Nutritional Needs of Low-Birth-Weight Infants

Optimal nutrition is critical in the management of the ever-increasing number of surviving small premature infants. Although the most appropriate goal of nutrition of the low-birth-weight (LBW) infant is not definitively known, achieving a postnatal growth that approximates the in utero growth of a normal fetus at the same postconception age appears to be the most logical approach at present.

In uncomplicated cases, growth will usually begin by the second week after birth, after the initial changes in body water distribution have taken place, and after the infant has accommodated in a nonstressful way to the provision of enteral feeds and parenteral supplements. The fetal standards of growth that will be considered here include not only weight and length, but also values for rate of retention of individual nutrients and minerals (Table 1).

The quality of postnatal growth may differ from the quality of fetal growth, depending on the type of milk consumed, eg, ex utero weight gain of a premature infant given formula includes more fat gain than that of a fetus of the same maturity.

CALORIC REQUIREMENT

Energy expenditure for maintenance and growth determines the caloric requirements of the infant. The energy expenditure for growth includes both the energy value of the new tissue and the energy cost of the tissue synthesis. The estimated "basal" or maintenance metabolic rate of LBW infants, including an irreducible amount of physical activity, is lower in the first week after birth than later, and in a thermoneutral environment is approximately 50 kcal/kg/d by 2 to 3 weeks of age. Each gram of weight gain, including the stored energy and the energy cost of synthesis, requires 5 to 6 kcal. Thus a daily weight gain of 15 g/kg requires a caloric expenditure of approximately 75 kcal/kg above the 50 kcal/kg maintenance expenditure. Estimated mean caloric requirements of premature infants during the neonatal period are shown in Table 2.

Individual infants vary in their activity, in their ease of achievement of basal energy expenditure at thermoneutrality, and in their efficiency of nutrient absorption. In practice, enteral caloric intakes of approximately 120 kcal/kg/d enable most LBW infants to achieve satisfactory rates of growth. A higher intake may be given if growth is unsatisfactory at these intakes, as may be seen with chronic illness such as bronchopulmonary dysplasia. Newborn infants with growth retardation often require an increased caloric intake for growth, because of both higher maintenance energy needs and higher energy costs of new tissue synthesis.

Protein Amount and Type

Until the 1940s, premature infants were usually fed human milk. Then Gordon et al found that LBW infants would gain more weight when fed various prepared formulas than when fed pooled human milk. Weight gain of the infants appeared to correlate more with the electrolyte, or ash, intake than with the protein intake. The estimated requirements based on the fetal accretion rate of protein are 3.5 to 4.0 g/kg/d (Table 1).

The type of protein most suitable for LBW infants was studied by Gaull, Raiha, and their co-workers in a series of papers comparing whey-predominant formulas (60:40 ratio of whey:casein protein) with casein-predominant formulas (18:82 ratio of whey:casein protein). Each formula was studied in two protein concentrations: 1.5 g/dL and 3.0 g/dL. The metabolic effects and resultant growth following feeding of each of the four formulas were compared with the effects of feeding pooled milk from mothers of term infants. The BUN was higher in infants fed both of the 3.0-g/dL formulas than with the 1.5-g/dL formulas, but the significance of the differences was not given. Metabolic acidosis and elevated plasma tyrosine and phenylalanine levels were found with the 3.0-
recognition of the magnitude of this fat malabsorption led to the use of low-fat formulas for feeding prematurely saturated triglycerides of cow's milk. The fat provides 40% to 50% of the energy, and in commercial formulas, fat provides 40% to 50% of the energy. The fat of human milk is well absorbed by the premature infant. Thus, the recently developed special formulas for premature infants contain a mixture of medium-chain triglycerides and predominantly unsaturated long-chain triglycerides. The essential fatty acid requirement of at least 3% of total calories in the form of linoleic acid is amply met by this fat mixture. However, medium-chain triglycerides are even better absorbed, presumably because their digestion and absorption are not dependent on duodenal intraluminal bile salt levels, which are low in the premature infant. Thus, the recently developed special formulas for premature infants contain a mixture of medium-chain triglycerides and predominantly unsaturated long-chain triglycerides.

The fat of human milk is well absorbed by the LBW infant if it is fed into the stomach and is not subjected to heat treatment, which can denature the lipase in the milk. One reason for the relatively efficient absorption of human milk fat is the distribution of fatty acids in the triglyceride molecule. Palmitic acid in the β position, as in human milk fat, leads to better absorption than is seen with cow’s milk fat, which has stearic acid in the β position. Lingual lipase acting in the stomach starts the digestion, and bile salt-activated lipase in the duodenum completes the digestion of triglycerides lipid.

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milk continues the digestion in the duodenum. These lipase activities substitute for the low pancreatic lipase of premature infants and appear to proceed well despite the low intraluminal bile salt concentrations of the premature infant.

**Carbohydrates**

The LBW infant may have difficulty in digesting lactose in the first days of life due to low intestinal mucosal lactase activity. In the absence of adequate lactase activity, undigested lactose may be present in high concentrations in the lower intestinal tract and serve as a substrate for proliferation of potentially pathogenic bacteria. Additionally, the lactose may cause intestinal distention by its osmotic effect. However, glycosidase enzymes for glucose polymers are active in small premature infants, and such polymers are well tolerated by LBW infants. Glucose polymers have the additional benefit of adding less osmotic activity to the formula per unit weight than does lactose or monosaccharides. On the basis of these advantages, the carbohydrate portions of the various special formulas for premature infants contain approximately 40% to 50% lactose and 50% to 60% glucose polymers.

**Minerals**

*Sodium and Potassium.* LBW infants, particularly those with birth weight less than 1,500 g, do not have well-developed renal sodium conservation mechanisms. The fractional excretion of sodium is high for the first ten to 14 days after birth. Thus, the low sodium concentrations of mature human milk or of some commercial formulas designed for the feeding of term infants lead to hyponatremia when these milks are used as the sole source of sodium for a small premature infant. Special formulas for premature infants should provide 2.5 to 3.5 mEq/kg/d of sodium at full feeding levels. Very LBW (<1,500 g) infants, however, may require 4 to 8 mEq/kg/d of sodium to prevent hyponatremia. The potassium requirement for LBW infants appears to be similar to that of term infants, 2 to 3 mEq/kg/d.

*Calcium and Phosphorus.* It is difficult to supply the small LBW infant with adequate amounts of calcium and phosphorus for normal bone growth and mineralization. As a result, osteopenia is a frequent feature in small premature infants and they have a lower but definite frequency of rickets. Human milk and infant formulas designed for term infants are both deficient in calcium and phosphorus relative to fetal accretion rates. The advisable intake of calcium for 800- to 1,200-g premature infants is 210 mg/kg/d in order to meet the fetal retention rate, while taking into account limited intestinal absorption. The commonly used formulas for term infants contain 44 to 52 mg/dL of calcium, and in LBW infants consuming such formulas, the bone mineral content by photon absorptiometry is far below the normal fetal values. But with calcium intakes of 200 to 250 mg/kg/d and phosphorus intakes of 110 to 125 mg/kg/d, the bone mineral content of LBW infants increases at the fetal rate. The role of vitamin D and its active metabolites in the genesis of osteopenia of small premature infants is discussed below.

There is good evidence that the special formulas now available for premature infants, which have been supplemented with calcium and phosphorus, can lead to postnatal bone growth and mineralization at fetal rates. Overall growth and clinical status of the infants fed these formulas have been normal, and serum calcium and phosphorus concentrations have been in the normal range.

**Zinc and Manganese.** Zinc metabolism is complex in the LBW infant. Theoretically, the fetal retention rate of 250 μg/kg/d could be met by the LBW infants’ consumption of their mothers' milk. However, when consuming heat-treated human milk, LBW infants are in negative zinc balance until about 70 days of age, apparently because of limitations in intestinal absorption of zinc. There is recent evidence that zinc absorption in LBW infants may be highly correlated with fat and nitrogen absorption. A positive zinc balance may appear earlier in the postnatal period when fat absorption is improved by having 40% to 50% of the fat as medium-chain triglycerides. The AAP Committee on Nutrition has proposed that infant formulas for full-term infants supply 0.5 mg of zinc and 5 μg of manganese per 100 kcal. There is no reason, at the present time, to modify these recommended levels for LBW infants.

**Copper.** Copper retention rate of the fetus is 51 μg/kg/d. This amount of copper is available from the milk of mothers of premature infants, with a copper content ranging from 58 to 72 μg/dL during the first month after birth. However, copper balances are negative in premature infants until the fifth week after birth.

Evaluation of copper nutrition in the neonatal period is complicated by the primary correlation of serum copper level with the serum ceruloplasmin level, which rises after birth. The serum copper level may increase in the face of a negative copper balance. Increases in copper concentration in formula from 50 μg/dL to 160 μg/dL did not lead to...
higher serum copper levels,\textsuperscript{23} although huge doses of 1,500 \(\mu g/D\) do increase serum levels.\textsuperscript{24}

Because clinical neonatal copper deficiency can occur with low copper intakes, close attention to the copper intake of LBW infants is important. The current AAP Committee on Nutrition\textsuperscript{1} recommended copper intake of 90 \(\mu g/100\ kcal\) continues to be appropriate.

Iron. On a weight basis, the iron content of premature infants at birth is lower than that of full-term infants. Much of the iron is in the circulating hemoglobin, so the frequent blood sampling that the premature infant is often subjected to may further deplete the amount of iron available for erythropoiesis. The early physiologic anemia of prematurity is not benefited by iron therapy\textsuperscript{1} and there are frequent clinical indications for maintaining the LBW infants' hematocrit above 40\% by transfusions of RBCs (apnea of prematurity, long-term requirement for supplemental oxygen, patent ductus arteriosus). In addition, high levels of oral iron supplementation can interfere with vitamin E metabolism in the small premature infant. Thus there is no clear indication for iron supplementation before 1 to 2 months of age. It has been suggested\textsuperscript{2,25} that oral iron supplements be started at about 2 weeks of age, or when enteral feedings are tolerated, at a dose of 2 to 3 mg/kg/d. If iron is administered this early, vitamin E supplements should be given.

Once the LBW infant reaches about 2,000 g in weight and/or goes home, iron supplementation is definitely needed. Infants fed human milk should receive 2 to 3 mg/kg/d of elemental iron as ferrous sulfate drops; formulas with iron usually contain sufficient supplemental iron.\textsuperscript{26} A somewhat higher total daily dose of iron (supplemental plus iron in the formula) for LBW infants has been recommended by Siimes\textsuperscript{27}; this regimen should be started by age 2 months and continued to age 12 to 15 months: birth weight 1,500 to 2,000 g, 2 mg/kg/d; birth weight 1,000 to 1,500 g, 3 mg/kg/d; birth weight less than 1,000 g, 4 mg/kg/d. There is, however, insufficient evidence that these increased amounts are necessary.

Iodine. The recommended minimum requirement of iodine for normal infants (5 \(\mu g/100\ kcal\))\textsuperscript{21} is based on the iodine content of human milk. The uptake of radioiodine by the thyroid gland of premature infants has been found to be in the normal range for children and adults; therefore, it is assumed that 5 \(\mu g\) of iodine per 100 kcal is also adequate for the low-birth-weight infant.

Other Trace Minerals. Although other minerals (such as cobalt, molybdenum, selenium, and chromium) are probably in trace amounts for infants, there is no information on which to base recommendations at this time. Fluoride is usually provided in supplements or as fluoridated water.

Vitamins

Vitamin A, Vitamin K, Thiamin, Riboflavin, Niacin, Pyridoxine, Pantothenic Acid, Vitamin B\textsubscript{12}, Biotin, and Folic Acid. The recommended oral intakes of these vitamins by LBW infants are the same as those recommended for full-term infants.\textsuperscript{21} It is essential that all LBW infants, as well as term infants, receive at least 1 mg of vitamin K at birth. The AAP Committee on Nutrition recommends that daily multivitamin supplements be considered, once enteral feedings are established, after taking into account the vitamin content of the un-supplemented formula. The most appropriate supplements are those that contain the National Research Council Recommended Dietary Allowance of vitamins A, C, D, and E and the B vitamins. It is important to realize that due to the instability of folic acid in solutions, the liquid multivitamin drops for infants do not contain folic acid. The Committee suggests that the National Research Council Recommended Dietary Allowance for folic acid can be added to the multivitamin preparation in the hospital pharmacy.\textsuperscript{28}

Vitamin C. There have been conflicting reports on the need for high ascorbic acid intakes in premature infants to enhance the activity of hepatic \(p\)-hydroxyphenylpyruvic acid oxidase and secondarily lower blood tyrosine and urinary tyrosine metabolite levels. Light et al\textsuperscript{29} found that 100 mg of vitamin C per day was useful, but this has not been substantiated by others.\textsuperscript{30} In addition, most studies show no detrimental effects of transient neonatal tyrosinemia,\textsuperscript{31-33} but one study showed a lowering of IQ values at age 7 to 8 years in affected children.\textsuperscript{34} Because of these uncertainties, there have not been consistent recommendations regarding vitamin C supplementation. Although the Nutrition Committee of the Canadian Paediatric Society recommended vitamin C supplementation of premature infants in 1976,\textsuperscript{35} it did not do so in 1981.\textsuperscript{36} Ziegler et al\textsuperscript{5} recommend vitamin C intake of 60 mg/d for premature infants. Because of the absence of compelling evidence for a high vitamin C requirement in LBW infants, the AAP Committee on Nutrition does not recommend a supplement in addition to the 35 mg of vitamin C in the daily oral multivitamin mixture.

Vitamin D. The role of vitamin D deficiency in the development of osteopenia and rickets in the small premature infant is uncertain. There have been two case reports\textsuperscript{37,38} suggesting that some small premature infants show a high vitamin D requirement due to a relative insensitivity to active
vitamin D metabolites. In addition, doses of 100 IU of vitamin D per kilogram per day were found not to maintain serum 25-dihydroxyvitamin D in a normal range, while 500 IU of vitamin D per kilogram per day did maintain serum 25-dihydroxyvitamin D levels.37 One series of balance studies on premature infants has shown that an oral dose of 1,200 to 2,000 IU of vitamin D is needed to achieve maximal calcium absorption.39 Studies of infants receiving a special formula for premature infants that was high in calcium plus 600 to 700 IU of vitamin D per day have shown maintenance of normal serum 25-dihydroxyvitamin D levels and calcium balances similar to the fetal retention rate.40

The prevention of severe bone disease in premature infants appears to rely on both high oral intakes of calcium and phosphorus and at least 500 IU of vitamin D per day. The latter can be achieved by giving 400 IU of vitamin D per day in a multivitamin supplement in addition to the vitamin D in the formula. There is no evidence that administration of the active vitamin D metabolites, 25-dihydroxyvitamin D or 1,25-dihydroxyvitamin D, to LBW infants is necessary or advisable.

Vitamin E. The requirement for vitamin E, α-tocopherol, in the small premature infant is higher than that of the term infant because the fat malabsorption of the premature infant also limits the absorption of fat-soluble vitamins such as vitamin E. The signs of vitamin E deficiency in the LBW infant include a mild hemolytic anemia and mild generalized edema.42 Vitamin E deficiency is exacerbated by a high intake of iron or polyunsaturated fatty acids, each of which increases the vitamin E requirement.1

The recommended intake of vitamin E is 0.7 IU (0.5 mg of d-α-tocopherol) per 100 kcal and at least 1.0 IU of vitamin E per gram of linoleic acid.1 In addition, it has been suggested that the premature infant receive 5 to 25 IU of supplemental oral vitamin E per day, because of concerns about the adequacy of its intestinal absorption.1 However, we lack fundamental knowledge about the pharmacology of vitamin E and its esters, the differences in the absorption and disposition of oral α intramuscular ν intravenous administration, and preservatives and the vehicles required to solubilize the fatty vitamin. This is highlighted by the recently reported43 premature infant deaths associated with an intravenous preparation of the acetate ester of vitamin E.

Folic Acid. Clinical deficiency of folic acid is unusual, although premature infants are particularly prone to show laboratory evidence of folate deficiency by hypersegmentation of their neutrophils. In LBW infants, a dose of 20 μg/d does not prevent low serum folate levels after 2 weeks, but 50 μg/d is effective, and Dallman1 has suggested that premature infants weighing less than 2,000 g receive that amount. It is important to note that due to the instability of folic acid in solutions, the liquid multivitamin preparations for infant use do not contain folic acid.

Caloric Density and Water Requirements

The caloric densities of preterm and term human milk are given in Table 3. These caloric densities have been used for feeding LBW infants, but many prefer to use more concentrated milks, 81 kcal/dL (24 kcal/oz), when commercial formulas are used. The increased concentration allows feeding volumes to be smaller, an advantage when gastric capacity may be limited. The volume given when formulas of this concentration are fed at the rate of 120 kcal/kg/d (150 mL/kg/d) provides most LBW infants with sufficient water for the excretion of protein metabolic products and electrolytes derived from the formula. However, if lower volumes are given, there may be insufficient water provided for renal excretion due to the relatively constant extrarenal losses.

Human Milk

A dramatic change in feeding of LBW infants has taken place recently because a number of studies have shown that LBW infants can be adequately fed with their own mothers' milk. Their mothers' milk leads to a more rapid rate of growth in weight, length, and head circumference, as well as a shorter time to regain birth weight, than does milk from the mothers of term infants.44 Pooled human milk from mothers of term infants does not meet all nutritional requirements of LBW infants and its use results in a slower rate of growth than is found with consumption of either milk from mothers of premature infants or commercial formulas.45-49 The low protein concentration of pooled term human milk is probably the major cause of the poor growth. Metabolic complications seen when feeding very LBW infants pooled human milk from mothers of term infants include hyponatremia at 4 to 5 weeks,42,50 hypoproteinemia at 8 to 12 weeks,1,51 and rickets at 4 to 5 months.62,63 An additional potential problem seen with use of pooled human milk is the transmission of cytomegalovirus through the milk to the infant.

Milk from mothers of premature infants, especially during the first 2 weeks after delivery, contains more calories; higher concentrations of fat, protein, and sodium; and lower concentrations of
lactose, calcium, and phosphorus than milk from mothers of term infants\(^5^4^-^5^7\) (Table 3). These differences in composition may be mainly a result of the lower daily volume of milk produced by the mothers of preterm infants as compared with mothers of term infants.\(^5^8\) The higher fat content leads to the higher caloric density of milk from mothers of preterm infants, which may be advantageous for the small infant with limited gastric capacity. The higher protein content of this “preterm” milk is sufficient to meet the fetal growth requirement of nitrogen\(^2\) when the milk is consumed at a rate of 180 to 200 mL/kg/d.

Human milk contains taurine, a sulfur-containing amino acid present in low concentrations in cow’s milk.\(^1\) The role of this amino acid in the human infant is not clear, and its essential nature has not been established. Recent studies of premature infants receiving taurine-supplemented, whey protein-predominant-commercial formula have shown that the added taurine did not enhance their growth,\(^5^9\) production of taurine-conjugated bile acids,\(^6^0\) or fat absorption.\(^6^1\)

The anti-infectious qualities of human milk are important attributes. The secretory immunoglobulin A (IgA) in the milk inhibits adherence and proliferation of bacteria at epithelial surfaces and has an important role in controlling the microbial environment of the intestinal tract. The secretory IgA is present in a higher concentration in milk from mothers of preterm infants than in milk from mothers of term infants.\(^6^2\)

Chessex et al\(^6^3\) have shown that the composition of the weight gain in LBW infants fed their own mothers’ milk was similar to that reported for fetuses of similar postconceptional age. However, a note of caution has been raised regarding the feeding of their own mothers’ milk to premature infants. Forbes\(^6^4\) is concerned by the marked variability in composition of human milk aliquots, and thus the difficulty of assuring an adequate nutrient intake for the infant. In addition, it is important to reemphasize that the nutritional advantages of the milk from the premature infant’s own mother are most obvious in the first month postpartum (Table 3), and these advantages rapidly diminish thereafter.

Mixtures of whey-predominant protein, carbohydrate, calcium, phosphate, trace minerals, and

### TABLE 3. Nutritional Composition of Milk from Mothers Delivering Preterm and at Term\(^*\)

<table>
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<tr>
<th>Nutrient</th>
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<th>3 Days Postpartum</th>
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<tr>
<td></td>
<td></td>
<td>Calories (kcal/dL)</td>
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<tr>
<td>Preterm</td>
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<td>51.4 ± 2.4</td>
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<tr>
<td>Term</td>
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<td>48.7 ± 2.0</td>
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<td>70.1 ± 3.3</td>
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<td></td>
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<td>69.7 ± 2.9</td>
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* Data from Gross et al.\(^5^8\) Values are means ± SEM.
vitamins for addition to milk from the mothers of preterm infants have been developed by commercial formula manufacturers. When the fortifiers are added to milk from mothers in the first postpartum month, the resultant nutrient, mineral, and vitamin concentrations approach those of the formulas developed for feeding premature infants. There have been no published studies, as yet, on the nutritional effects of human milk fortified by these mixtures.

COMMERCIAL FORMULAS FOR LBW INFANTS

Many findings from studies on nutrient, electrolyte, mineral, and vitamin needs and tolerances of LBW infants, which have already been discussed above, have been applied to the development of formulas specifically designed to meet the needs of the small premature infant. The common features of the formulas are whey-predominant proteins, carbohydrate mixtures of lactose and glucose polymers, and fat mixtures containing combinations of medium-chain triglycerides and relatively unsaturated long-chain triglycerides. The formulas differ in their sodium, calcium, phosphorus, vitamin, and mineral content (Table 4). Each of the special formulas has been shown to be associated with adequate growth and metabolic stability.16,44,45

| TABLE 4. Composition of Special Formulas for Premature Infants* |
|-------------------|------------------|------------------|
| Ingredient        | Enfamil Premature| SMA "Preemie"    |
| 2.4               | 2.0              | 2.2              |
| Fat (g/dL) 4.1    | 4.4              | 4.4              |
| Medium-chain triglycerides 40% | 12%          | 50%              |
| Oleo oil 0        | 20%              | 0                |
| Corn oil 40%      | 0                | 30%              |
| Oleic oil 0       | 25%              | 0                |
| Coconut oil 20%   | 25%              | 20%              |
| Soy Oil 0         | 18%              | 0                |
| Carbohydrate (g/dL) 8.9 | 8.6          | 8.6              |
| Lactose 40%       | 50%              | 50%              |
| Glucose polymers 60% | 50%          | 50%              |
| Minerals (mg/dL)* |                   |                   |
| Calcium 95 [48]   | 75 [37]          | 144 [72]         |
| Phosphorus 48     | 40 [23]          | 72               |
| Magnesium 8       | 7                | 10               |
| Zinc 0.8          | 0.5              | 1.2              |
| Copper 0.073      | 0.07             | 0.2              |
| Manganese 0.021   | 0.02             | 0.02             |
| Iron 0.13         | 0.3              | 0.3              |
| Iodide 0.006      | 0.008            | 0.015            |

| Vitamins          | Enfamil Premature| SMA "Preemie" |
|                   | 2,540            | 3,200          |
|                   | 5,500            |                 |
| A (IU/L) 2,540    | 3,200            | 5,500           |
| D (IU/L) 507      | 510              | 1,200           |
| E (IU/L) 16       | 15               | 30              |
| C (mg/L) 69       | 70               | 300             |
| B1 (mg/L) 0.63    | 0.8              | 2               |
| B2 (mg/L) 0.74    | 1.3              | 5               |
| Niacin (mg/L) 10.1| 6.3              | 40              |
| B6 (mg/L) 0.53    | 0.5              | 2               |
| B12 (g/L) 2.5     | 2                | 4.5             |
| Folic acid (g/L) 240| 100             | 300             |
| K1 (mg/L) 0.08    | 0.07             | 0.1             |
| Osmolality (mosm/kg of water) 300| 270           | 300             |

* All formulas have a 60:40 whey protein:casein ratio; all contain 81 calories per deciliter.
† Values in brackets are milliequivalents per liter.
the risk of aspiration and to conserve energy.

Gastric feeding of boluses of milk can lead to disturbances of blood gas tensions in infants with respiratory problems; thus, in some, continuous transpyloric feedings by nasal or oral tubes may be better tolerated. Clinical results of this feeding mode have been excellent in many centers, but there has been some criticism that bypassing the stomach and duodenum by a jejunal tube may cause inefficient utilization of the nutrients in the formula. Continuous gastric feeds may be tolerated by many small infants better than are bolus gastric feeds, and are satisfactory if gastric emptying is not limiting in the infant. Bolus feeds into the stomach via gavage tube or by nipple, every two to three hours, is the goal once the LBW infant has shown a clearing of the respiratory distress and gastric emptying is not a problem. Whatever the mode of feeding, the formula volume should be advanced slowly—over at least ten to 14 days in infants weighing less than 1,000 g and over six to eight days in LBW infants weighing more than 1,500 g. This allows adaptation of the intestinal tract to enteral feeds without the development of vomiting, distention, and diarrhea.

**PARENTERAL NUTRITION**

Parenteral administration of glucose, fat, and amino acids is frequently an essential part of the nutritional care of premature infants, particularly those weighing less than 1,500 g. The high incidence of respiratory problems, limited gastric capacity, and intestinal hypomotility in very small premature infants dictates the need to advance the volume of enteral feeds slowly. The availability of parenteral nutritional components enables supplementation of the slowly advancing enteral feedings so that the total daily intake by both routes meets the nutritional needs of the infant. When necessary, full nutritional requirements can be met for long periods by the parenteral route alone.

A positive nitrogen balance, and thus the achieving of an anabolic state, can occur with parenteral lipid and/or glucose caloric intakes of 60 kcal/kg/d and amino acid intakes of 2.5 to 3.0 g/kg.d. With higher nonprotein caloric intakes of 80 to 85 kcal/kg/d and amino acid intakes of 2.7 to 3.5 g/kg/d, nitrogen retention occurs at the fetal rate. Growth requires a minimal parenteral nonprotein caloric intake of 70 kcal/kg/d.

The nonprotein caloric sources are glucose and lipid. Use of glucose as the sole nonprotein caloric source presents several problems. The osmolality of a solution, dependent largely on the glucose content, limits to about 13 g/dL the concentration that can be used via peripheral veins. Higher concentrations cause undue local irritation. In addition, small premature infants have a poor glucose tolerance in the first days of life, with hyperglycemia (>125 mg/dL) appearing frequently at glucose infusion rates exceeding 6 mg/kg/min. Thus, in order to avoid the potentially damaging effects of widely varying serum osmolality, and in order to avoid the dehydrating effects of an osmotic diuresis from significant glycosuria, glucose infusion should start at a rate less than 6 mg/kg/min. Usually a steady increase of the glucose infusion rate stimulates endogenous insulin secretion and an infusion rate of 11 to 12 mg/kg/min (130 to 140 mL/kg/d of a 13-g/dL solution) is tolerated after five to seven days. If not, insulin may have to be administered to achieve a caloric intake sufficient for growth. Care must be exercised in the use of insulin because the very low-birth-weight infant may experience wide swings of blood glucose level with resulting periods of hypoglycemia. Blood glucose levels also may be augmented by intravenous lipid supplements through effects of serum free fatty acids on glucose and insulin metabolism.

The availability of intravenous lipid preparations has allowed the provision of calories adequate for growth via peripheral veins. The lipids have a high concentration of calories, 1.1 kcal/mL in the 10% preparations, and the solution is isosmotic with plasma and thus is not irritating to the veins. The tolerance for parenteral fat is less in the newborn than in the older child and is further diminished in the very small premature infant. In addition, intrauterine growth retarded infants have even less parenteral fat tolerance than would be predicted from their gestational ages. Thus, in LBW infants, lipids should be administered around the clock, should be started at 0.5 to 1.0 g/kg/d, and should be increased by 0.5 g/kg/d to a maximum of 2.0 to 3.0 g/kg/d. To avoid hyperlipemia, the rate of lipid infusion should not exceed 0.25 g/kg/h. Fat tolerance can be only roughly assessed on the ward because visual estimation of plasma lactescence in a spun hematocrit tube is not reliable. Thus, such monitoring can be supplemented by periodic estimations of the serum triglyceride levels, which should be kept below 150 mg/dL.

The use of intravenous lipids should be restricted in the presence of hyperlipemia. Hyperlipemia should be avoided because it can interfere with pulmonary gas diffusion. Additional possible pulmonary complications of parenteral lipid in premature infants include fat globules in capillaries or alveolar macrophages and fat in pulmonary arterial lining cells. However, such changes can also occur in premature infants who have not received parenteral lipids. The relationship of car-
nitine deficiency to poor lipid tolerance of the parenterally fed premature infant is uncertain. Such infants are not receiving carnitine in the parenteral solutions and their blood and tissue carnitine levels are low.\textsuperscript{66-68} However, there is no evidence that providing carnitine would be beneficial.

The use of intravenous lipids should be restricted in the presence of hyperbilirubinemia.

The nitrogen in parenteral nutrition solutions is most commonly provided as a mixture of crystalline amino acids. Such amino acid mixtures have generally replaced the protein hydrolysates used previously. Not only is the nitrogen of the amino acid solutions utilized better than the nitrogen of protein hydrolysates,\textsuperscript{72} there is also a lower incidence of hyperammonemia. However, hyperammonemia as well as metabolic acidosis can be seen when parenteral amino acids are given at a rate exceeding 3.5 g/kg/d.

The commercially available parenteral amino acid solutions are not specifically designed for the premature infant. Moreover, the ideal composition of these solutions for the premature infant is not known. In addition, it is not clear whether specific amino acid requirements for newborn infants extend to parenteral amino acid needs. Cysteine has been considered to be an essential amino acid for newborn infants because of low activities of cystathionase, the enzyme that converts methionine to cysteine, in newborn hepatic tissue.\textsuperscript{1} However, cysteine supplementation of cysteine-free parenteral amino acid solutions did not improve nitrogen balance or growth of a group of premature and term newborn infants.\textsuperscript{88}

The intravenous requirement of elemental calcium and phosphorus is at least 30 to 40 mg/kg/d each. The estimated intravenous requirement of magnesium is 15 to 25 mg/d.

The parenteral trace metal requirements for infants have been estimated by Shils et al\textsuperscript{90} to be: zinc, 300 μg/kg/d; copper, 20 μg/kg/d; chromium, 0.14 to 0.2 μg/kg/d; and manganese, 2 to 10 μg/kg/d. Approximate amounts, based on these estimates, should be added to each daily fluid volume. More recent studies by Zlotkin and Buchanan,\textsuperscript{91} however, suggest that higher intakes, 438 μg/kg/d of zinc and 63 μg/kg/d of copper, are needed for LBW infants to duplicate intrauterine accretion rates of these metals.

Other trace elements, the need for which is based on animal experiments or presence in human enzyme systems, include selenium, vanadium, molybdenum, nickel, tin, silicon, and arsenic. Specific recommendations for their use await further studies.

Recommended vitamin requirements for infants can be met by giving the daily amount recommended for children,\textsuperscript{92} now available commercially in a lyophilized preparation (MVI-Pediatric). The provision of fat-soluble vitamins parenterally is complicated by adherence of some of the administered vitamins to the plastic bags and tubing.\textsuperscript{93}

**CONCLUSION**

Nutrition supply to LBW infants plays a major role in the ultimate outcome of the ever-increasing number of surviving prematurely born infants. Recognizing the potential damage from inadequate nutrition during the early neonatal period, the dilemma of feeding the premature infant is that of attempting to provide sufficient nutrition to assure optimal development without additional morbidity or mortality associated with feeding. Nutritional needs can be provided by enteral or parenteral means or a combination of both. Current research has focused on the promising use for premature babies of their own mothers’ milk as well as new special formulas for those babies needing breast milk substitutes. The use of parenteral supplements and, indeed, long-term total parenteral nutrition has allowed for the more optimal provision of nutrition to these vulnerable infants.
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