Fortification of Human Milk

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Human milk may confer nutritional and nonnutritional advantages in feeding the preterm infant, including protection against infections and enhanced intestinal development. In addition, recent studies have suggested that human milk is superior to formula for feeding preterm infants with respect to both short-term and long-term outcome data (1,2). However, many studies have shown that preterm milk and banked term milk do not provide adequate quantities of several nutrients, specifically protein and minerals, to meet the nutritional needs of the preterm infant (3–5).

HUMAN MILK FORMULA

To overcome the nutritional inadequacies of human milk, Lucas et al. introduced the term lactoengineering and produced a “human milk formula”—that is, a formula made entirely with human milk components (6). The original formula prepared by Lucas was based on fortification of human milk with protein, fat, calcium, and phosphorus. However, since it has been shown that increasing the energy intake of very-low-birthweight (VLBW) babies to more than 115 to 120 kcal/kg-d does not improve linear growth but only increases fat accretion (7,8), current fortification schedules are designed primarily to increase the protein content of human milk, while also providing an additional source of minerals and vitamins (9–12).

In our Center for Infant Nutrition in Milan, Italy, a human milk protein concentrate is obtained by an ultrafiltration process (13). Briefly, defatted milk is pasteurized at 72°C for 15 seconds, ultrafiltrated, freeze-dried, and stored in small, sealed-glass ampoules (Fig. 1). The concentrate is composed of 65% to 70% protein, 12% lactose, 9% fat, and small quantities of minerals. The final concentrate is used to supplement human milk and produce a “human milk formula” for feeding VLBW infants. The infants assigned to receive our human milk formula also receive a daily supplement of calcium (30 mg/kg from calcium lactate) and phosphorus (20 mg/kg from sodium phosphate). Beginning on the 15th day of life, all infants also receive a daily vitamin supplement providing 1,200 IU of vitamin A, 1,200 IU of vitamin D, 30 mg/kg of vitamin E, and 50 mg/kg of vitamin C. Starting at 30 days of age, all infants also receive supplemental iron (2 mg/kg from ferrous sulfate).
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**POOLED HUMAN MILK**

1. **Bacterial Test 1**
   - **PASTEURIZATION**
     - 72°C – 15 sec
2. **Bacterial Test 2**
   - **SEPARATION OF CREAM**
     - Cream freezing
   - **ULTRAFILTRATION**
     - cut off 20,000
   - **CONCENTRATED HUMAN MILK**
     - Pasteurization
     - 72°C – 15 sec
   - **PACKING IN GLASS – BOTTLES**
   - **FREEZE – DRYING**
3. **Bacterial Test 4**
   - **PROTEIN POWDER**

**FIG. 1.** Human milk lactoengineering: processing used in the Center for Infant Nutrition, Maternity Hospital Macedonio Melloni, Milan, to separate protein concentrate from human milk.

**HUMAN MILK FORTIFIERS**

Human milk enriched with human milk protein, salts, and vitamins seems to meet the protein requirements of the VLBW infant, preserves the unique immunological and nutritional properties of human milk, and produces growth, metabolism, and plasma amino acid concentrations that should be considered the basis for feeding VLBW infants (11–14).

No human milk protein preparation is currently commercially available. Furthermore, it is not likely that one will become available in the future owing to the high cost of processing human milk and the difficulty in collecting adequate amounts of milk without the risk of transmitting viral infections. These problems have necessitated the development of fortifiers based on other sources of protein, primarily bovine milk proteins or protein hydrolysates, with or without the addition of amino acids (11,12,15–18). Although some differences in plasma amino acid concentrations have been observed, other metabolic responses and growth have generally been similar, regardless of the source of protein.

There are several different forms (liquid and powder) of cow’s milk based human milk fortifiers available (Table 1). Powdered fortifiers have the advantage of providing supplementation without displacing milk volume, thus allowing a larger intake of human milk. However, adding a powdered source of protein and minerals to preterm milk could result in excessive intake of one or more of these nutrients, depending on the nutrient content of the milk itself. Liquid supplementation randomly dilutes the higher levels of nutrients contained in some mothers’ milks. A disadvantage of a
<table>
<thead>
<tr>
<th>Packaging (Added to 100 ml human milk)</th>
<th>NENATAL-F and COW &amp; GATE (Nutricia)</th>
<th>EOPROTIN (Milupa)</th>
<th>FM-85 (Nestlé)</th>
<th>ENFAMIL HUMAN MILK FORTIFIER (Mead Johnson)</th>
<th>SIMILAC NATURAL CARE (Ross Laboratories)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powder 1.5 g packets (2 packets)</td>
<td>Per 100 kcal Added to 100 ml HM</td>
<td>Per 100 kcal Added to 100 ml HM</td>
<td>Per 100 kcal Added to 100 ml HM</td>
<td>Per 100 kcal Added to 100 ml HM</td>
<td>Per 100 kcal Per 100 Mixed</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>100</td>
<td>10</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>7.0</td>
<td>0.7</td>
<td>5.4</td>
<td>0.6</td>
<td>5.0</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>20</td>
<td>2</td>
<td>18.8</td>
<td>2.1</td>
<td>20.1</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>0</td>
<td>0</td>
<td>0.4</td>
<td>0.04</td>
<td>0.1</td>
</tr>
<tr>
<td>Minerals</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Vitamins</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
</tbody>
</table>

HM = human milk.
liquid supplement is that it contributes to the total volume of the intake, thus decreasing the amount of human milk ingested.

**ANALYSIS OF HUMAN MILK BEFORE FORTIFICATION**

In many neonatal units, human milk is routinely enriched in a fixed proportion with commercial fortifiers containing protein, carbohydrates, and electrolytes. Because of the large variation in human milk concentrations of protein and fat—particularly in the mother's own milk but also in banked milk—there is an obvious risk of under- or overnutrition of the vulnerable VLBW infant (19). Unfortunately, routine analysis of the macronutrient composition of the human milk given to VLBW infants is rarely performed before fortification, despite recommendations that it should be (10,20–22). Thus quality control of human milk used for VLBW infant feeding is mandatory, both to monitor the nutritional value of the milk supplied and to decide on the amount of fortifier to be added. To monitor the macronutrient composition of human milk, we use an infrared analyzer, as suggested by Michaelsen et al. (23,24).

The infrared technique has been used for the routine analysis of bovine milk for several years. The equipment has a higher precision and accuracy than direct methods and is very simple to use. The classical analysis of protein, fat, and carbohydrate content in human milk is time-consuming and requires three different analytical approaches. Infrared analysis overcomes this problem and allows almost real-time results to be obtained (with a milk sample of 6 ml, the measurement takes less than 1 minute). We evaluated the precision and accuracy of this method using a Milko-Scan 133 B infrared analyzer (Foss Electric, Denmark). A comparative study was performed on 62 samples of milk (33 human, 29 bovine). The results of the infrared analysis were compared with those of reference methods (25,26). No differences were found between infrared analysis and reference methods both for human and bovine milk, and the coefficients of variation (CV) were similar to those already reported by Michaelsen et al. (23). Figure 2, panel A, shows the linear regression for all 62 milk samples for protein determination. The equation of the curve was $y = 0.64 + 0.62x$ and the correlation coefficient ($R$) was 0.79. The equations and the correlation coefficients calculated for the linear regression were, respectively, $y = 0.08 + 0.86$ and $R = 0.90$ for human milk, and $y = 1.35 + 0.27x$ and $R = 0.55$ for bovine milk (see Fig. 2, panel B). The data obtained confirm that infrared analysis may be a valuable method for measuring macronutrients in milk, especially in human samples, since precision and accuracy seem to be better for human milk than for bovine milk. Moreover, this method offers the advantage of being quicker and simpler than reference methods, and for this reason it may be recommended for use in neonatal intensive care units.

Protein analysis of human milk before fortification offers the possibility of improving the nutritional management of VLBW infants—with a few simple calculations the protein concentration of human milk can be adjusted to achieve the desired daily protein intake (generally 3.5 g/kg).
FORTIFICATION OF HUMAN MILK

FIG. 2. Relation between protein content measured by infrared analysis and by Lowry reference method for all 62 samples (panel A) and for human (○) and bovine (●) milk samples considered separately (panel B). The correlation coefficient (R) for all 62 milk samples was 0.79 (panel A). The correlation coefficients calculated separately for human milk and bovine milk were 0.90 and 0.55, respectively (panel B).

VARIABLE FORTIFICATION REGIMEN

Because the nutrient needs of the VLBW infant change markedly as the infant grows and because the composition of human milk is variable, fortification of milk with predetermined, fixed amounts of nutrients is apt to result in a mismatch between nutrient needs and nutrient intakes during at least part and probably most of an infant's rapid growth period. To increase the likelihood of obtaining a good match between
intake and requirement, a variable fortification regimen has been proposed that uses the metabolic response of the infant (serum urea concentration) to guide the level of fortification (27).

Using this regimen in an initial cautious study, we showed (27) that the new regimen did lead to higher nutrient intakes, and these in turn led to a somewhat higher rate of growth. An experimental bovine milk protein–based fortifier (BMF) prepared from ultrafiltrated bovine whey protein concentrate (casein-to-whey-protein ratio = 40/60) was used either in the new fashion, with amounts determined by serum urea monitoring (regimen VAR), or in the conventional fixed proportion (regimen FIX). Using the fixed proportion, we also compared the new fortifier with a fortifier based on human milk protein (regimen HMP). Twelve infants were studied on each of the three regimens.

At study entry, fortification in regimen VAR was the same as in regimen FIX; that is, 3.5 g of BMF were added to each 100 ml of breast milk (fortification level 0). In regimen VAR, fortification was subsequently adjusted on the basis of twice-weekly determinations of corrected serum urea nitrogen (SUN): SUN × 0.5/SCr, where 0.5 is the "normal" serum creatinine concentration and SCr is serum creatinine concentration determined at the same time as serum urea nitrogen.

Adjustment of the fortification level after each determination of corrected serum urea nitrogen was performed as shown in Table 2. Fortification level was not changed from the standard 3.5 g per 100 ml of milk when corrected serum urea nitrogen was between 9.1 and 12.0 mg/dl (fortification level 0); fortification level was increased by one level (+0.6 g) if the corrected urea nitrogen was less than 9 mg/dl, and decreased by one level (−0.6 g) if it was more than 12 mg/dl. The fortification level was not changed by more than one level at a time. Levels −3 and +3 were the limits of adjustment (see Table 2).

As a result of this fortification schedule, fortification levels greater than level 0 were used most of the time in the regimen VAR. During study weeks 1 and 2, fortification levels of +1 and +2 were used with few exceptions, and mean fortification levels were +1.54 and +1.79, respectively. During study week 3, fortification was lower, with a mean value of +0.86 (Table 3).

As expected, fortification with the VAR regimen led to a higher energy and protein intake, mainly in the first 2 weeks of the study, with the difference for protein

<table>
<thead>
<tr>
<th>TABLE 2. Adjustment of fortification</th>
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<tbody>
<tr>
<td>Fortification level</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>+3</td>
</tr>
<tr>
<td>+2</td>
</tr>
<tr>
<td>+1</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>−1</td>
</tr>
<tr>
<td>−2</td>
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<tr>
<td>−3</td>
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CSUN = corrected serum urea nitrogen.
intake reaching statistical difference \((p < 0.01)\) during week 2 (Table 4). Weight gain, whether expressed as g/d or g/kg·d, was lowest with regimen HMP (27.8 g/d or 17.2 g/kg·d), higher with regimen FIX (30.0 g/d or 18.3 g/kg·d), and highest with regimen VAR (32.3 g/d or 18.8 g/kg·d). Differences in gains in length and head circumference were small and not statistically significant. The difference in weight gain among the feeding groups resulted in earlier discharge of infants in the VAR group. Since a body weight of 2,200 g is required in our department before discharge of VLBW infants, a difference in weight gain of 4.5 g/d between HMP and VAR groups led to a 4.5-day reduction in hospital stay in the infants in the VAR group; the difference between FIX and VAR groups resulted in a 2-day reduction in hospital stay in the VAR group. Plasma concentrations of several amino acids were higher in the VAR group than in the FIX group, but none, including threonine, was outside the range reported by other investigators in infants receiving fortified breast milk (28–30). Thus, it appears that in VLBW infants protein fortification of human milk beyond the standard fixed level is metabolically safe.

**CONCLUSIONS**

The results of our study and data from published reports strongly support the use of fortified human milk in VLBW infant feeding. Considering all the clinical and neurodevelopmental implications of the nutritional management of these infants, we

<table>
<thead>
<tr>
<th>Week of study</th>
<th>Mean fortification level</th>
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<tbody>
<tr>
<td>Week 1</td>
<td>+ 1.54</td>
</tr>
<tr>
<td>Week 2</td>
<td>+ 1.79</td>
</tr>
<tr>
<td>Week 3</td>
<td>+ 0.86</td>
</tr>
</tbody>
</table>

**TABLE 4. Intakes of energy and protein**

<table>
<thead>
<tr>
<th>Intake of energy (kcal/kg·d)</th>
<th>HMP</th>
<th>FIX</th>
<th>VAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>118 (6)</td>
<td>116 (9)</td>
<td>125 (3)</td>
</tr>
<tr>
<td>Week 2</td>
<td>121 (7)</td>
<td>119 (7)</td>
<td>125 (7)</td>
</tr>
<tr>
<td>Week 3</td>
<td>119 (6)</td>
<td>117 (7)</td>
<td>120 (7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intake of protein (g/kg·d)</th>
<th>HMP</th>
<th>FIX</th>
<th>VAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>3.50 (0.26)</td>
<td>3.35 (0.46)</td>
<td>3.69 (0.40)</td>
</tr>
<tr>
<td>Week 2</td>
<td>3.67 (0.29)</td>
<td>3.45 (0.34)*</td>
<td>4.00 (0.46)*</td>
</tr>
<tr>
<td>Week 3</td>
<td>3.55 (0.27)</td>
<td>3.44 (0.42)</td>
<td>3.73 (0.28)</td>
</tr>
</tbody>
</table>

Mean (SD).  
* \(p < 0.01\).
make the following practical suggestions:

- Human milk may confer nutritional and nonnutritional advantages to VLBW infants, including protection against infections, enhanced intestinal maturation, and improved long-term developmental outcome.
- Human milk alone cannot meet the considerable nutrient needs of the VLBW infant. Thus, human milk fed to VLBW infants must be fortified with protein, minerals, and vitamins.
- Human milk protein should be considered the gold standard for human milk fortification.
- In view of the practical problems of preparing and using human milk protein for fortifying human milk, mother's own milk (when available) or banked milk fortified with protein of nonhuman origin should constitute the basis for feeding VLBW infants.
- To improve the nutritional management of VLBW infants fed human milk, an individualized feeding system should be used, based on infrared analyses of human milk before fortification.
- The simple addition of a fortifier to human milk in fixed proportion, as is the current practice, is not entirely satisfactory because it often leads to inadequate nutrient intakes.
- Individual differences among VLBW infants call for precise interindividual and intraindividual adjustments of protein intake during the stay in the nursery. This means a variable protein intake based on the metabolic responses of each premature infant.
- When a variable fortification regimen is used in feeding VLBW infants, metabolic monitoring of the protein intake is mandatory.
- Serum urea nitrogen responds promptly to changes in protein intake and is proportional to protein intake, so it could be considered the most suitable metabolic indicator of protein adequacy.
- Different strategies of variable fortification should probably be applied to different categories of VLBW infants.

REFERENCES


DISCUSSION

Prof. Koletzko: In your experience with measuring human milk composition with the infrared system, do you find it helpful to preferentially select milks with a high lipid content and energy content, to provide an increased energy intake?

Prof. Moro: When we evaluate milk by infrared analysis, we determine the whole macronutrient composition. This means that we know the protein content, the fat content, and the carbohydrate content of the milk. So we are able to separate milks of different energy densities and use them appropriately. Sometimes it is not even necessary to add a fortification; for example, milk from mothers who have given birth preterm may be quite rich in protein—up to 2 g/100 ml, and in fat also.

Prof. Koletzko: My second question relates to the vitamin content of human milk fortifiers. The available fortifiers contain different amounts of vitamins. Has there been any evaluation of the potential benefit of vitamin supplementation of human milk fortifiers?

Prof. Moro: I think all the vitamin preparations are suitable for VLBW infants. In our unit we seldom use artificial fortifiers. We routinely use human milk protein fortifiers and we add vitamins and minerals separately.

Prof. Cooper: Could you explain why the group that was fortified with human milk protein had a slightly lower weight gain.

Prof. Moro: The mean growth rate was numerically somewhat lower, but the difference was not significant. When you use human milk protein for fortification, a proportion of the measured protein is immunoglobulin. The immunologic components have obvious advantages but are not absorbed. So you need to exclude this component from the calculations of growth rate.

Prof. Cooper: If you could measure the actual amount of protein given with infrared, why didn’t you use serum urea nitrogen as your indicator to evaluate how much fortifier to add?

Prof. Moro: Infrared analysis gives you only the protein content of the milk, not the metabolic response of the baby. If you want to know whether the protein intake you are giving is well tolerated, you need a metabolic index. We decided on serum urea nitrogen, because it was most responsive to variations in the protein intake.

Dr. Walker: In the process of preparing your fortified milk, you put it through several stages that would have considerably reduced its protective value—that is, you freeze dried it and you put it through two pasteurization cycles. Have you looked at the fecal flora in the infants, and is there any difference in necrotizing enterocolitis incidence compared with infants fed their own mothers’ raw milk?

Prof. Moro: We generally use fresh breast milk from the infant’s own mother as the basic feed. The human milk fortification that we add is only a supplement to the protein intake. Thus the fresh maternal milk can operate in the usual way to defend the baby from necrotizing enterocolitis. The pasteurization that is performed during the separation of the protein will result in the loss of some nutritional properties, such as lipase activity, but there is plenty of evidence that at least some of the immunologic properties are retained.

Prof. Heird: I am uncertain why the fortifiers contain an energy source. In your analysis, did you really find human milk that had a sufficiently low energy content to require the addition of both protein and energy?

Prof. Moro: The problem is to give the correct protein energy ratio. If you decide to increase the protein intake above, say, 4 g/kg·d, you will have to enrich the milk with some other source of energy.
Prof. Heird: How often does human milk contain less than, say, 67 kcal/dl?

Prof. Moro: Generally, preterm milk contains about 70 kcal/dl in the first weeks.

Prof. Endres: How often do you perform the infrared analyses? And who does the work?

Prof. Moro: Nurses do the analyses at the start of each day in the department. Analyses are done for each baby, and feed is prepared for 24 hours.

Dr. Rigo: When you use human milk fortifiers, you increase the osmolality of the milk. When we use fortifiers, the increase is about 100 mOsm/kg H$_2$O. But because of the dextrin content of some human milk fortifiers and the amylase activity of human milk, the increase could be greater. What do you feel about feeding preterm infants on milk with osmolality reaching, say, 400 mOsm/kg H$_2$O?

Prof. Moro: We measured the osmolality of the feeds at the beginning of our clinical studies. With human milk protein fortifier, it never exceeded 350 mOsm/kg H$_2$O.

Dr. Filho: In Brazil we are very aware of the problem of osmolality. The only human milk fortification product available causes a large increase in osmolarity. Thus unsupplemented milk from our milk bank has an osmolality of about 270 mOsm/kg, but when we add the fortifier, it increases to 396 mOsm H$_2$O. We are very concerned that this may cause problems.

Prof. Moro: The value of 350 mOsm H$_2$O refers to human milk fortified with human milk protein, not with a commercially available fortifier. Commercially available fortifiers are enriched with protein, carbohydrates, and minerals, so you must be very careful about their composition. When you add them to human milk you must check the osmolality. We give minerals and vitamins separately.

Prof. De Vonderweid: There is a big difference if you add the fortifier to banked milk that has been pasteurized and to fresh human milk. If you add the fortifier to fresh human milk, the enzyme activity is much higher and you may reach osmolalities of 600 to 800 mOsm/kg H$_2$O. This is not the case when you use banked pasteurized human milk.

Prof. Haschke: You showed us a study where you compared a variable and a fixed fortification regimen. You said that it is absolutely necessary to measure the protein content in human milk when you fortify it. Let’s go back to practical issues. Most hospitals do not have these facilities, so my question concerns safety. Are there any safety studies that have raised concern over the fixed model as compared with the flexible model you are using?

Prof. Moro: If you can measure the macronutrient composition of human milk, you can look at the metabolic responses of the baby to evaluate whether the protein intake you are giving is suitable or not. If you measure serum urea nitrogen twice a week, you can see whether the baby is tolerating the protein intake from a metabolic point of view. You can’t then decide whether to increase or decrease the protein intake without knowing exactly how much you are giving.

Prof. Haschke: This is exactly the point I was making. Did you see any problem with the fixed supplementation regimen in terms of the metabolic outcome?

Prof. Moro: No, the metabolic responses were practically the same.

Prof. Haschke: The efficacy of the fortification did not seem very impressive. The weight gain was almost the same as in the unsupplemented babies.

Prof. Moro: Well, the number of babies studied was small, only 12 in each group. In spite of this, the weight difference between the variable group and the group fed with human milk protein fortification was 4.5 g/day. This brought to a reduction in hospital stay of about 4 days. I think that is important.
Prof. Haschke: But you showed that the weight gain in g/kg body weight/day was the same.

Prof. Moro: But if you look at the weight increment per day, the babies fed with variable fortification were able to reach discharge weight, which is 2,200 g in our department, 4 days before the group fed with human milk protein fortifier and 2 days before the group fed with fixed fortifier.

Prof. Lucas: In response to Prof. Haschke’s question about safety, when we did our own fortification trial, which we published in the *American Journal of Clinical Nutrition* [1], we did not do monitoring, and we used a fixed fortification schedule. Our previous analytic data based on breast milk suggested that fortification would take a certain number of infants into the particularly high-protein-intake range in the early weeks. We decided to accept that but to monitor plasma amino acids. Though I accept that it is difficult to define hyperaminoacidemia in the newborn preterm infant, we did not identify any cases with our policy of fortifying human milk with 0.7 g of protein per 100 ml right from the start.

Prof. Pohlandt: If you measure serum urea several times a week, which I think is reasonable because it reflects the individual metabolic situation in the baby, then I doubt whether you also have to do the infrared measurement. Have you seen any benefit from doing both? I think that a better basis for increasing the amount of fortifier would be twice weekly urea measurements rather than the average protein concentration of the milk.

Prof. Moro: You can use the metabolic response of the baby to evaluate whether the protein intake is appropriate, but you don’t know how much protein the baby is receiving.

Prof. Pohlandt: But all you need to do is to increase the protein intake stepwise until you reach the appropriate blood urea.

Prof. Moro: I agree, but you will never know how much protein the baby is receiving.

Prof. Pohlandt: I’m not interested in that!

Prof. Ziegler: I think there is some confusion about what Prof. Moro actually did. He did a study comparing fixed to variable fortification, but in that study he did not use the infrared analyzer. I think Prof. Pohlandt assumed that he did both, but he did not. He is now recommending that infrared analysis should be used routinely, but that was not done in that study, so he cannot say whether it would have made any difference to the results.

Prof. Moro: That is correct.

Dr. Sedaghatian: Has anybody determined the amount of protein needed at different gestational ages in premature babies? Surely we should be recommending an appropriate intake according to gestational age rather than a fixed amount of protein from 24 to 36 weeks gestation, which I can’t imagine is really physiological. Doesn’t maternal milk protein content reflect the premature infant’s requirements?

Prof. Moro: Papers from Atkinson and other groups [2,3] evaluated the composition of human milk from mothers delivering at different gestational ages, and it was clearly shown that there was a correlation between gestational age and the macronutrient composition of the milk. The protein content of preterm milk is at least 20% higher than that of term milk. This difference lasts for 3 to 4 weeks.

Prof. Lucas: The high protein of preterm milk is a volume artifact. That has been shown very clearly. The more milk the mother produces, the lower the protein con-
tent; it’s as if there was a fixed protein synthetic rate. This is not an evolutionary phenomenon in preterm milk. It is only that mothers of preterm infants produce very little milk, so it has a high protein content. You would do better to relate the protein level to the volume of milk produced rather than to gestation.

Prof. Fazzolari: Could you describe the amino acid profile you find on your different dietary regimens. Did you find any difference in amino acids that can affect the central nervous system—I mean tryptophan, tyrosine, phenylalanine, and so on?

Prof. Moro: In the variable group the values of practically all the amino acids were higher than in the other groups. In spite of that, all the levels remained in the normal range.

Prof. Heird: What is the cost of the infrared system, and how much does that add to the daily cost of providing milk for a baby.

Prof. Moro: The equipment costs about $30,000 in US currency. Each sample costs about $13.

Prof. Heird: The whole issue of cost and effectiveness is going to have to be addressed. I can see the advantages of such a system for research purposes, but I wonder if a better use of the resources might not be to do a thorough evaluation of the effects of a fixed supplementation program.

Prof. Nowak: Could you tell us about viral safety of your milk fortifier? I believe that in certain countries there has been controversy about the use of banked milk, because of the risk of cytomegalovirus transmission.

Prof. Moro: We performed Holder pasteurization that is heating the milk at 63°C for 30 minutes. With that schedule you don’t have any risk of viral contamination. All viruses are inactivated.

Dr. Schanler: Short, high-temperature processing kills viruses, and specifically kills cell-associated CMV. I think such a procedure is virally safe.

Prof. Haschke: Are you sure that it is safe in terms of hepatitis C?

Dr. Schanler: We haven’t tested that. When we did the studies we did not know about it.

Prof. Polberger: The question about pasteurization and the killing of viruses is a tricky one. Holder pasteurization, 63°C for 30 minutes, seems to be the most valid method at present. There has been some concern about other methods. I also would like to mention the issue of cytomegalovirus infection. There have been reports that you should always freeze mother’s own milk before supplying her own infant because of the risk of CMV. I don’t know if everybody is doing that. It is stated that you should not use fresh milk at all in preterm infants, even if it is from the infant’s own mother.

REFERENCES

