Introduction

The nutrient needs and appropriate growth rates of the hospitalised premature infant have been reviewed elsewhere [1]. In the post-discharge period, however, such data are not available. Although the rate of foetal growth serves as the standard for the infant less than 36 weeks gestation and breastfeeding meets the needs of the healthy term infant, neither goal has been shown to apply to the premature infant post-hospital discharge [2]. The graduate of the newborn intensive care unit (NICU) frequently enters into the home setting at a physical size that is significantly less than that of the foetus of the same postmenstrual age [3]. Nutrient needs may be further altered by gender, ethnicity, hospital course and clinical status [4-6].

Post-discharge formulae recently have been developed and a few have been subjected to randomised trials that include term infant formulae. Clinical studies on post-discharge nutrition are few and they differ in the population studied, specific diet investigated, duration of study diet and outcome measures. No data are available to determine how these formulae compare with actual nutrient needs for particular populations. Continued monitoring of dietary intake, anthropometry and clinical status will aid in understanding how these formulae meet nutrient needs.

Available diets

Human milk remains the primary choice for feeding infants, even premature infants in the post-discharge period. Published data suggest that premature infants have fewer upper respiratory symptoms post-discharge if they were fed human milk in hospital and continue, even on a partial human milk diet, post-discharge [7, 8]. There are no studies that describe effects of human milk fortifier use post-discharge. There are three groups of available formulae: term, preterm, and enriched (or post-discharge). The nutrient content of enriched formula falls between that of a term formula and preterm formula. The composition of some typical formulae marketed in the United States (US) are described in table I.

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Human milk</th>
<th>Term formula</th>
<th>Enriched or post-discharge formula</th>
<th>Preterm formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>~67</td>
<td>67</td>
<td>73</td>
<td>81</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>~1.0</td>
<td>1.4</td>
<td>2.1</td>
<td>2.4</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>~3.5</td>
<td>3.6</td>
<td>4.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>~7.0</td>
<td>7.3</td>
<td>7.6</td>
<td>8.7</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>~26</td>
<td>53</td>
<td>83</td>
<td>140</td>
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<tr>
<td>Phosphorus (mg)</td>
<td>~14</td>
<td>32</td>
<td>47</td>
<td>74</td>
</tr>
<tr>
<td>Sodium (mmol)</td>
<td>~0.9</td>
<td>0.8</td>
<td>1.1</td>
<td>1.8</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>~0.04</td>
<td>1.2</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>~0.3</td>
<td>0.6</td>
<td>0.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Vitamin A (µg)</td>
<td>~68</td>
<td>61</td>
<td>102</td>
<td>300</td>
</tr>
</tbody>
</table>

Post-discharge growth and body composition

Premature infants can achieve rates of weight gain postnatally similar to that of the foetus, at least 15 g/kg/day. Although this rate parallels...
the rate of weight gain in the foetus, it does not allow for catch-up growth during the hospital stay because this rate of weight gain commences only after 1 to 2 weeks [9]. Although most premature infants are appropriately grown at birth, they are frequently discharged at a weight less than the 10th percentile for age [10]. This 'in-hospital undernutrition' may be related either to deficient nutrient intake or a result of a complicated clinical course that heightens nutrient demand and/or interferes with nutrient intake [9, 11]. The complications of prematurity, such as chronic lung disease, sepsis and necrotising enterocolitis, are associated with lower rates of growth compared with infants not manifesting these conditions [9].

Post-discharge formulae recently have been developed and a few have been subjected to randomised trials. Continued monitoring of dietary intake, anthropometry and clinical status will aid in understanding how these formulae meet nutrient needs.

To achieve catch-up, premature infants must grow at a rate greater than that of the term infant [3]. Several investigations suggest that premature infants remain smaller than term infants at 3 and at 8 years corrected age [12, 13]. However, some reports indicate that they catch-up in physical growth during adolescence [14]. By 20 years of age, females demonstrate catch-up in weight, height and body mass index, but males remain smaller in all three parameters as compared with term infants [15]. Other studies report that head growth of premature infants lags behind term infants, even as late as 8 years corrected age [13, 16]. In addition, poor head growth has been linked to poor neurodevelopmental outcome [16]. To what degree appropriate nutrition during infancy affects ideal brain growth and neurodevelopmental outcome is unknown since in several studies the nutrient intake of infants was not explored.

Very little data exist on body composition in the post-discharge period. Bone mineralisation has been investigated. Metabolic bone disease during the neonatal period may affect linear growth at 18 months and continue to be a factor associated with height through 12 years of age [17, 18]. It is unknown whether post-discharge formula will enhance linear growth for the infant who suffered from osteopenia in the NICU. Optimal rates of growth in the post-discharge period are ill-defined but caregivers need some targets to assist in their evaluation of these infants. Table II provides an approximation for rates of growth in the post-discharge period.

Table II: Target growth parameters (from ref. [30, 34]).

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (g/day)</th>
<th>Length (cm/week)</th>
<th>Head circumference (cm/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>25-35</td>
<td>0.7-0.8</td>
<td>~0.4</td>
</tr>
<tr>
<td>3-12 months</td>
<td>10-20</td>
<td>0.2-0.6</td>
<td>~0.2</td>
</tr>
</tbody>
</table>

Post-discharge formulae studies

Prior to the development of enriched post-discharge formulae, premature infant graduates were fed either human milk or a term formula. Because of the concerns about post-discharge nutritional status, enriched formulae were developed. The following section discusses the studies evaluating post-discharge diets. An early nonrandomised study of 59 premature infants (born at approximately 30 weeks gestation and weighing 1.2 kg) fed for 8 weeks one of three formulae (term, preterm, or low-birth-weight formula) and then switched to term formula. Infants were followed to 16 weeks [19]. The low-birth-weight formula had a nutrient composition between the term and preterm formulae. A parallel group of human milk-fed infants also was studied. The investigation identified no differences among the three formula groups in rates of growth or biochemical assessments to 16 weeks. Bone mineral content was greater at 8 weeks in the group fed preterm formula, but there were no differences among
Nutrition of premature babies post-discharge

formula groups at 16 weeks. Although this small study suggested that diet did not impact growth, nutritional status or body composition, an important observation concerning the group fed human milk was reported. The infants fed human milk had lower rates of growth, bone mineral content and more abnormal nutritional status assessments (see below) [19].

Post-discharge diets also were studied in randomised trials of premature infants fed for 6 to 9 months either preterm formula, enriched (post-discharge) formula or term formula [5, 6, 20-22]. The outcomes measured at 9 to 18 months included growth, biochemical assessments of nutritional status, feeding tolerance and neurological development. Investigations varied in the populations studied, types of milk, lengths of time study milks were consumed and lengths of follow-up.

In a preliminary study conducted in the United Kingdom (UK), post-discharge or term formulae were assigned randomly to 32 infants weighing less than 1,850 g at birth [23]. The formulae were fed in the NICU beginning at approximately 37 weeks gestation and continued to 9 months corrected age. The infants fed the post-discharge formula had greater weight and length gains (approximating the 50th percentile) through 9 months compared with the group fed term formula (approximating the 10th percentile). No differences were observed between groups for head circumference, skinfold thickness, feeding tolerance or milk consumption. At 3 and 9 months of corrected age, the group fed post-discharge formula had greater bone mineralisation and skeletal growth (assessed by bone width) compared with the group fed term formula [24].

Growth and neurodevelopmental outcomes at 9 and 18 months corrected age in premature infants assigned randomly to either term or post-discharge formula were examined in a larger (n=284) multicenter trial in the UK [21]. Entry criteria included a birthweight of less than 1,750 g and gestational age of less than 37 weeks. Study diets were initiated at approximately 36 weeks and continued until 9 months corrected age. Infants who were fed the post-discharge formula had greater weight and length at 9 months, but at 18 months there were no differences in attained weight and length. However, the Z-score for length was significantly closer to the 50th percentile in the post-discharge formula group. When examined by sex, only males' weight and length appeared to benefit significantly from post-discharge formula. There were no differences between groups in head circumference, mid-arm circumference, skinfold thickness, incidence of illness and feeding tolerance. Neurodevelopmental assessments using a variety of measures revealed no differences between groups. Thus, this large randomised trial suggested that, while receiving an enriched post-discharge diet, premature infants have greater growth than those fed term formula, but the advantages disappear once the diet is normalised.

For infants with a birthweight less than 1,250 g, post-discharge formula confers an advantage for physical growth and nutritional status compared with term formula.

One multicenter study in the US evaluated infants with a birthweight <1,800 g [20]. Study infants were randomised to either a term or a post-discharge formula that were fed to 12 months corrected age. A difficulty with this study is the high drop-out rate, only 42% of the 125 enrolled infants completed the study. Overall, when adjusted for site, birthweight group and sex, infants fed post-discharge formula had greater body weight and length than those fed term formula. Importantly, differences between groups in weight, length and head circumference were magnified by birthweights <1,250 g. Male infants also appeared to benefit more than females. The biochemical markers of protein nutrition, i.e. prealbumin, retinol binding protein and blood urea nitrogen (BUN), were greater in the group fed post-discharge formula. In summary, it appears that, for infants with a birthweight less than 1,250 g, post-discharge formula confers an advantage for physical growth and nutritional status compared with
term formula. These data may explain the lack of beneficial effects in the previously described UK studies where a heterogeneous group of premature infants were enrolled. It is speculated that in a selected population, such as infants with birthweights less than 1,250 g, post-discharge formula would be most beneficial.

A study in Newcastle, UK, identified that improved growth and body composition outcomes persisted if infants were fed a more-enriched diet than previously had been studied [5, 6, 22]. This 6-month intervention study enrolled infants with birthweight ≤1750 g and gestation ≤34 weeks. The randomised groups were fed either preterm formula to term-equivalent age followed by term formula to 6 months, preterm formula to 6 months, or term formula to 6 months; follow-up was conducted to 12 and 18 months corrected age. Milk intakes were greater for the groups fed term formula versus those fed the preterm formula, but energy intakes remained equal, suggesting that dietary intake adjusted to meet energy needs (approximately 140 kcal/kg/day at term and 100 kcal/kg/day at >3 months) [5]. The study identified sex (i.e. males) and preterm formula as major factors affecting outcomes. When fed preterm formula, weight, length and head circumference were greater than in other diet groups, primarily in males. The beneficial effects in males persisted at 18 months [6]. Body composition data indicated that post-discharge formula supported greater mineral, lean and fat mass in males through 12 months, but only at sporadic time points for females [22]. Mental and psychomotor development at 18 months did not differ among groups [6].

The investigators also noted that sex affected nutrient utilisation and/or need during infancy. They suggested that, because of slower rates of growth, a larger sample size of girls was needed to determine whether diet affects their growth. It should be emphasised that a beneficial outcome was observed when preterm formula, not post-discharge formula, was fed. Moreover, this is the only study to report a persisting outcome and that evaluated a preterm formula. Thus, the Newcastle study reported beneficial dietary effects following a 6-month intervention using preterm formula; these effects persist beyond the intervention. The Newcastle study also reported detailed information on nutrient intakes. This information is useful in thinking about usual nutrient intakes for this population in the immediate post-discharge period (Table III). When computed from ad libitum intakes, the protein/kilocalories ratio is 2.6 g/100 kcal and calcium/kcal ratio is 120 mg/100 kcal. These intakes approximate those of enriched post-discharge formulae (Table I).

Table III: Energy, protein and calcium intakes in the post-discharge period (adapted from ref. [5]).

<table>
<thead>
<tr>
<th></th>
<th>Term-equivalent age</th>
<th>1 month-corrected age</th>
<th>2 months-corrected age</th>
<th>3-4 months-corrected age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/kg)</td>
<td>150</td>
<td>140</td>
<td>120</td>
<td>100</td>
</tr>
<tr>
<td>Protein (g/kg)</td>
<td>4</td>
<td>4</td>
<td>3.5</td>
<td>3</td>
</tr>
<tr>
<td>Calcium (mg/kg)</td>
<td>180</td>
<td>180</td>
<td>160</td>
<td>140</td>
</tr>
</tbody>
</table>

Studies of breast-fed infants post-discharge

The provision of human milk post-discharge has received limited study. No randomised trials have been conducted on premature infants breast-fed in the post-discharge period. An early nonrandomised study compared 3 groups of formula-fed infants with infants fed human milk for 8 weeks post-discharge [19]. Growth, biochemical assessments and bone mineral content were similar among the 3 formula groups, especially when followed to 16 weeks. However, the group fed human milk had lower rates of weight gain, bone mineral content and lower serum phosphorus concentration, and higher serum alkaline phosphatase activity. Another study observed that when premature infants continued to receive human milk post-discharge, their bone mineral content was less at one year corrected age compared with similar infants who were switched to a formula post-discharge [25]. Continued follow-up of this cohort found that bone mineral content at 2 years was similar between those infants
fed human milk or formula. Nevertheless, at 2 years, the growth of both groups approximated the 25th percentile [25]. These data suggest that post-discharge growth of premature infants fed human milk should be monitored closely. Furthermore, the data support the need for standards of growth and nutrient intakes in the post-discharge period. Additional evidence that human milk-fed premature infants should be monitored carefully post-discharge comes from the UK randomised trial of post-discharge formula [21]. Along with two formula groups, 65 breast-fed infants were followed for the first 9 months as a reference group. That group received term formula when human milk was not available. The breast-fed group differed from the others in that mothers providing human milk were older, had more years of formal education and were of a higher socioeconomic status. They breast-fed their infants a minimum of 6 weeks. The breast-fed infants, however, were significantly smaller in weight than either formula group at 6, 12, and 26 weeks, but at 9 months the breast-fed group’s weight differed only from that of the post-discharge formula group. Breast-fed infants’ length was significantly less than that of the post-discharge formula group at 6 and 12 weeks and 9 months. Unfortunately, no follow-up was conducted for the breast-fed group beyond 9 months. Although the breast-fed premature infants’ slower growth suggests a need for nutrient supplementation post-discharge, their lesser rate of growth has been associated with better health and shorter hospital stay than those fed formula [21, 26].

Studies in small-for-gestational-age term infants

There is one report of small-for-gestational-age term infants who had slightly improved length gains with the use of post-discharge formula when compared with term formula for 9 months [27]. However, at 9 months the infants fed post-discharge formula had significantly lower developmental quotient (DQ=99.5) compared with infants fed term formula (DQ=102). When analysed by sex, the difference was only noted for female infants. By 18 months of life, this difference disappeared [28]. At present, the use of post-discharge formulae for the small-for-gestational-age term infant is not recommended.

In this investigation, a reference group of breast-fed, small-for-gestational-age term infants also was followed for 18 months [27]. The breast-fed infants had greater gains in weight, length and head circumference, gains that persisted to 18 months compared with infants fed formula. However, after adjustment for confounding factors of social class, maternal education, parental size, infant sex, size at enrollment, age at follow-up and birth order, no differences were observed between breast- and formula-fed infants [27, 28]. Most importantly, the breast-fed group had higher developmental scores than both formula-fed groups at 18 months [28]. Thus, human milk offers the small-for-gestational-age term infant the advantage of better neurodevelopmental outcomes while not compromising physical growth. These data suggest that recommendations for term small-for-gestational-age term infants be distinct from weight-matched premature infants.

Discharge planning

Discharge planning should be started well in advance of the planned hospital departure. In doing so, potential risk factors for poor growth post-discharge can be identified. Milestones that potentially ensure optimal growth outcomes include the ability to consume ad libitum quantities of milk orally, a satisfactory rate of weight gain, and normalisation of biochemical markers of nutritional status.
Before discharge, the infant should have an established pattern of weight gain while consuming the planned diet. Physiologically, the infant should be able to breast- or bottle-feed without cardiorespiratory compromise [29]. Parents should demonstrate their ability to feed their infant by breast, bottle or alternative methods if indicated. In addition, they should demonstrate correct formula preparation and supplement dosage. Nutritional risks should be assessed and the appropriate therapies and dietary modification should be made.

There are several options for milk selection and supplementation at discharge. The lack of data sufficient to support one recommendation over another provides significant latitude in management [30]. An individual approach is indicated.

**Breastfeeding premature infants**

As identified through discharge planning, if the infant is breastfeeding well, weight gain is adequate and there are no persisting nutritional biochemical abnormalities, post-discharge diets should include exclusive breastfeeding. In this scenario, the infant also should receive a multivitamin and an iron supplement. The infant should be seen for follow-up at 1 week, and then monthly. Growth should be assessed at each visit and measurement of biochemical indices (serum alkaline phosphatase, phosphorus, albumin, BUN) may be helpful at 1 week and 1 month.

If discharge planning identifies issues with either growth, ability to feed, or biochemical measurements, then a supplement must be provided in addition to breastfeeding. Supplemental nutrition usually is in the form of commercially prepared formula. The enriched post-discharge formulae have been used for this purpose because the nutrient density is greater than that of term formula, and there are powdered preparations that can be mixed to the desired concentration. In this scenario, mothers should breast-feed the majority of the day (if their milk production is adequate and the infant can consume adequate volume), but supplemental enriched formula should be used for 2 to 3 feedings each day. These formula feedings could comprise enriched formula mixed with breast-milk or prepared as usual. Potential mixtures of human milk and post-discharge formula powder are included in table IV. For the infant who requires fluid restriction, breastfeeding may be possible if powdered enriched formula is used as a supplement. When breastfeeding and supplemental enriched formula are used, the infant should receive supplemental multivitamins and iron. Follow-up growth and biochemical measurements should be done at 1 week, and then as indicated serially. If the supplemental formula is used, it should be con-

<table>
<thead>
<tr>
<th>Component (unit/liter)</th>
<th>Enriched post-discharge formula</th>
<th>Human milk</th>
<th>Human milk + enriched formula*</th>
<th>6 feedings of human milk + 2 feedings of enriched formula†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>730</td>
<td>670</td>
<td>790</td>
<td>686</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>21</td>
<td>10</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>835</td>
<td>280</td>
<td>415</td>
<td>419</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>475</td>
<td>147</td>
<td>222</td>
<td>229</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>13.3</td>
<td>0.4</td>
<td>2.5</td>
<td>3.6</td>
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<tr>
<td>Zinc (mg)</td>
<td>9</td>
<td>1.2</td>
<td>2.6</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Prepared by adding approximately 2.25 g enriched post-discharge formula powder to 100 ml human milk; average values for comparison purposes only.
† Computed by assuming 75% of diet is human milk and 25% is post-discharge formula prepared per manufacturer’s recommendations; average values for comparison purposes only; enables “exclusive” breastfeeding for most (75%) of the day.
continued for approximately 6 months. Although this plan for post-discharge support is used frequently, the major concern is that it lacks experimental validation with adequate post-discharge follow-up. This is one area where intense research efforts are needed.

**Formula feeding premature infants**

For the formula-fed premature infant, the same discharge criteria should be considered: infants who are unable to ingest quantities of milk in excess of 180 ml/kg/day, have rates of weight gain less than 20 g/day, or have persisting biochemical abnormalities should be given enriched, post-discharge formula near discharge. In general, these infants tend to have birth weights <1,250 g, restricted milk intake, and/or biochemical evidence of rickets or hypoproteinemia. If the exclusive diet is enriched post-discharge formula, then no additional vitamins or iron are required. If term formula is fed, the infant should be given iron-fortified formula. If term formula is fed, the infant also should be given multivitamins for about 2 months.

Discharge planning should include nutritional factors, such as whether breastfeeding, formula feeding or combination are anticipated post-discharge. Continued evaluation of growth and nutritional status must take place to ensure the best outcome for the premature infant.

**Duration of feeding and use of supplements post-discharge**

When supplemental nutrition is provided post-discharge, it should be continued for 6 to 9 months corrected age [31]. Only iron-fortified formulae should be given and, if used, no additional iron supplementation is indicated. Iron intake should be 2 mg/kg/day for the exclusive breast-fed infant in the first year [32]. The dose of iron should be adjusted if the infant is breast-fed and also receive formula. Multivitamins are not indicated for infants receiving only post-discharge formula, or if consuming term formula and weigh more than 3 kg. Multivitamins should be given to exclusively breast-fed premature infants. These recommendations ensure a vitamin D intake of 200 IU per day [33].

**Post-discharge monitoring**

There must be good communication between the in-hospital and the post-discharge caregivers to ensure that the plan for nutrition post-discharge is understood and carried out appropriately. The follow-up physician should be apprised of the importance of providing the supplemental nutrition or the serial monitoring, as indicated. The frequency of office or home visits will be determined by the clinical condition of the infant. When there are concerns about milk intake, growth or abnormal biochemical indices prior to discharge, the infant should be seen more frequently, beginning at 1 week post-discharge. After the first week, serial weekly and then monthly visits become appropriate as the infant demonstrates adequate growth and biochemical measurements.

Growth velocity can be utilised to monitor growth. Weekly weight trends are helpful to assess the infant who is demonstrating poor growth and requires diet manipulations. Laboratory assessment for mineral status should include serum alkaline phosphatase activity levels, serum calcium, and serum phosphorus for infants who have a history of osteopenia or are considered at risk for this disease due to poor calcium and phosphorous intakes while in the intensive care unit. For protein status, albumin and BUN can be followed. When growth is poor or laboratory values are abnormal, the diet should be re-evaluated. The post-discharge formula could be further concentrated, or additional formula feedings per day are possible considerations for the breast-fed infant. As indicated, experimental validation is needed in this area.
Conclusions

Discharge planning should include nutritional factors, such as whether breastfeeding, formula feeding or combination are anticipated post-discharge. Prior nutritional status (derived from serial biochemical monitoring), ability to feed orally and rate of growth are factors that will determine the nutrition plan post-discharge. If none of these issues are a concern, then exclusive breastfeeding or feeding term formula are indicated. If any of these factors are a concern, then supplemental nutrition from an enriched post-discharge formula should be used along with breastfeeding or as an exclusive diet if no breastfeeding is anticipated. Continued evaluation of growth and nutritional status must take place to ensure the best outcome for the premature infant. Suggested guidelines are provided but it is expected that research will continue to elucidate more clearly the specific nutrient needs of this high-risk infant population.

References