Calcium, Phosphorus, Magnesium, and Vitamin D Requirements in Premature Infants

Bernard L. Salle, *Jacques Senterre, and Guy Putet

Department of Neonatology, Edouard Herriot Hospital, Place d'Arsonval 69437 Lyon, France; and *Department of Pediatrics, State University of Liège, Liège, Belgium

Ninety-nine percent of the calcium and most of the phosphorus in the body is in the skeleton; these elements and magnesium are also constituents of the intracellular and extracellular spaces. Metabolic homeostasis of calcium, phosphorus, and magnesium and mineralization of the skeleton are complex functions that require an adequate supply of minerals, the development of the intestinal absorption process, and the metabolism of vitamin D.

Premature infants and particularly very low birthweight infants show disturbances of calcium, phosphorus, and magnesium metabolism much earlier and more frequently than older infants because of their fast rate of growth and the immaturity of their physiologic systems. The amount of calcium, phosphorus, and magnesium that can be accumulated by a preterm infant is not yet certain. In the fetus, accumulation of calcium, phosphorus, and magnesium during the last trimester of pregnancy is about 20 g, 10 g, and 0.4 g, respectively, or 120 to 130 mg/kg.d, 65 to 70 mg/kg.d, and 3 to 4 mg/kg.d, respectively (1,2).

This chapter presents the results of balance studies of minerals and discusses the influence of some factors on the absorption and retention of minerals in preterm infants fed human milk or various formulas. Bone mineral content in low birthweight infants of less than 1500 g or with gestational age less than 32 weeks, fed either human milk or formula, is also reported. This allows us to make reasonable recommendations for the required intakes of minerals in low birthweight infants.

VITAMIN D REQUIREMENTS

The vitamin D requirements of the premature infant are controversial and have been reported to vary between 400 and 5000 IU/d (3–8). This wide range of variation is largely the result of studying populations with very different vitamin D status at birth. In premature infants with cord blood 25-hydroxyvitamin D greater than 20
ng/ml, as is frequently the case in the United States, administration of 400 IU/d of vitamin D appears to be sufficient to maintain adequate plasma concentrations of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D (8). When cord blood 25-hydroxyvitamin D falls to between 10 and 20 ng/ml, Hillman and co-workers (5) have shown that vitamin D requirements are met by a daily dose of 800 IU. In premature infants with cord blood 25-hydroxyvitamin D less than 10 ng/ml, as often happens in some part of Europe, 1000 to 1200 IU of vitamin D per day are necessary during the first few weeks of life (4).

Some investigators have suggested that the vitamin D requirements of premature infants are greater than those of term neonates because of an immaturity of the hepatic or renal conversion of vitamin D to 25-hydroxyvitamin D and 1,25(OH)\(_2\)D. This has not been confirmed in recent studies (4,6). The increased needs of premature infants are probably partly due to malabsorption of vitamin D resulting from a low secretion of bile acids. The presence of a large quantity of polyunsaturated fatty acids in the diet might unfavorably influence vitamin D absorption, although medium-chain fatty acids may have an opposite effect (4).

Recommendations for increased vitamin D intake stem from the belief that rickets or osteopenia of prematurity can be treated or prevented by giving more than the recommended 400 IU/d (9,10). It can be argued that the relatively large requirements for calcium and phosphorus in the rapidly growing preterm infant, associated with poor intestinal absorption of calcium, necessitates a higher vitamin D intake. Nevertheless the etiology of rickets of prematurity is multifactorial and the most important factors are likely to be a deficiency of calcium and phosphorus rather than of vitamin D, as we shall show further (9).

MINERAL BALANCES

We carried out 3-day balance studies in healthy preterm infants in the second or the third week of life. All infants weighed less than 1300 g and were less than 31 weeks gestational age. Each infant received only one type of feeding—human milk or low birthweight formula—and one vitamin D dosage from birth to the end of the study period. Infants were enrolled in the study if they had no pathologic conditions except for apneic spells (some infants received xanthine treatment) (11-13).

The infants were kept in incubators throughout the study under conditions of thermal neutrality. Feeding by nasogastric tube was well tolerated, and the infants grew at a steady rate for at least 1 week. A shaped metabolic bed, specially designed to fit inside an incubator, allowed the separate collection of urine and feces (11).

Two different balance techniques can be used to assess the effect of different milks in premature infants: (a) infants are given different formulas in succession and act as their own controls; or (b) infants receive one milk only and are compared with aged-matched controls receiving a different formula. We prefer the latter method in premature infants because of the relatively rapid maturation of several physiologic intestinal functions with age. Furthermore if various formulas are tested at different
ages in the same infant, the physiologic changes that occur are difficult to discriminate from those attributable to the formula itself.

**BONE MINERAL CONTENT**

In order to assess bone mineral content and bone mineral density in premature babies, dual energy x-ray absorptiometry was used to make longitudinal measurements in the lumbar spine during the first year of life. This technique is a new, non-invasive, accurate, and precise method for measuring small amounts of mineral (14).

Working with dual energy x-ray as the radiation source, bone mineral content and density were measured on a Hologic 1000 densitometer (Hologic Inc., Waltham, MA, USA). A special program for small bone measurements was used to scan the lumbar spine. The scanning time for a lumbar spine in babies is short (2 to 3 minutes). All five vertebrae were included in the scan. The precision was assessed by measuring the lumbar spine in 10 newborns two to three times with repositioning. The mean coefficient of variation was 2.4% and 1.55% for bone mineral content and bone mineral density, respectively (14,15).

**CALCIUM REQUIREMENTS**

Calcium needs could be defined by comparison with the fetal accumulation in utero as the premature baby can be considered as a fetus ex utero.

There are two processes of calcium absorption in the intestine, one involving non-saturable passive absorption, the other being saturable and involving active transport under the influence of vitamin D and 1,25(OH)_{2}D (16). If vitamin D is lacking, too little calcium is absorbed (30% of the supply), but administration of vitamin D or 1,25(OH)_{2}D significantly improves intestinal absorption.

**Human Milk** (Table 1)

Metabolic balance studies showed that the percentage absorbed depends on dietary intake of vitamin D. Mean calcium absorption was 70% when vitamin D was given. Calcium retention, however, unlike absorption, depends on phosphorus intake; calcium retention is only 25 to 28 mg/kg.d in premature babies fed on human milk alone without supplementation. This is because mother’s milk provides a limited supply of phosphorus (15 to 16 mg/dl). Preterm infants respond to a low phosphorus intake in exactly the same way as adults, with hypophosphaturia, hypophosphatemia, and hypercalciuria (Table 1). The deficiency of phosphorus is exacerbated if human milk is enriched with calcium and/or protein (12,13).

Table 1 shows that when human milk is supplemented with phosphorus, calcium retention improves to 35 mg/kg.d, though this is nevertheless far below calcium retention in utero. The effect of phosphorus and calcium supplementation of human milk
TABLE 1. Calcium, phosphorus, and fat balance in premature infants (BW ≤1300 g) fed human milk (HM) with or without supplementation or low birthweight (LBW) formula; all premature babies received 1200 IU of vitamin D

<table>
<thead>
<tr>
<th></th>
<th>HM 10</th>
<th>HM + P 10</th>
<th>HM + P + Ca 8</th>
<th>HM + HM fortifier 7</th>
<th>LBW formula 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca intake (mg/kg.d)</td>
<td>58 ± 11</td>
<td>53 ± 8</td>
<td>90 ± 1.1</td>
<td>101 ± 19*</td>
<td>118 ± 10*</td>
</tr>
<tr>
<td>Ca feces (mg/kg.d)</td>
<td>17 ± 10</td>
<td>14 ± 7*</td>
<td>24 ± 13*</td>
<td>35 ± 11*</td>
<td>42 ± 18*</td>
</tr>
<tr>
<td>Ca urine (mg/kg.d)</td>
<td>16 ± 8</td>
<td>3 ± 1*</td>
<td>3 ± 2*</td>
<td>2 ± 1*</td>
<td>7.3 ± 5</td>
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<tr>
<td>Ca retention (mg/kg.d)</td>
<td>25 ± 12</td>
<td>35 ± 7*</td>
<td>63 ± 12*</td>
<td>65 ± 14*</td>
<td>68 ± 11*</td>
</tr>
<tr>
<td>Ca absorption (%)</td>
<td>71 ± 14</td>
<td>74 ± 13*</td>
<td>73 ± 13</td>
<td>66 ± 7.3</td>
<td>65 ± 14</td>
</tr>
<tr>
<td>P intake (mg/kg.d)</td>
<td>24 ± 6</td>
<td>40 ± 11*</td>
<td>62 ± 5*</td>
<td>78 ± 13*</td>
<td>72 ± 3*</td>
</tr>
<tr>
<td>P feces (mg/kg.d)</td>
<td>2 ± 1</td>
<td>3 ± 1</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>6 ± 2</td>
</tr>
<tr>
<td>P urine (mg/kg.d)</td>
<td>Traces</td>
<td>12 ± 2</td>
<td>5 ± 4*</td>
<td>12 ± 8*</td>
<td>6 ± 6</td>
</tr>
<tr>
<td>P retention (mg/kg.d)</td>
<td>21 ± 5</td>
<td>34 ± 5*</td>
<td>53 ± 4*</td>
<td>62 ± 9*</td>
<td>60 ± 6*</td>
</tr>
<tr>
<td>P absorption (%)</td>
<td>92 ± 4</td>
<td>91 ± 5</td>
<td>93 ± 2</td>
<td>94 ± 22</td>
<td>92 ± 21</td>
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<tr>
<td>Fat intake (g/kg.d)</td>
<td>6.2 ± 0.9</td>
<td>5.9 ± 0.8</td>
<td>5.70 ± 1.1</td>
<td>4.17 ± 1</td>
<td>6.81 ± 2.2</td>
</tr>
<tr>
<td>Fat net absorption (%)</td>
<td>79 ± 10</td>
<td>80 ± 10</td>
<td>71 ± 23</td>
<td>79 ± 6</td>
<td>87.5 ± 3</td>
</tr>
</tbody>
</table>

* Values significantly different (p ≤ 0.01) compared with HM group.

P, phosphorus; Ca, calcium.

is also illustrated in Table 1 (human milk + phosphorus + calcium, or human milk + European human milk fortifier). Calcium retention increased steadily to about 60 mg/kg.d in both groups when human milk was supplemented with calcium and phosphorus (17).

**Low Birthweight Formula (Table 1)**

With formula adapted for feeding premature infants, absorption ranges from 40% to 60% depending on the amount of calcium provided and the quality of calcium salts added. Utilization of medium-chain triglycerides (20–30% of total fat) improves fat absorption and consequently calcium absorption. Calcium retention is therefore between 60 and 90 mg/kg.d.

**Net Calcium Absorption in Preterm Infants Fed Human Milk or Formula**

Figure 1 shows the correlation between net calcium absorption and calcium intake in two groups of infants supplemented with vitamin D and fed low birthweight formula or human milk with or without calcium supplementation. The slopes of the two relationships do not differ significantly from one another (p > 0.05) (cf. legend). Thus overall net calcium absorption in vitamin D–supplemented infants fed low birthweight formula was as efficient as that of the infants fed human milk supplemented with
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vitamin D. However, the intercepts of the two relationships shown in Fig. 1 were markedly different, the one in infants fed human milk being essentially zero (−2 ± 10 mg/kg.d) as expected, while the other infants given low birthweight formula being significantly negative (−32 ± 14 mg/kg.d). The latter can be explained if the actual amount of calcium available for absorption was less than the amount of calcium fed to the infants. Such a situation might arise if some of the ingested calcium precipitated in the intestine and was therefore neither solubilized nor absorbed. We showed that fecal calcium was 2.5 times higher relative to fecal fat in the group fed low birthweight formula than in the group fed human milk (with or without supplementation with calcium), even though the calcium intakes of the two groups were similar (16). This suggests that the absolute amount of calcium absorbed by the infants fed low birthweight formula was indeed less, while their fractional net calcium absorption (Fig. 1) was comparable (16).

In other words, the apparent net calcium absorption of infants fed low birthweight formula was lower than that of infants fed human milk (Table 1). In our metabolic studies, the actual amount of calcium provided by feeding was experimentally measured in every case and not calculated. Thus the amount of calcium ingested is a reliable value. Yet fecal calcium output of the infants fed the low birthweight formula was greater and can only reflect an overall lower bioavailability of the calcium provided. Lower availability could result if some fraction of the calcium was insoluble or precipitated in the gut and was thus unavailable for absorption. Because of the apparent unavailability of some of the calcium in the low birthweight formula, a simple increase in calcium content in a formula may not necessarily lead to increased calcium absorption.

![Graph showing relationship between calcium intake and net calcium absorption](image)

**FIG. 1.** Relationship between calcium intake and net calcium absorption in premature infants receiving vitamin D supplementation fed either banked human milk ($y = -2 \pm 10 + 0.76 \pm 0.08 \times n = 44$, $r = 0.81$, $p < 0.01$) or low birthweight formula ($y = 32 \pm 14 + 0.88 \pm 0.12 \times n = 83$, $r = 0.63$, $p < 0.01$). $y$, net calcium absorption (mg/kg.d); $x$, calcium intake (mg/kg.d).
PHOSPHORUS REQUIREMENTS (Table 1)

Phosphorus is not only an important skeletal constituent but is also an important intracellular anion. In bone, the calcium/phosphorus ratio is constant from the fetus to the adult (2.2:1). Phosphorus is correlated to protein content: the ratio of total nitrogen to phosphorus is 17:1. Phosphorus accumulation in the premature infant is thus proportional to calcium and nitrogen retention, and follows the formula:

\[ P \text{ retained} = \frac{\text{Ca retained}}{2.2} + \frac{\text{N retained}}{17} \]

We have shown that phosphorus retention calculated from the balance is correlated to calculated retention when retained calcium and nitrogen are known (12).

During fetal life, 75% of phosphorus, i.e., 55 mg/kg.d, is retained in bone and 18 mg/kg.d is retained in tissues. Absorption in the intestine is achieved through two processes, as for calcium—one is nonsaturable (passive), and the other is active, coupled to sodium. In premature infants fed mother’s milk, absorption always exceeds 90%. In premature babies fed artificially with a special formula, absorption ranges from 80% to 95%, but does not depend in any way on calcium absorption or circulating vitamin D levels.

Special milk formulas for premature infants always provide much more phosphorus than needed, and absorption too is greater. Phosphaturia amounts to 10 to 20 mg/kg.d. When there is a deficit in calcium absorption, phosphorus is absorbed in excess, causing hyperphosphatemia and hyperphosphaturia, with hypocalcemia. The calcium/phosphorus ratio in a formula should be nearer 2 than 1, with an ideal ratio of 1.7:1.8.

MAGNESIUM REQUIREMENTS

There is little information on the absorption and retention of magnesium in preterm infants. Factors that affect magnesium absorption include endogenous fecal losses, intake of calcium and magnesium, vitamin D status, fat intake, gestation, and postnatal age.

Magnesium is absorbed by simple diffusion. The amount of magnesium absorbed is about 35% to 50% of the intake in adults. In low birthweight infants, increased calcium retention has no effect on magnesium retention (9). Widdowson (1) demonstrated that phosphate supplements to human milk improved magnesium absorption and retention.

The results of magnesium and fat balance studies in low birthweight infants fed human milk or low birthweight formula at two postnatal ages (21 to 27 days and 41 to 45 days) are shown in Table 2. With a low birthweight formula magnesium absorption was 50% and magnesium retention was about 3 mg/kg.d, 90% of fat being absorbed. There was no difference in magnesium retention at the two postnatal ages. With human milk, the improvement of magnesium absorption and retention was due
TABLE 2. Magnesium and fat balance in premature babies fed human milk (HM) with or low birthweight (LBW) formula at two different postnatal ages: 21–27 days and 44–45 days; all premature babies received 1200 IU of vitamin D

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<tr>
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<th>Human milk</th>
<th>LBW formula</th>
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<tr>
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<td>n</td>
<td>6</td>
</tr>
<tr>
<td>Study I—age of study: 21–27 days</td>
<td></td>
<td></td>
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<tr>
<td>Mg intake (mg/kg.d)</td>
<td>4.8 ± 0.9</td>
<td>8.1 ± 0.5</td>
</tr>
<tr>
<td>Mg feces (mg/kg.d)</td>
<td>2.6 ± 0.5</td>
<td>4.3 ± 1.6</td>
</tr>
<tr>
<td>Mg urine (mg/kg.d)</td>
<td>0.4 ± 0.2</td>
<td>0.8 ± 0.6</td>
</tr>
<tr>
<td>Mg retention (mg/kg.d)</td>
<td>1.8 ± 1.0</td>
<td>3.0 ± 1.6*</td>
</tr>
<tr>
<td>Mg absorption (%)</td>
<td>46 ± 12</td>
<td>47 ± 20</td>
</tr>
<tr>
<td>Fat intake (g/kg.d)</td>
<td>5.30 ± 0.69</td>
<td>5.35 ± 0.23</td>
</tr>
<tr>
<td>Fat absorption (g/kg.d)</td>
<td>3.80 ± 0.54</td>
<td>4.63 ± 0.37</td>
</tr>
<tr>
<td>Fat absorption (%)</td>
<td>72 ± 6</td>
<td>87 ± 4*</td>
</tr>
<tr>
<td>Study II—age of study: 44–45 days</td>
<td></td>
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<tr>
<td>Mg intake (mg/kg.d)</td>
<td>4.9 ± 0.8</td>
<td>9.3 ± 2.1</td>
</tr>
<tr>
<td>Mg feces (mg/kg.d)</td>
<td>1.4 ± 0.4</td>
<td>4.6 ± 1.9</td>
</tr>
<tr>
<td>Mg urine (mg/kg.d)</td>
<td>1.0 ± 0.8</td>
<td>1.3 ± 1.0</td>
</tr>
<tr>
<td>Mg retention (mg/kg.d)</td>
<td>2.5 ± 0.9</td>
<td>3.4 ± 1.1</td>
</tr>
<tr>
<td>Mg absorption (%)</td>
<td>70 ± 10</td>
<td>52 ± 12</td>
</tr>
<tr>
<td>Fat intake (g/kg.d)</td>
<td>5.74 ± 0.70</td>
<td>5.56 ± 0.23</td>
</tr>
<tr>
<td>Fat absorption (g/kg.d)</td>
<td>5.23 ± 0.70</td>
<td>5.04 ± 0.15</td>
</tr>
<tr>
<td>Fat absorption (%)</td>
<td>91 ± 4</td>
<td>91 ± 3</td>
</tr>
</tbody>
</table>

* p < 0.05.

to improvement of fat absorption over time; fat absorption increased from 72% to 91% and subsequently magnesium absorption increased from 46% to 70% and retention from 1.8 to 2.5 mg/kg.d. Nevertheless, magnesium retention was lower with human milk than with low birthweight formula due to the low content of magnesium in human milk (1.5 to 2 mg/dl).

BONE MINERAL CONTENT

Twenty premature babies were studied over 1 year. The mean birthweight and SD was 1229 ± 30 g and the mean gestational age was 30 ± 0.25 weeks. Subjects were studied on days 41, 89, 184, and 365. All babies received 1200 IU of vitamin D per day during the first 3 months of life and then 800 IU per day. Figure 2 shows bone mineral content and density in premature babies versus full-term infants over the first year of life. The deficiencies in lumbar spine mineral content and density in premature infants decreased with postnatal age from 62% to 22% and from 30% to 13%, respectively. There was no significant difference in the values between premature babies fed their own mother's milk supplemented with phosphorus and calcium and premature babies fed low birthweight formula over 6 months (15).
Our latest results in 15 babies obtained at 2 years of age showed that the deficiencies in bone mineral content and density were still present and projection of these results suggest that catch-up of bone mineral content will occur at around 4 years of age.

PRACTICAL RECOMMENDATIONS

Premature infants and particularly very low birthweight infants suffer from bone hypomineralization, osteopenia, and rickets. In preterm newborns, dual energy X-ray absorptiometry of the lumbar spine shows that, in comparison with normal full-term infants, osteopenia is present over the first 2 years of life. The etiology as demonstrated by metabolic balance studies is an inadequate calcium absorption and calcium and phosphorus supply.
Premature infants fed human milk need phosphorus, calcium, and magnesium supplements. Ready-to-use additives are now on the market for enrichment of human milk in order to provide an adequate intake of these minerals and consequently a high retention.

Premature babies fed low birthweight formula should have a calcium supply of between 120 and 160 mg/kg.d (80 to 120 mg/100 kcal). The calcium/phosphorus ratio should be close to 2, due to a poor bioavailability of calcium salts in formula feeds and consequent poor calcium absorption. Retention never exceeds 80 to 90 mg/kg.d with formulas currently available on the European market.

Magnesium intake and retention is always sufficient in premature babies fed low birthweight formula.

Bone mineralization in premature babies is less than in full-term babies but nevertheless catch-up of bone mineral content will occur over the first 3 or 4 years of life.

CONCLUSION

Calcium and phosphorus retention in low birthweight infants is far from that observed in utero at the same gestational age. As demonstrated by measurement of bone mineral content in lumbar spine, osteopenia is common in premature babies. The neonatologist should keep in mind that calcium and phosphorus intake should be monitored when feeding premature babies, particularly those of very low birthweight. Dual energy absorptiometry is a new tool, non-invasive and precise, which facilitates following these infants’ bone mineral content.

REFERENCES


**DISCUSSION**

*Dr. Vonderweid:* We know that we can achieve calcium retentions of 60 to 70 mg per day in low birthweight infants by parenteral and enteral nutrition. We also know that these babies will be osteopenic for a long while, at least during their first 2 years. It appears that the osteopenia does no harm during this period. Do you think it is reasonable to try to increase the amount of calcium retained in the first month of life by giving more of it, or by giving more vitamin D?

*Dr. Salle:* The ESPGAN recommendations for calcium intake in European preterm babies are 100 to 140 mg/kg.d, which means a retention of around 70 to 80 mg/kg. The American Academy of Pediatrics recommends giving more, to achieve a retention of 100 to 140 mg/kg.d. The problem is that people involved with calcium metabolism in North America do not really believe that the addition of so much calcium to the diet results in increased retention. We have demonstrated that an increase in calcium intake results in increased fecal calcium excretion, not increased retention (personal data). In my opinion and the opinion of Jacques Senterre it is very difficult to exceed a calcium retention of 80 to 85 mg/kg.d in a premature baby.

Another point is that the bone of a preterm infant is not the same as the bone of a fetus. Fetal bone is very quiet, with no turnover and no osteoclast activity. A 1-month-old preterm baby has a very active bone with a high turnover. The need for calcium in this bone is probably not the same as in the fetus.

*Dr. Hernell:* Your formula-fed infants had greater fractional fat absorption, yet had more calcium in the stool. It used to be said that fat excretion correlated with calcium excretion because of the formation of calcium soaps. If you have improved fat absorption but increased fecal calcium, in what form is the calcium excreted?

*Dr. Salle:* Probably as calcium salts—chloride, phosphate, citrate, and carbonate. Phosphate salts should be avoided in formulas since they result in high calcium excretion. The best salts for absorption are chloride and carbonate.

*Dr. Singh:* Why do the infants on breast milk feeds, who are getting less calcium than infants on formula feeds, still lose more calcium in the urine?

*Dr. Salle:* This is due to deficient phosphorus intake. If phosphorus intake is too low, absorbed calcium cannot be utilized and is excreted in the urine. For every molecule of calcium deposited in bone you need a molecule of phosphorus. The same thing happens if you enrich human milk with protein without adding phosphorus. Hypercalciuria will occur
because increased protein turnover requires increased phosphorus utilization, so less is available for combination with calcium in bone. With low birthweight formulas the situation is completely different—calcium is not so well absorbed and there is plenty of phosphorus. The calcium/phosphorus ratio needs to be about 1.7 or 1.8 under these conditions, otherwise there will be considerable urinary phosphorus losses.

It is important to remember that the calcium/phosphorus composition of human milk is appropriate for the term baby, not the preterm one. The preterm baby needs more calcium than is provided in human milk. Fomon showed that retention in term babies is only around 20 mg/kg.d, while preterm babies need to retain around 80 to 100 mg/kg.d. More phosphorus is therefore needed, and because human milk is low in phosphorus it needs to be enriched.

Dr. Micheli: Is calcium retention a limiting factor for linear growth in preterm infants?

Dr. Salle: I cannot answer this from our data.

Dr. Fukagawa: Do you have any evidence of impaired bone matrix synthesis in preterm infants? In other words do they have osteoporosis?

Dr. Salle: We have performed many histomorphometric studies on bones of preterm infants. There is no osteoporosis, only osteomalacia.

Dr. Fukagawa: In old people it has been shown that lumbar bone mineral content does not necessarily reflect whole body bone density.

Dr. Salle: We have measured total body bone mineral content in 55 preterm babies from 28 weeks of gestation to term. The correlation with lumbar spine mineral content measured at the same time was 1.

Dr. Priolisi: You showed the association between nitrogen retention and phosphorus retention and you reminded us that during growth some of the phosphorus is preferentially directed toward soft tissues if not enough is provided in the intake. Should we be checking urinary phosphate excretion to monitor for possible phosphate depletion?

Dr. Salle: Yes, this is certainly worth doing. On a daily protein intake of 3 to 3.5 g/kg and a calcium intake of 100 to 120 mg/kg, urinary phosphate excretion should be about 10 to 20 mg/kg. If it is less than this you are probably not giving enough phosphorus.

Dr. Lucas: I am a little concerned about some of the comments that have been made about the long-term implications of metabolic bone disease. I don’t think it can be regarded as benign. We know for certain that there are longer-term consequences for growth, though we cannot yet extrapolate to the more distant future. We have recently obtained data, not yet published, showing that babies fed on human milk who are calcium and phosphorus depleted have an increase in their bone mineral content 5 years later compared with babies who were fed on a fortified formula, perhaps suggesting that they were programmed to be more frugal with calcium, having been depleted early on. This is hypothesis only. The important thing is that there are long-term differences that are in an unexpected direction.