Nutrition, Growth, and Body Composition


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The most widely accepted guideline for nutritional management of the low birthweight (LBW) infant is to provide sufficient intakes of all nutrients to achieve postnatal rates of growth and nutrient accretion approximating those of a normal fetus during the same period of development (1,2). However, most LBW infants lose from 10% to 15% of body weight soon after birth and do not regain this weight until 2 or 3 weeks of age. As a result, infants who gain weight at the intrauterine rate after birthweight is re-achieved will remain 2 to 3 weeks behind the fetus of comparable age. Hence, achieving rates of weight gain and nutrient accretion in excess of intrauterine rates seems desirable. In fact, the argument can be advanced that failure to do so may contribute to the subsequent poor growth performance of a large number of LBW infants (3,4).

Many studies published during the past decade have shown that rates of weight gain up to 50% greater than the intrauterine rate can be achieved (4-22); however, the higher rates of weight gain are usually associated with rates of fat accretion far in excess of the intrauterine rate (i.e., 20–30% versus 11–12% of weight gain). This raises the important question of whether significant postnatal catch-up growth can be achieved without excessive fat deposition relative to that of the developing fetus or whether the excessive fat deposition simply reflects the nature of the intakes fed.

At the outset, it is important to note that the consequences of the composition of weight gain of LBW infants are unknown. On the one hand, “excessive” fat accretion is generally thought to be undesirable. In the LBW infant, however, there is no clear definition of “excessive” fat accretion. Moreover, in this population, fat deposits may be an important nutritional buffer for intervals between feedings and may be useful for insulation against thermal stress. Thus rates of fat accretion in excess of intrauterine rates may be advantageous for the LBW infant’s successful adaptation to extrauterine life. In this regard, it has been estimated that fat accretion accounts
over the past several years we have studied growth, nutrient retention, and metabolic response in over 200 LBW infants fed protein intakes ranging from 2.25 to 4.3 g/kg.d and energy intakes ranging from 100 to 150 kcal/kg.d (20–22,24–25). Moreover, the intakes of protein and energy were varied independently, making it possible to differentiate the independent effects of protein intake and energy intake as well as the effect of energy intake on protein utilization. The results of these studies strongly for roughly 40% of the weight gain of term infants from birth to 4 months of age (23). Perhaps the most pressing reason to know more about the extent to which composition of weight gain of LBW infants can be manipulated by diet is the fact that it will be easier to study the consequences of one composition of weight gain versus another if the composition of weight gain can be manipulated predictably by diet.

Over the past several years we have studied growth, nutrient retention, and metabolic response in over 200 LBW infants fed protein intakes ranging from 2.25 to 4.3 g/kg.d and energy intakes ranging from 100 to 150 kcal/kg.d (20–22,24–25). Moreover, the intakes of protein and energy were varied independently, making it possible to differentiate the independent effects of protein intake and energy intake as well as the effect of energy intake on protein utilization. The results of these studies strongly
suggest that protein deposition is largely a function of protein intake and that fat deposition is largely a function of energy intake. The primary data are illustrated in Figs. 1 and 2 which show, respectively, the relationship between protein intake and protein accretion and the relationship between energy intake and fat accretion. Figure 3 illustrates the close relationship between the ratio of protein and energy of the diet and the ratio of protein and fat (i.e., protein stored/fat stored) in newly deposited tissue.

These close relationships between protein and energy intakes and body composition suggest that these data can be used to develop a model for predicting the protein and energy intakes likely to produce both specific rates and specific compositions of weight gain. Our attempts to develop such a model are described below along with a discussion of how the model might be used and its limitations.

DEVELOPMENT OF THE MODEL

The multiple regression equations summarizing the relationship between nitrogen intake ($N_{in}$) and nitrogen retention ($N_r$) as well as that between energy intake ($E_{in}$) and energy retention ($E_r$) of a subset of the infants studied by us are:

$$N_r = 0.712 N_{in} + 0.0157 \quad (r = 0.85) \quad [1]$$

$$E_r = 0.714 E_{in} - 35.08 \quad (r = 0.72) \quad [2]$$

The multiple regression equation summarizing the rate of weight gain ($\Delta W$) of the same infants is:

$$\Delta W = 0.095 E_{in} + 3.6 P_{in} - 0.00468 BW + 1.699 \quad (r = 0.62) \quad [3]$$
where $P_{in}$ is protein intake. Substituting the average birthweight of infants participating in these studies, i.e., 1400 g, equation 3 becomes:

$$\Delta W = 0.095E_{in} + 3.6P_{in} - 4.86$$  \[4\]

The equation expressing the relationship between nitrogen retention and nitrogen intake can be converted to one summarizing the relationship between protein accretion ($P_s$) and protein intake ($P_{in}$) by substituting $P_s/6.25$ and $P_{in}/6.38$ for $N_r$ and $N_{in}$:

$$P_s = 0.6975P_{in} + 0.098$$  \[5\]

The general relationship between energy retention ($E_s$), i.e., metabolizable energy intake minus energy expenditure, and fat accretion ($F_s$) is expressed by the following equation, in which the constants 5.65 and 9.25 are the energy values (kcal/g) of protein and fat:

$$F_s = E_s - 5.65P_s/9.25$$  \[6\]

Replacing $E_s$ and $P_s$ with equations 2 and 5, the equation for fat accretion becomes:

$$F_s = 0.077E_{in} - 0.426P_{in} - 3.85$$  \[7\]

The next step in developing a model for predicting the protein and energy intakes required to produce a specific rate and a specific composition of weight gain is to choose the composition of weight gain desired. A reasonable choice, but not necessarily the optimal choice or in fact the only choice, is that of the developing fetus, as summarized by Ziegler et al. (27). Having made this choice, it is possible to determine the relationship between the intakes of protein and energy necessary to produce the desired relationship between the rates of protein and fat accretion. The data summarized by Ziegler et al. indicate that the "reference fetus" increases in weight from 770 g at 25 weeks' gestation to 2450 g at 35 weeks. During this interval, which is a reasonable one for our purposes, protein increases from 69.3 g to 274.4 g and fat increases from 5.4 g to 198.5 g. From these data, the ratio of protein stored to fat stored during this developmental interval can be calculated, i.e., $P_s/F_s = 205/193 = 1.062$.

Assuming that the water lost permanently as part of the apparently inevitable postnatal weight loss is replaced by protein and fat in the same proportions as occur in utero, the infant who continues to deposit protein and fat in these proportions will have on discharge the same body composition, at least with respect to protein and fat, as would have been the case had birth not occurred prematurely.

Substituting the above equations for $P_s$ (equation 5) and $F_s$ (equation 7) into the ratio equation (i.e., $P_s/F_s = 1.062$) and solving it for either protein intake or energy intake yields an equation expressing the relationship between the intakes of protein and energy necessary to produce the desired relationship between the rates of protein and fat accretion. Solving it for energy intake yields:

$$E_{in} = 14.15P_{in} + 51.33$$  \[8\]
This equation can now be substituted into the multiple regression equation summarizing the rate of weight gain:

$$\Delta W = 4.94P_{in} + 0.016$$ \[9\]

The resulting equation along with equation 8 permits calculation of the protein and energy intakes likely to result in any desired rate of weight gain with the same composition as that of the fetus during the 25th and 35th weeks of gestation. The remaining task is thus to decide upon the "desired" rate of weight gain.

**USE OF THE MODEL TO PREDICT INTAKES**

If the infant born at 25 weeks of gestation does not regain birthweight until 3 weeks of age and yet is expected to achieve catch-up by 10 weeks of age, the weight gained during a 10 week period in utero must occur over a 21-day-shorter period, or in 49 rather than 70 days. Thus the infant must gain an average of 34.3 g/d rather than 24 g/d, or roughly 21 g/kg.d rather than 15 g/kg.d. Substituting this greater rate of weight gain into equation 9 indicates that the protein intake required to produce this rate of weight gain is 4.3 g/kg.d. Substituting this protein intake into equation 8 in turn indicates that the concomitant energy intake required is 112.3 kcal/kg.d.

Clearly, the rate of weight gain required to produce complete catch-up growth of this theoretical infant is entirely feasible. However, the reasonably high protein intake that is theoretically required to produce this rate and composition of weight gain is unlikely to be completely utilized at the predicted energy intake. For example, we have shown that a protein intake of 3.9 g/kg.d is not utilized as completely at an energy intake of 120 kcal/kg.d as at a concomitant energy intake of 144 kcal/kg.d (21); thus it is unlikely that a protein intake of 4.3 g/kg.d with a concomitant energy intake less than 120 kcal/kg.d will be utilized any more completely than the previously studied intake of 3.9 g/kg.d. This suggests that complete catch-up growth with the same composition of weight gain that occurs in utero cannot be achieved within 49 days.

However, complete catch-up growth without fat accretion at rates in excess of the intrauterine rate might be achievable if birthweight were regained sooner, thereby prolonging the time required to "catch up." If birthweight is regained by 2 weeks of age, for example, the rate of weight gain necessary to result in complete catch-up by 10 weeks of age, i.e., within 56 rather than 49 days, is 18.6 g/kg.d rather than 21 g/kg.d. The protein and energy intakes required to produce this rate of weight gain are 3.76 g/kg.d and 105 kcal/kg.d. Again, however, this protein intake may not be completely utilized unless concomitant energy intake, and hence the resulting rate of fat accretion, is higher.

A very practical approach is to assume that catch-up without excessive fat deposition by a postnatal age equivalent to 40 weeks' gestation rather than by hospital discharge is reasonable. This approach takes advantage of the greater rate of fat accretion during the latter weeks of intrauterine development. For example, over the
interval from 25 to 40 weeks, the "reference fetus" deposits 344.7 g of protein and 381 g fat; thus, over this interval, $P_s/F_s = 0.905$. Forty percent of this protein (139.6 g) and 49% of this fat (188 g) are deposited during the last 5 weeks of gestation, i.e., weeks 35 to 40, during which time $P_s/F_s = 0.743$. Thus the infant who deposits protein and fat at appropriate rates and at a ratio of 0.9 from the time birthweight is regained at 3 weeks of age until the equivalent of 40 weeks' gestation should, at that time, weigh the same and have the same body composition as a "normal" term infant.

According to model predictions, a protein intake of 3.4 g/kg.d and an energy intake of 100 kcal/kg.d should achieve this goal. These intakes should result in a rate of weight gain of 16.6 g/kg.d. Thus the infant fed these intakes will be about 2 weeks behind the fetus of comparable age at the equivalent of 35 weeks' gestation and also somewhat fatter but should catch up both in weight and in protein content over the ensuing 5 weeks.

**LIMITATIONS OF THE MODEL**

The predictions based on the model described and illustrated above, like the predictions based on any such model, represent, at best, hypotheses to be tested. Thus until this is done the validity of the predictions remains unknown. We have approached this issue in two ways. First, a similar model based on the same data was used to predict protein and energy intakes necessary to produce partial and complete catch-up growth with the same composition as that of the developing fetus by hospital discharge at a body weight of 2200 g and these intakes were tested in LBW infants. Second, the model described above was used to predict rates of weight gain as well as rates of protein and fat accretion of several groups of infants described in published studies, and these predicted rates were compared to reported rates.

With respect to the first approach, the protein and energy intakes predicted by the model to result in specific rates and compositions of weight gain in general resulted in the expected rates of weight gain, protein accretion, and fat accretion, and the expected ratio of protein stored to fat stored (25). For all variables, the relationship between predicted and observed responses was highly significant. In addition, the slopes of the regression lines relating observed outcomes to predicted outcomes did not differ from the lines of identity. These observations indicate that the model can be used prospectively to predict protein and energy intakes likely to result in specific rates and compositions of weight gain.

Figures 4 to 6, respectively, illustrate the relationship between the rates of weight gain, protein accretion, and fat accretion of LBW infants reported by several investigators (6,10,12–16,19) and the rates of weight gain, protein accretion, and fat accretion predicted by the model described above. It is obvious that the reported data agree reasonably closely with the predictions of the model. Thus when evaluated prospectively or retrospectively the model appears to be reasonably useful. This suggests that the protein and energy intakes required to produce various rates and
FIG. 4. The relationship between the rate of weight gain (g/kg.d) of groups of low birthweight infants reported by a number of investigators (6,10,12–16,19) and that predicted by the equation, \( \Delta W = 0.095E_m + 3.6P_m - 0.0047BW + 1.7 \) (see text). The regression (broken) line, \( y = 0.7x + 4.9 \) \((r^2 = 0.38)\), does not differ significantly from the (solid) line of identity. Compositions of weight gain can be predicted with reasonable accuracy. Hence it should be possible to determine if the magnitude and composition of weight gain of LBW infants have short-term and/or long-term functional consequences.

The above conclusions, of course, are based on the assumption that estimates of body composition computed from rates of nutrient retention in fact reflect rates of actual protein and fat deposition. To date, with the exception of some measurements of total body water, actual measurements of the body composition of LBW infants have not been reported. Since calculation of fat-free mass from total body water data necessitates assumptions concerning the hydration of lean body mass, which, in the

FIG. 5. The relationship between protein accretion (\( P_s \)) of groups of low birthweight infants reported by a number of investigators (6,10,12–16,19) and that predicted by the equation, \( P_s = 0.698P_m + 0.098 \) (see text). The regression (broken) line, \( y = 1.12x - 0.5 \) \((r^2 = 0.85)\), does not differ significantly from the (solid) line of identity.
LBW infant, is highly variable, the total body water data are not very helpful. We have had some experience with measuring body composition of LBW infants by densitometry, i.e., measuring the infant’s volume by an air displacement device (28), measuring total body water as the dilution space of deuterium, and using these data, as well as the infant’s weight, to calculate rates of protein and fat deposition (29). The limited fat mass of LBW infants imposes severe limitations on this approach until the infant weighs 3.5 to 4 kg. However, as shown in Fig. 7, the observed change in density was at least qualitatively similar to that expected—i.e., density decreased less rapidly in those fed diets with higher P/E ratios and consequently accreting tissue with a higher P/F ratio.

**FIG. 6.** The relationship between fat accretion ($F_s$) of groups of low birthweight infants reported by a number of investigators (6,10,12–16,19) and that predicted by the equation, $F_s = E_s - 5.65P_s/9.25$ (see text). The regression (broken) line, $y = 0.7x + 1.33$ ($r^2 = 0.37$), does not differ significantly from the line of identity.

**FIG. 7.** The relationship between the change in density of low birthweight infants (g/ml.kg) from the time desired intake was tolerated until discharge at 2200 g and the protein/energy ratio (g/kcal) of the intake. [From Dell RB, et al. (29).]
Whole body counters capable of measuring total body $^{40}\text{K}$ content of LBW infants within a short period of time are now available and are beginning to be used in studies of LBW infants. These data should provide reasonable estimates of total body potassium and hence of lean body mass. Although this approach also may be limited by the lack of data concerning the hydration of lean body mass of LBW infants, it will be quite interesting to see how the rate of change in lean body mass predicted from total body $^{40}\text{K}$ measurements compares with the rate of change calculated from rates of nitrogen and energy retention.

OTHER CONSIDERATIONS

It should be noted that the above exercise predicting the protein and energy intakes likely to result in catch-up growth of LBW infants without exceeding the intrauterine rate of fat accretion applies only to infants whose weight at birth is appropriate for gestational age. Further, the validity of the exercise depends to some extent upon the assumptions made concerning the composition both of the immediate neonatal weight loss and the tissue with which it is replaced. While the assumptions made are reasonable, although perhaps not entirely valid, for the infant whose size at birth is appropriate for gestational age, they may not be reasonable for the infant who is growth retarded in utero. Yet catch-up growth is probably more important for growth-retarded infants than for those whose size at birth is appropriate for gestational age.

Despite the limitations of the above approach with respect to the infant who is growth retarded in utero, its application to such infants helps to illuminate the magnitude of the problems in achieving catch-up growth in this population. In the absence of data concerning the body composition of infants who are born small for gestational age, it will be assumed that this is the same as that of a normally grown infant of the same size. For example, an infant who is born after 29 weeks of gestation weighing 770 g is assumed to have the same body composition as an infant born after 25 weeks of gestation and weighing the same. It also will be assumed that the infant experiences the same initial weight loss, that birthweight is regained at 2 weeks of age, and that body composition at 2 weeks of age is the same as that at birth. Thus at this time the hypothetical infant is 6 weeks behind the fetus of comparable postmenstrual age.

To catch up by 40 weeks postmenstrual age, the hypothetical infant described above must increase from 770 g to 3450 g within a 6-week-shorter time interval than the appropriately grown 770 g fetus, within a 4-week-shorter time interval than the 770 g infant who is born at 25 weeks’ gestation and regains birth weight by 2 weeks of age, and within a 3-week-shorter time interval than the more typical appropriately grown 770 g infant who regains birth weight by 3 weeks of age. Thus the growth retarded infant must gain weight at an average rate of almost 50 g/d, or 22.8 g/kg.d, in order to catch up by 40 weeks postmenstrual age. Such a rate of weight gain, perhaps, is achievable. However, this rate is as great as any reported and was observed in infants increasing in weight from, roughly, 1000 g to 2000 g. Moreover, as illustrated above (and with the additional proviso that the composition of weight gain
be the same as that which occurs in utero), this rate is almost certainly not achievable unless the small-for-gestational-age infant handles nutrients differently from the infant whose size is appropriate for gestational age.

While many believe that the small-for-gestational-age infant handles nutrients more efficiently than the normally grown infant, our data suggest otherwise. The equations summarizing the nutrient retention data of infants studied by us are based on data from both normally grown and growth-retarded infants. Further, although size for gestational age was a potential independent or confounding variable for all multiple regression equations, it did not contribute significantly to the equations for any of the relevant independent variables (e.g., rate of weight gain, nitrogen retention, energy retention).

Another important issue concerns the impact of the composition of weight gain during a relatively finite period on body composition later in life. This general issue is related to the issue of "imprinting," which will not be addressed, but it also includes the simpler issue of whether a perhaps excessive rate of fat accretion during the early neonatal period, e.g., from birth until weight reaches 3450 g, is likely to exert a detectable effect on body composition at specific times thereafter. Table 1 summarizes the predicted body composition at a postmenstrual age of 40 weeks and at 4 and 12 months thereafter of infants whose composition of weight gain differed only during the interval from birth to 3500 g. These theoretical data suggest that the impact of the composition of weight gain during the neonatal period wanes as the infant's weight doubles between the equivalent of term birth and 4 months of age and again between 4 and 12 months of age.

These predictions are based on data summarized some time ago by Fomon (23) and may not reflect the rate or the composition of weight gain of modern infants.

TABLE 1. Impact of composition of neonatal weight gain on body composition of LBW infants at 40 weeks postmenstrual age ("Term") and at 4 and 12 months later

<table>
<thead>
<tr>
<th></th>
<th>Infant A</th>
<th>Infant B</th>
<th>Infant C</th>
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</thead>
<tbody>
<tr>
<td>&quot;Term&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>12.0%</td>
<td>10.3%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Fat</td>
<td>11.2%</td>
<td>15.3%</td>
<td>22.7%</td>
</tr>
<tr>
<td>4 Months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>11.7%</td>
<td>10.9%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Fat</td>
<td>26.2%</td>
<td>28.2%</td>
<td>31.9%</td>
</tr>
<tr>
<td>12 Months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>14.8%</td>
<td>14.2%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Fat</td>
<td>24.1%</td>
<td>25.5%</td>
<td>27.9%</td>
</tr>
</tbody>
</table>

Assumptions: All "infants" were born at 26 weeks' gestation and increased in weight to 3500 g over the next 14 weeks. Weight gained during this period was 12.9% protein and 14.2% fat in infant A, 11% protein and 20% fat in infant B, and 11% protein and 30% fat in infant C. In all infants, the composition of weight gain from "term" to 4 months (weight = 7000 g) was 11.4% protein and 40.8% fat; from 4 to 12 months (weight = 10.5 kg), the composition was 21% protein and 19.9% fat (23).
between birth and 4 months of age and, particularly, between 4 and 12 months of age (30). Thus, to the extent that the composition of weight gain of modern infants differs from that used in the predictions, the conclusion that the impact of early composition of weight gain exerts little effect on body composition at 4 months of age and virtually no effect at 12 months of age may be faulty. This exercise also fails to account for any "imprinting" effect of the early diet and the possibility that this phenomenon, whether manifested through increased appetite or through nutrient disposition, may alter the composition of subsequent weight gain.

REFERENCES


**DISCUSSION**

*Dr. Guesry:* I was struck by the fact that you were unwilling to say whether it is a good or a bad thing to gain weight at the intrauterine rate or to deposit fat at a very high rate!

*Dr. Swyer:* You appear to accept that there is an inevitable loss of weight over the first 3 weeks. Would it be desirable or possible to avoid this loss, particularly since it appears that it is largely body mass rather than water?

*Dr. Heird:* This issue was addressed in some studies that I did not describe. We examined nitrogen excretion in babies with a mean birthweight of around 1000 g during the first few days of life, with and without intravenous amino acids. We showed clearly that if amino acids are given from very early on the babies are in positive nitrogen balance, whereas if only glucose is given they are in negative balance. The assumption is often made that preterm infants are unable to tolerate amino acids during the first few days of life but this seems to be untrue. It seems likely that the early administration of suitable feeding regimens will reduce the postnatal weight loss and begin to solve the problems encountered in achieving catch-up growth.

*Dr. Swyer:* You put the major emphasis on nitrogen intake. In view of the importance of fatty acid intake for brain development at this very active stage I should like to know when you start to give lipid preparations and if you think these are important components of early feeding.

*Dr. Heird:* I am not sure that the lipid preparations that are available in North America are likely to be very helpful. Very low birthweight babies are also relatively intolerant to glucose and lipids in the early days. However, my approach is to start giving lipids early and to increase the amount given according to tolerance.
Dr. Pusponegoro: But when would you recommend actually starting to use intravenous fat solutions in babies on total parenteral nutrition?

Dr. Heird: Babies such as we have been discussing develop signs of essential fatty acid deficiency within a few days if they are growing and are not receiving any lipids, though it will take longer for symptoms to develop if they are not growing. There are some problems with the fat emulsions we have at present, which are based on soybean oil. These emulsions contain considerable amounts of linolenic acid, which inhibits the conversion of linoleic acid to arachidonic acid. In general fat emulsions should be started as soon as clinically feasible but with the reservation that, at least in North America, we don’t at present have access to really appropriate preparations. I think that by the time you start giving amino acid solutions you can also start with 0.5 g/kg per day of fat. If that is tolerated it can be increased.

Dr. Manz: Normal infants show a decrease in weight gain before and after birth. Should we really be thinking about a continuous growth curve or should we in fact be thinking about a transient decrease in growth during this period?

Dr. Heird: I am always uncomfortable about applying normal fetal standards to the baby after premature birth. I feel that the important thing is to ensure somehow that the preterm infant catches up with the growth curve of the normal infant at some point, but where that point should be I don’t know. From animal studies one would assume the sooner the better but this may not necessarily be the case for humans. The real issue is how to produce catch-up growth. We should be asking to what extent the smallness of prematurely born children at 3 years of age, or 10 years, is related to failure to achieve catch-up during the period when catch-up is still possible.

Dr. Lucas: In relation to postnatal weight loss, neurologists like Arand in Dallas would argue that you are born with an intracellular-to-extracellular ratio of 1:2 and you have to reverse this postnatally, so there will be an obligatory loss of extracellular water after birth. To what extent does this confuse the calculations about catch-up growth? How much of the weight loss after birth is actually obligatory weight loss due to water loss and cannot be retrieved?

Dr. Heird: We assume that about half the weight loss is water from the calculations based on obligatory water loss data. At the time the baby has regained birthweight we assume that the water was replaced by protein and fat in the same proportions as were accumulated in utero. This may be only an assumption but it does not have much bearing on the subsequent calculations.

Dr. Priolisi: Did you measure plasma amino acids in your very low birthweight babies while on total parenteral nutrition?

Dr. Heird: The plasma amino acid pattern prior to the addition of amino acids looked similar to the pattern in malnourished babies—overall the concentrations were low. After adding the parenteral amino acids the pattern became like that of babies fed their own mothers’ milk. The concentration of no amino acid exceeded the concentration observed in babies fed their own mother’s milk by more than two standard deviations.

Dr. Putet: Do you think that the protein-energy ratio of the nutrient intake should change with gestational age? There was some indication from your data that the infants you studied appeared to need more nitrogen in the very early weeks and rather less later on.

Dr. Heird: From multiple regression analyses of roughly 250 babies with birthweights ranging from 750 to 1750 g and who have had, on average, three balances during their stay in neonatal care, we have not been able to show that birthweight or gestational are significant factors in determining the optimum protein-energy ratio of the diet.

Dr. Putet: What in your opinion, and taking into account all your accumulated data on
blood amino acids and so on, is the optimal daily protein intake for infants around 1000 g weight?

**Dr. Heird:** Up to 3.6 g/kg/d protein and 120 kcal/kg/d is well tolerated by all the babies we have studied. On this level of intake, and using a whey-predominant formula, all the plasma amino acids are within the range of 95% confidence limits of cord blood amino acids, either obtained *in utero* or at delivery.

**Dr. Lucas:** In our experience some small-for-gestational-age (SGA) infants have extremely high energy expenditures. Do you recognize within your population subgroups of babies who need different nutritional management from the rest and in whom your regression equations of energy expenditure versus protein intake may not apply?

**Dr. Heird:** Those regression equations were obviously generated from the babies that we studied. About 25% of them were SGA. We took the approach early on that we needed to establish whether it made a difference if the baby was born SGA. We depended on stratified randomization with respect to birthweight so that we should have equal numbers of all possible confounding variables in each group that we studied. We then did multiple regression analyses of the outcome variables of interest to us, controlling for about 25 other possible confounding variables. At the end of the exercise none of these potentially confounding variables appeared in the equation. Thus it does not seem that there is a subgroup of babies who require special attention. That is not to say, however, that there are no babies who require a different nutritional approach. Babies with bronchopulmonary dysplasia, for example, were excluded from the analyses, as were babies with necrotizing enterocolitis, obviously.