimated gestational age is accurate to within one week. Items of neuromuscular maturity and physical maturity are scored from –1 to 5, a total score obtained, and gestational age estimated based on maturity rating score.

Infants are considered low birth-weight if birth weight is less than 2500 g regardless of gestational age. Very-low-birth-weight defines infants with weight less than 1500 g, with an additional classification of extremely low-birth-weight describing infants less than 1000 g.

Crown–heel length performed by two examiners is measured by achieving full extension of the infant on a measuring board with a fixed headpiece and movable footpiece. The

infant needs to be supine, head held in the Frankfurt plane vertical, legs extended, and ankles flexed, and the movable footpiece is brought to rest firmly against the infant's heels. An average of two measurements documents the length. If crown–heel length cannot be measured due to limb anomalies or if there is a discrepancy between weight and length, a crown–rump length is sometimes measured.

Head circumference measured with a non-stretchable tape is the largest of three measurements around the head, with the tape held snugly above the ears.

Weight, length, and head circumference are then plotted on standard curves to classify an infant as appropriate, small, or large for gestational age for each measurement. Most measurements define appropriate for age as measurements that fall within the 10th to 90th percentiles, ideally based on charts constructed for similar race and height above sea level. Infants who are appropriate for age on the three measures are at the lowest risk, within that gestational age grouping, for problems associated with neonatal morbidity and mortality. An example of growth curves commonly used in neonatal nurseries is depicted in Figure 6.1.

Growth and Nutrient Requirements

Estimation of nutrient requirements in premature infants is based on the goals for growth of this cohort of infants. The common goal has been to achieve growth similar to that of the "reference fetus."[4,5] These growth standards serve as a reference to judge the adequacy of growth; however, postnatal changes in energy requirements as well as environmental stresses are likely to be different, and the ideal growth of these infants remains to be defined. An alternative approach may be to achieve the best possible growth without adverse metabolic consequences.

Nutrient requirements for preterm infants have been estimated by various methods, including the factorial method based on the reference fetus, nitrogen balance studies, and turnover studies, or based on nutrient values in the serum. For example, Figure 6.2 depicts the composition of weight gain in normal human fetuses.[4] This reference fetus (Table 6.1) has not only served as a basis for calculation of nutrient needs, but also as a measure of sufficiency of particular nutrients, as discussed above. The factorial approach is based on the assumption that the requirement for a nutrient is the sum of losses (fecal, urine, dermal, and other, if any) and the amount required for growth, i.e., incorporation into new tissues. An example of such an approach to calculate protein requirements of preterm infants is that of Ziegler.[6] Advisable intakes of protein are obtained by adding 8–10% of the estimated requirement.

Provision of Nutrients

Energy Needs

Energy needs are based on basal metabolic rate, cost of growth, and losses in stool and urine. The factorial method cannot be used to estimate energy requirements. It is generally recognized that preterm infants have higher energy requirements compared to their term counterparts.[7] To gain the predicted growth in weight for premature infants

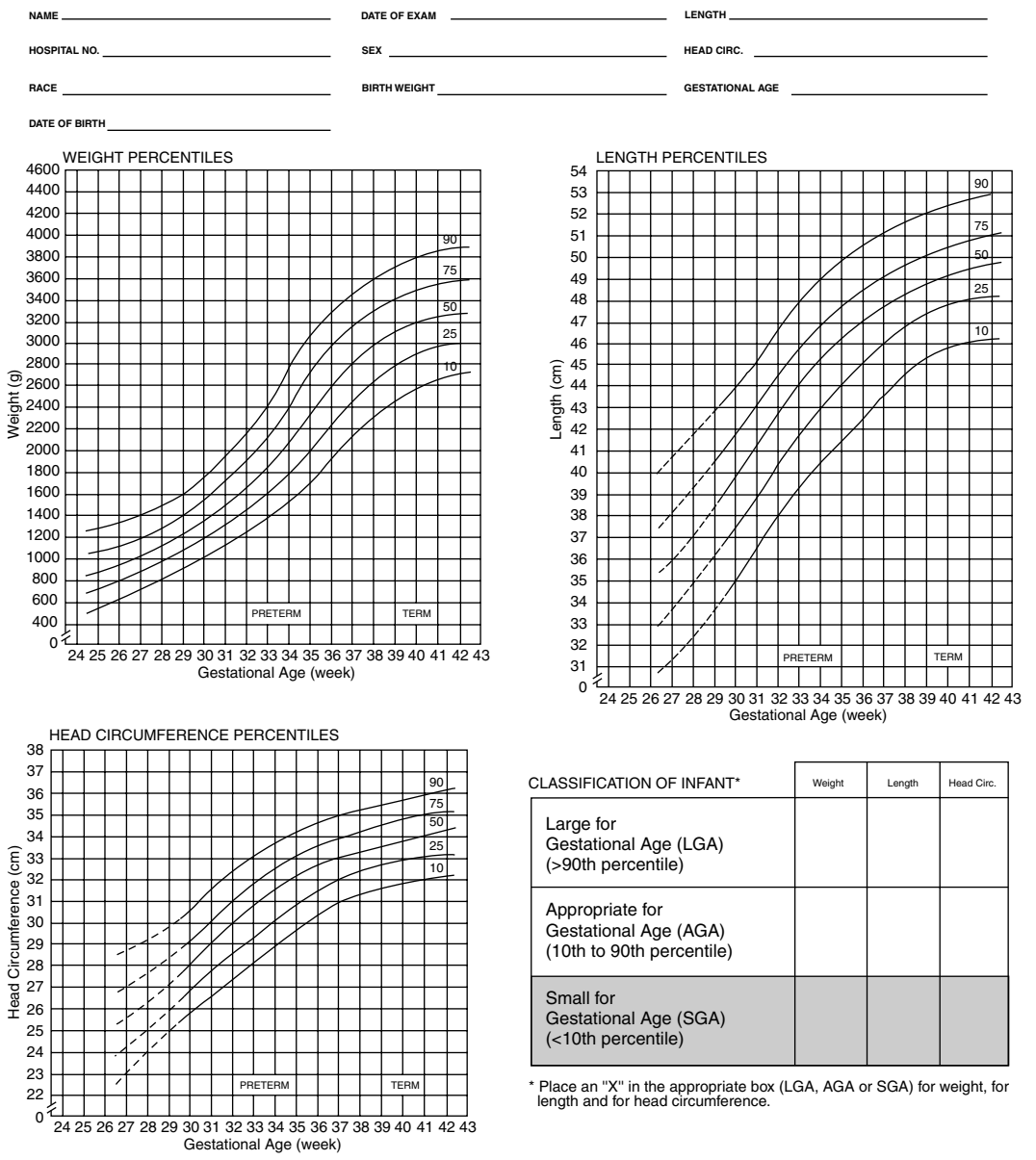

FIGURE 6.1
Classification of newborns by intrauterine growth and gestational age.

(10 to 15g/kg/d), it is estimated that premature infants would need 110 to 130 kcal/kg/d. Energy requirements must take into account the route of administration, enteral vs. parenteral, since 90 to 95 kcal/kg/d may satisfy energy requirements by the parenteral route. Disease states such as sepsis, chronic lung disease,[8,9] and concomitant use of corticosteroids will increase energy needs. The mainstay of energy support should be balanced between carbohydrates, fat, and amino acids.

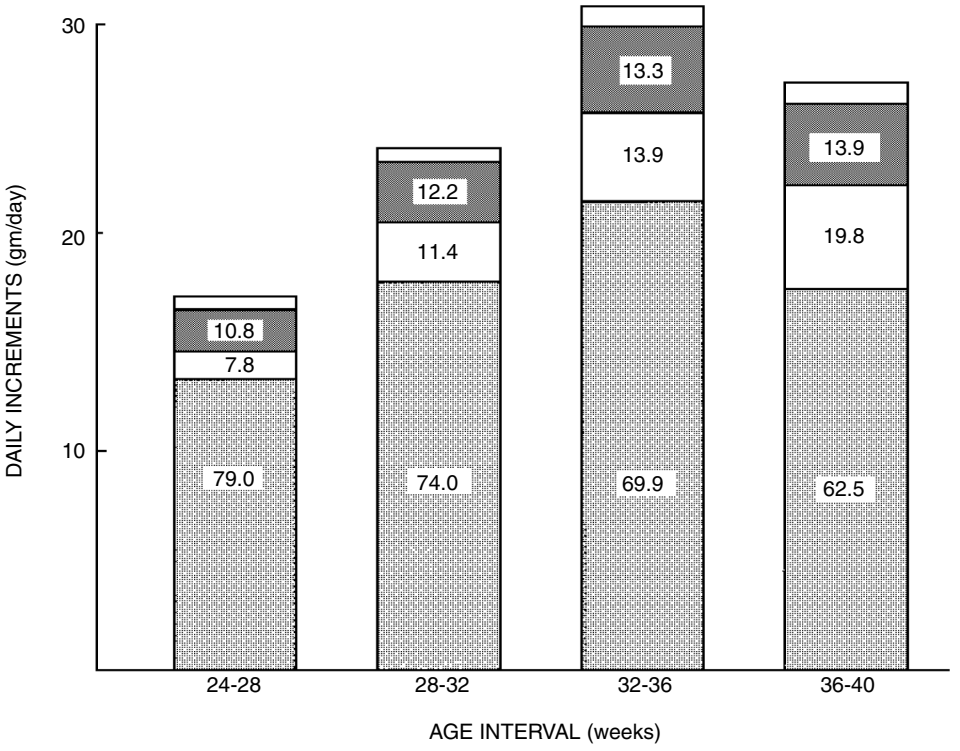

FIGURE 6.2
Average composition of weight gain of the reference fetus; numbers indicate percentages of gained accounted for by components. From Ziegler E.E., O'Donnell A.M., Nelson S.E., Fomon S.J. *Growth* 40: 329; 1976. With permission.

TABLE 6.1

Daily Increments of Body Weight and Body Composition of the Reference Fetus

Age Interval (Weeks)	Weight (g)	Protein (g)	Lipid (g)	Ca (mg)	P (mg)	Mg (mg)	Na (mEq)	K (mEq)	Cl (mEq)
24–25	11.4	1.25	0.5	61	39	1.8	0.9	0.5	0.8
25–26	15.7	1.67	1.2	84	54	2.4	1.3	0.6	1.0
26–27	18.6	2.00	1.6	101	65	2.8	1.5	0.8	1.1
27–28	21.4	2.37	2.0	119	76	3.3	1.7	0.9	1.3
28–29	22.6	2.59	2.3	129	83	3.5	1.7	0.9	1.3
29–30	23.1	2.76	2.6	138	89	3.7	1.7	1.0	1.3
30–31	24.3	3.00	2.9	152	97	4.0	1.8	1.0	1.3
31–32	25.7	3.28	3.2	171	109	4.4	1.8	1.1	1.3
32–33	27.1	3.55	3.5	193	123	4.8	1.9	1.1	1.3
33–34	30.0	3.97	4.0	228	144	5.5	2.1	1.2	1.4
34–35	31.4	4.23	4.4	258	162	6.0	2.2	1.3	1.4
35–36	34.3	4.62	5.1	301	189	6.9	2.4	1.4	1.4
36–37	35.7	4.83	5.6	341	212	7.5	2.5	1.5	1.4
37–38	31.4	4.34	5.6	344	211	7.1	2.1	1.3	1.1
38–39	24.3	3.44	5.4	325	197	6.1	1.6	1.0	0.7
39–40	17.1	2.50	5.0	302	179	5.0	1.0	0.6	0.3

From Ziegler E.E., O'Donnell A.M., Nelson S.E., Fomon S.J. *Growth* 40: 329; 1976. With permission.

Amino Acid Needs

The factorial approach is commonly used to estimate protein requirements. The protein need will be greater if catch-up growth is also to be produced. It is generally accepted that the newborn infant will lose up to 10% of his/her body weight. In sick premature infants where nutrition cannot be provided or is not tolerated, the amount of catch-up may be greater. Several studies suggest that endogenous protein losses in the absence of exogenous protein intake are at least 1 g/kg/d.[10,11] When fed in the conventional manner, premature infants run the risk of under-nutrition. Therefore, strategies to optimize amino acid intakes to include provision for catch-up growth need to be developed, since early initiation of parenteral nutrition results in positive nitrogen balance and has been shown to be safe.[11,12-14]

Cysteine and tyrosine are provided as cysteine hydrochloride (40 mg/g/amino acid, not to exceed 100 mg/kg/d) and N-acetyl-L-tyrosine (0.24 g%);[15] it has been demonstrated that infants receiving cysteine retain significantly more nitrogen that do infants receiving an isonitrogenous amino acid intake without cysteine.[11]

It is generally accepted that infants receiving 80 to 90 kcal/kg/d from parenteral nutrition with an adequate amino acid intake should gain weight similar to the intrauterine rate.[16] Most of this energy intake is provided by glucose and lipids. However, premature and sick infants may not tolerate increasing glucose concentrations/delivery without concomitant hyperglycemia, making the goal of achieving adequate energy intake difficult in the first week of life.

Lipid Needs

Lipid emulsions are used in conjunction with glucose and amino acid solutions. Generally, lipids are started at 0.5 g/kg/d intravenously, increasing by 0.5 g/kg to a maximum of 3.0 g/kg/d. Infusion rates are maintained between 0.15 to 0.25 g/kg/h in order to avoid hypertriglyceridemia (triglycerides > 175 mg/dL). Essential fatty acid deficiency may be prevented by lipid intakes as low as 0.5 to 1.0 g/kg/d.

Fat particle size is between 0.4 and 0.5μ in diameter, similar to that of endogenous chylomicrons. Clearance of lipids by premature infants may be limited, thereby requiring frequent assessment of tolerance. Emulsions of 20% are preferred due to lower total phospholid and liposome content per gram of triglyceride.[17,18]

Parenteral Nutrition

It is common practice to provide initial nutrient requirements, especially in a sick neonate, by the parenteral route. A typical parenteral regimen is depicted in Table 6.2. Commonly available lipid products are listed in Table 6.3. Currently, two amino acid formulations are available in the U.S. specifically designed for preterm infants: Trophamine® and Aminosyn-PF®. These amino acid formulations were designed to result in a plasma amino acid profile similar to that of a 30-day-old breastfed infant.[19] It is generally recommended that parenteral nutrition be started within the first two days of life in preterm infants and advanced in a systematic fashion to achieve 3.0–4.0 g/kg/d of amino acids, 90–100 kcal/kg/d of energy. Most preterm infants do not achieve these intakes until well into the second week of life because of issues such as glucose and lipid intolerance.

Mineral Requirements

Mineral requirements have also been estimated based on body composition and the reference fetus.[4,5] From a practical standpoint, daily needs for sodium, potassium, and

TABLE 6.2

Parenteral Nutrition Regimen

Component		Amount/kg/d
Amino acids (g)		3–4
Glucose (g)		15–25
Lipid (g)		0.5–3.0
Sodium (mEq)[1]		2–5
Potassium (mEq)[2]		2–4
Calcium (mg)		80–100
Magnesium (mg)		3–6
Chloride (mEq)		2–3
Phosphorus (mg)[2]		40–60
Zinc (μg)		200–400
Copper (μg)		20
Iron (μg)		100–200
Other trace minerals[3]		
Vitamins[4]		
Total Volume		120–150 mL
Nutrient	**<14 d**	**>14 d**
Manganese (μg)	0.0–0.75	1.0
Chromium (μg)	0.0–0.05	0.2
Selenium (μg)	0.0–1.3	2.0
Iodide (μg)	0.0–1.0	1.0
Molybdenum (μg)	0	0.25
C (mg)		80
A (mg)		0.7
D (μg)		10 (= 400 μ)
B_1 (mg)		1.2
B_2 (mg)		1.4
B_6 (mg)		1
Niacin (mg)		17

[1] Sodium requirements may vary between infants and within the same infant, and should be tailored to serum values.

[2] Phosphorus intakes are maintained in a ratio of 1:2 to 1:2.6 with calcium (mEq:mM) and may be limiting in parenteral nutrition because of insolubility; in general, the more acidic the TPN, the more calcium and phosphorus can be dissolved in the solution without precipitation. Care must be taken to avoid hyperphosphatemia with its resultant hypocalcemia.

[3] amount/kg/d.

[4] Provided as MVI-Pediatric®; each 5 mL provides (MVI is to be provided in amounts not exceeding 2.0 ml/kg/d).

chloride are based on serum measurements, while calcium and phosphorus needs are based on the factorial method.[4,5] Requirements are listed in Table 6.2. In general, the preterm infant has higher requirements of most minerals than term infants. During total parenteral nutrition, requirements for calcium and phosphorus may not be met because of the insolubility of calcium salts. Human milk may not provide adequate amounts of sodium, and hyponatremia has been reported.[20] Calcium and phosphorus needs of preterm infants cannot be met by human milk from mothers delivering preterm or term infants, and will need to be supplemented.[21] Since calcium transfer across the placenta occurs in the third trimester, the very premature infant is relatively osteopenic, and prolonged

TABLE 6.3

Fatty Acid Composition of Commonly Used Lipid Emulsions

	Intralipid® 20%	Liposyn III® 20%
Oils %	—	—
Safflower	0	0
Soybean	20	20
Fatty acid content (%)	—	—
Linoleic	50	54.5
Oleic	26	22.4
Palmitic	10	10.5
Linolenic	9	8.3
Stearic	3.5	4.2
Egg yolk phospholipid %	1.2	1.2
Glycerine %	2.25	2.5
kcal/mL	2	2
mOsm/L	260	292

parenteral nutrition and/or unfortified human milk feedings puts the infant at great risk for metabolic bone disease.

Iron is accumulated in the fetus in the third trimester with an iron content of 75 mg/kg at term. Small-for-gestational-age infants, preterm infants, and infants of diabetic mothers have low iron stores at birth. Coupled with the need for frequent blood sampling, the premature infant is at great risk for the development of iron deficiency anemia, and the exact time for supplementation remains controversial. However, given that the criteria for blood transfusion have become more stringent,[21] iron should be supplemented as early as two weeks. If recombinant erythropoietin is used to stimulate endogenous iron production,[22] iron requirements may be 6.0 mg/kg/d or higher.

Nutrient Delivery

Delivery of enteral nutrients is based on gestational age. In general, infants of 33 weeks gestation and beyond can be fed orally soon after birth. However, if medical or surgical illness precludes enteral feedings, parenteral nutrition is indicated. Parenteral nutrition can be considered as total (where all nutrients are delivered, for example in an infant with a surgical condition precluding enteral nutrition: gastroschisis) or supplemental (to complement enteral nutrition). It can be further described as peripheral parenteral nutrition (provided by a peripheral intravenous line) or central (where the tip of the catheter is in a central location or deep vein). The latter should be the route if long-term parenteral nutrition (for example, greater than 2 weeks) is anticipated, since it allows for higher glucose delivery compared to the peripheral vein (>12.5% dextrose in water). A typical nutrition plan for a very-low-birth weight infant is depicted in Table 6.4, and indications for parenteral nutrition are listed in Table 6.5.

The metabolic complications (Table 6.6) can be avoided by careful assessment of tolerance to the macronutrients as nutrition delivery is advanced. Premature infants do not tolerate high concentrations of glucose or rapid advances in glucose delivery; similarly, rates of fat infusion of greater than 2.0 g/kg/d may result in hypertriglyceridemia, particularly in the small or ill preterm infant (triglycerides >175 mg/dL). A suggested regimen of monitoring parenteral nutrition is depicted in Table 6.7. A multidisciplinary approach with physicians, pharmacists, nutritionists, and nursing staff who are knowledgeable in parenteral nutrition and monitoring should be implemented for the care of such infants. Early recognition of metabolic effects (pharmacist/nutritionist) or catheter-related effects

TABLE 6.4

Initiation and Advancement of Parenteral and Minimal Enteral Feedings in an Infant with a Birthweight of <1000 g

Age, d	Parenteral Amino Acid [g/kg]	Glucose	Lipids [g/kg]	Electrolytes	Enteral mL/h
1	0.0	D_5W	0.0	0.0	0.0
2	1.0	D_5W	0.5	Add if Na <130 mEq/l	0.25
3	1.5	Increments of 2.5%	1.0[a]	Standard	0.25
4	2.0	Increase as tolerated	1.5[a]	Standard	0.5
5	2.5	Increase as tolerated	2.0[a]	Standard	0.5
6	3.0	Increase as tolerated	2.5[a]	Standard	0.75
7	3.0 or higher[b]	Same or higher	3.0[a]	Standard	0.75

[a] Monitor triglycerides to assess lipid tolerance.

[b] Optional; infants requiring catch up growth, on corticosteroids or demonstrating low BUN despite adequate protein intakes may need higher amino acid intakes at later stages.

TABLE 6.5

Parenteral Nutrition is Indicated in the Following Conditions

Condition	Indication
Medical	Inadequate enteral nutrition
	Necrotizing enterocolitis
	Feeding intolerance/difficulty
	Ileus
Surgical	Omphalocele
	Gastroschisis
	Tracheo-esophageal fistula
	Atresias of the intestine (duodenal/jejunal/ileal)
	Diaphragmatic hernia
	Hirschsprung's disease

TABLE 6.6

Complications of Parenteral Nutrition

Type	Complication
Metabolic	Hypo- or hyperglycemia
	Electrolyte imbalance
	Metabolic bone disease
	Hepatic dysfunction
Infectious	Bacterial sepsis
	Fungal sepsis
Mechanical	Extravasation
	Thrombosis
	Pericardial effusion
	Diaphragmatic palsy

(nursing) could help to minimize the potential complications of parenteral nutrition. The most common metabolic complications observed are hepatic dysfunction and metabolic bone disease.

Hepatic dysfunction is defined as an increase in serum bile acids followed by an increase in direct bilirubin, alkaline phosphatase, and gamma-glutamyl transferase. The hepatocellular enzymes, ALT and AST, are late to increase, and are often seen in the more severe cases. Gamma-glutamyl transferase is probably the most sensitive but least specific

TABLE 6.7

Suggested Monitoring during Parenteral Nutrition

Component	Initial	Later
Weight	Daily	Daily
Length	Weekly	Weekly
Head circumference	Weekly	Weekly
Na, K, Cl, CO_2	Daily until stable	Weekly
Glucose	Daily	PRN
Triglycerides	With every lipid change	Weekly or biweekly
Ca, PO_4	Daily until stable	Weekly or biweekly
Alkaline phosphatase	Initial	Weekly or biweekly
Bilirubin	Initial	Weekly or biweekly
Mg	Initial	Weekly or biweekly
Ammonia	PRN	PRN
Gamma GT	Initial	Weekly or biweekly
ALT/AST	Initial	Weekly or biweekly
Complete blood count	Initial	Weekly or PRN

indicator, whereas elevation in direct bilrubin is the most specific and least sensitive indicator of hepatic dysfunction. The etiology is multi-factorial,[23-25] but the incidence appears to be declining as a result of both specialized amino acid solutions and early provision of enteral nutrients.

Premature infants are at high risk for the development of metabolic bone disease most commonly due to inadequate intakes of calcium and phosphorus during parenteral nutrition. Infants born before 32 weeks of gestation have some degree of hypomineralization which is worsened during the subsequent period of hospitalization, especially coupled with inadequate intakes of calcium and phosphorus. In general, both calcium and phosphorus levels are maintained in serum, while the bones appear more osteopenic on radiographs, and ultimately hypophosphatemia with increasing alkaline phosphatase is observed. Rising alkaline phosphatase in the absence of elevated liver enzymes is a strong indicator of metabolic bone disease. Incidence of rickets (metabolic bone disease) is inversely proportional to birth-weight, and has been reported to be as high as 50–60% in very-low-birth-weight infants.[26] Diagnosis is made by routine radiographs which in the initial stages would demonstrate bone undermineralization, especially in the ribs and scapula, subsequently showing the classic forms of rickets in the wrists and long bones. Strategies to increase calcium and phosphorus delivery should be considered. Unfortunately, the very small preterm infant is more often at risk for these complications, given the duration of parenteral nutrition and the coexistence of hepatic dysfunction.

Enteral Nutrition

Even if enteral nutrition is started in the first days after birth, it is suggested that supplemental parenteral nutrition be started because immaturity, feeding intolerance, and GI motility may affect the rate of advancement of enteral nutrition. Further, intakes are also dictated by the feedings used: human milk or formula. Composition of formulas available in the U.S. is depicted in Table 6.8. Composition of human milk (Table 6.9), especially from a mother delivering a preterm infant, is different from that of mothers delivering at term; further, differences between and within the same woman makes the average content difficult to estimate. The route of enteral nutrition is dictated not only by the gestational age of the infant, but also the coexistence of medical or surgical morbidity. Routes and types of delivery are depicted in Table 6.10.

TABLE 6.8

Composition of Formulas Commonly Used in Premature Infants

Nutrients per 100 Calories	Enfamil® Premature Formula 24 with Iron	Similac® Special Care® 24 with Iron	Enfamil 22™ with Iron	Similac® NeoCare™ 22 with Iron
Protein, g	3	2.71	2.8	2.6
Whey:casein	60:40	60:40	60:40	50:50
Fat, g	5.1	5.43	5.3	5.5
Source	MCT, soy, coconut oils	MCT, soy, coconut oils	High oleic sunflower, soy, MCT, coconut oils	Soy, MCT, coconut oils**
Carbohydrate, g	11.1	10.6	10.7	10.3
Source	Corn syrup, solids, lactose	Corn syrup, solids, lactose	Corn syrup solids,* lactose	Corn syrup solids, lactose
Water, g	108	109	120	120
Lineoleic acid, mg	1060	700	950	750
Vitamin A, IU	1250	1250	450	460
Vitamin D, IU	270	150	80	70
Vitamin E, IU	603	4	4	3.6
Vitamin K, mcg	8	12	8	11
Thiamin (B_1), mcg	200	250	200	220
Riboflavin (B_2), mcg	300	620	200	150
Vitamin B_6, mcg	150	250	100	100
Vitamin B_{12}, mcg	0.25	0.55	0.3	0.4
Niacin, mcg	4000	5000	2000	1950
Folic acid, mcg	35	37	26	25
Pantothenic acid, mcg	1200	1900	850	800
Biotin, mcg	4	37	6	9
Vitamin C, mg	20	37	16	15
Choline, mg	12	10	15	16
Inositol, mg	17	5.5	30	6
Calcium, mg	165	180	120	105
Phosphorus, mg	83	100	66	62
Calcium: phosphorus	2:1	1.8:1	1.8:1	1.7:1
Magnesium, mg	6.8	12	8	9
Iron, mg	108	1.8	1.8	1.8
Zinc, mg	105	1.5	1.25	1.2
Manganese, mcg	603	12	15	10
Copper, mcg	125	250	120	120
Iodine, mcg	25	6	15	15
Selenium, mcg	1.8	1.8	2.3	2.3
Sodium, mg	39	43	35	33
Potassium, mg	103	129	105	142
Chloride, mg	85	81	78	75
Osmolality, m0sm/kg water	310	280	260	250

* Powder form only. Ready-to-use form contains maltodextrin.

** Ready to feed.

TABLE 6.9

Composition of Human Milk

	Human milk (2 wks postpartum)	
	Term	**Preterm**
Volume (ml)	147–161	139–150
Water (ml)	133–145	125–135
Protein		
Content (gm)	1.8–2.5	2.4–3.1
% of energy	7–11	9.6–12
Whey/casein ratio	80:20	80 : 20
Lipid		
Content (gm)	4.4–6	4.9–6.3
% of energy	44–56	42–55
Composition		
Saturated (%)	43	41–47
Monosaturated (%)	42	39–40
Polyunsaturated (%)	15	12–14
Carbohydrate		
Content (gm)	9–10.6	8–9.8
% of energy	38–44	31–38
Lactose (%)	100	100
Minerals and Trace Elements		
Calcium (mg)	39–42	31–40
(mmol)	0.9–1	0.7–1
Chloride (mg)	69–76	76–127
(mmol)	1.9–2.1	2.1–3.6
Copper (mg)	37–85	107–111
Iodine (µg)	16	—
(mmol)		
Iron (mg)	0.04–0.12	0.13–0.14
Magnesium (mg)	3.9–4.5	4.3–4.7
(mmol)	0.16–0.18	0.17–0.2
Manganese (µg)	0.9	—
Phosphorus (mg)	22–25	20–23
(mmol)	0.7–0.9	0.6–0.7
Potassium (mg)	90–91	81–93
(mmol)	2.2–2.4	2.1–2.4
Sodium (mg)	37–43	44–77
(mmol)	1.6–1.9	1.9–3.3
Zinc (mg)	0.18–0.50	0.61–0.69
Vitamins		
Fat-soluble		
Vitamin A (IU)	155–333	72–357
Vitamin D (IU)	0.7–3.3	0.7–12
Vitamin E (IU)	0.45–0.75	0.42–1.42
Vitamin K (µg)	0.29–3	0.29–3

TABLE 6.9 *(Continued)*

Composition of Human Milk

	Human milk (2 wks postpartum)	
	Term	**Preterm**
Water-soluble		
Vitamin B_6 (μg)	15–119	9–129
Vitamin B_{12} (μg)	0.01–1.2	0.01–0.07
Vitamin C (mg)	6.6–7.8	6.3–7.4
Biotin (μg)	0.01–1.2	0.01–1.2
Folic Acid (μg)	7.5–9	5–8.6
Niacin (mg)	0.2–0.25	0.24–0.3
Pantothenic acid (mg)	0.26	0.33
Riboflavin (μg)	15–104	14–79
Thiamin (μg)	3–31	1.4–31
Other		
Carnitine (mg)	1.04	—
Choline (mg)	13.4	10–13
Inositol (mg)	22.2–83.5	21.3

TABLE 6.10

Routes of Feeding Preterm Infants

Route	<34 weeks	>34 weeks
Per os	No	Yes
Continuous gastric	<1250 g	Failure to tolerate bolus gastric, significant GER
Bolus gastric (every 3 h)	>1250 g; infants <1250 g not tolerating continuous	Failure to tolerate per os
Transpyloric, continuous	Failure to tolerate gastric feeds, gastric distention due to positive pressure, poor gastric emptying	Same as <34 weeks

Motor responses to feedings are similar whether feedings are provided by the gastric or transpyloric route.[27] However, when feeds are provided slowly over 120 min as compared to 15 min, gastric emptying is better, suggesting that in the smaller premature infant, slow infusions may be better tolerated.[28,29]

Oral Feeding

Term and preterm infants greater than 33 to 34 weeks gestation may be fed soon after birth by the oral route. This should be attempted in the delivery room in healthy infants or initiated soon after birth. Human milk feedings (i.e., breast feeding) should be encouraged, and all steps should be taken by the medical team and hospital staff to encourage breast feeding once the decision is made.[30] If breast feeding is precluded due to craniofacial anomalies such as cleft lip or palate, feeding devices are available and speech and/or feeding teams may need to be involved. Lactation consultation should be sought for mothers who have difficulty in either initiation or maintenance of breast feeding. Hospitals should avoid supplementing breastfed infants and the use of pacifiers.[30]

Most mothers delivering preterm infants have not made a decision about breast feeding, and should be counseled appropriately. All delivery sites should have facilities to pump

breast milk if actual breastfeeding is not possible and the mother wishes to breastfeed. Teaching should include appropriate techniques for pumping and storing milk.

Nutrient Delivery

For infants born after 33 to 34 weeks of gestation, enteral feedings may be started *per os*. Although it is recognized that infants at this gestational age can coordinate their suck, swallow, and respiratory activities, thus enabling feedings, not all infants respond in such a fashion and careful assessment is warranted. In the event that nipple feedings are not achieved, the infant may be fed by the gastric route.

In general, the alternatives to feedings by mouth are gastric and transpyloric. Gastric feedings can be further described as bolus or continuous, where the feedings are either provided intermittently every 2 to 3 hours, or by a pump continuously. Transpyloric feeds are provided continuously, with the tip of the feeding tube in the second part of the duodenum. General indications for the latter include failure to tolerate gastric feeding due to delayed gastric emptying, gastric distention due to positive pressure ventilation, or gastroesophageal reflux. Feedings can also be planned based on birth-weight. In general, infants below 1250 g are fed by the continuous gastric method, whereas bigger infants are fed by the intermittent method.

Special Considerations

Essential Fatty Acids

Vegetable oils contain the precursor essential fatty acids linoleic acid (18:2w-6) and in most cases alpha linolenic acid (18:3w-3). Linoleic and linolenic acids serve as precursors for the synthesis of long-chain polyunsaturated fatty acids (LC-PUFA) including arachdonic (20:4w-6), eicosopentaenoic (20:5w-3), and docosahexaenoic (22:6w-3) acids. Human milk lipids contain preformed LC-PUFA; LC-PUFA are essential components of membrane systems and are incorporated in membrane-rich tissues such as the brain during early growth.[31,32] Some of the LC-PUFA serve as precursors for prostaglandins, prostacyclin, thromboxanes, and leukotrienes. The fetus and the fully breastfed infant do not depend on active synthesis of LC-PUFA, since the placenta and human milk provide LC-PUFA in amounts considered appropriate.[33-36] Premature infants fed formulas without LC-PUFA develop depletion of LC-PUFA in plasma and red cell membranes, indicating limited endogenous LC-PUFA synthesis.[37] Recent studies by Carlson et al. demonstrate that preterm infants have high cord blood phosphatidlyethalonamine (PE), phosphatidlycholine (PC), docosahexanoic acid (DHA), and arachadonic acid (AA), but that these levels decline rapidly.[38] Further, PE, PC, DHA, and PC AA declined in formula-fed infants, but were maintained in human milk-fed infants;[38] at the end of the six-week study period, although PE, PC DHA, and AA were significantly higher in human milk-fed than formula-fed infants, these levels did not reach cord blood levels.[38] These declines in erythrocyte PE DHA could be prevented with supplementation of DHA.[39] However, supplementation with DHA (0.5% total fatty acids) resulted in decreased AA concentrations compared to feeding with 0.2% DHA, suggesting adverse effects on AA synthesis at the higher concentration.[40] Similar effects on AA were observed in premature infants fed formulas with similar linoleic acid content (16%) but different alpha-linolenic acid contents (1 vs. 3.2%); high alpha-linolenic acid-supplemented infants had lower AA and despite a higher DHA content, rate of weight gain was significantly less than the lower-supplemented infants throughout the study.[41] There were no demonstrable effects on visual evoked potential or

latency at 56 weeks between the two groups of infants, although mean latency in both groups was higher and mean amplitude lower than in age-matched breastfed term infants or in term infants fed similar formulas. Higher visual acuity in DHA-supplemented infants has been reported at 2 and 4 months[42-44] but not at 6, 9, and 12 months. Further studies are required before the optimal dose of DHA can be determined on growth and longer term followup of premature infants.

Carnitine

Current parenteral nutrition regimens do not contain carnitine. Low plasma concentrations of carnitine and its decline with postnatal age has been demonstrated in infants receiving carnitine-free nutrition.[45,46] Although fatty acid metabolism has not been shown to be impaired in short-term parenteral nutrition, carnitine is an accepted additive for infants requiring parenteral nutrition for longer periods.[47-49] Carnitine is provided at doses of 8.0 to 20 mg/kg/d.

Glutamine

Glutamine is the most abundant amino acid in the human body and is the most important "nitrogen shuttle," accounting for 30 to 35% of all amino acid nitrogen transported in the blood.[50] Glutamine concentrations in blood and tissue fall following starvation, surgery, infection, and trauma.[51,52] In addition, glutamine plays an important role in protein and energy metabolism, nucleotide synthesis, and lymphocyte function.[53] Glutamine is known to be an important fuel for small intestinal enterocytes;[54] however, an absolute need of glutamine for gut growth has not been demonstrated with either detrimental or negligible effects reported in the literature.[55-57] Nonetheless, absence of glutamine in the diet has been shown to cause villous atrophy, fall in lumina propria lymphocyte populations, and increased bacterial translocation.[58-62] While optimal intakes of glutamine for premature infants is not known, enteral supplementation with glutamine has been shown to decrease feeding intolerance,[63] and there is a possible decrease in hospital costs[64] with glutamine supplemented up to 0.3 g/kg/d. Further studies on optimal supplementation of glutamine, enterally and parenterally, in preterm infants are required.

Summary

Despite the many questions that remain regarding optimal nutritional management of the neonate, it is nonetheless important to develop rational protocols for the management of nutritional issues that arise. This chapter has provided some guidelines and the framework from which these guidelines arose. There are numerous different approaches to feeding a neonate. The ultimate goal should be to optimize nutrition, and hence growth and ultimately development in this ever-increasing population of small premature infants.

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