What Are the Risks and Benefits to Increasing Dietary Bone Minerals and Vitamin D Intake in Infants and Small Children?

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Abstract

Bone minerals and vitamin D are crucial for infants and small children. Human milk has little vitamin D, and supplemental vitamin D must be given to all infants either via drops or as contained in infant formula or foods. The calcium and phosphorus in human milk are adequate for infants in the first six months of life, with supplemental minerals coming from weaning foods after six months. Long-term benefits to providing bone minerals at greater levels than in human milk have not been shown. There is no evidence to support high-dose bone mineral supplementation or high-dose vitamin D supplementation in infancy, and controlled trials are needed before these can be advocated.

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INTRODUCTION

Considerable discussion has occurred over the past several decades regarding the concept that osteoporosis originates in childhood and the related perspective that providing high dietary intakes of the bone minerals, calcium, and phosphorus as well as vitamin D may delay or prevent this disease in the elderly. However, although optimizing mineral intake during the adolescent growth spurt is a well-accepted nutritional goal, the mineral and vitamin D needs of infants and small children are less clear. Human milk has a relatively low content of calcium, phosphorus, and vitamin D. There is a complete lack of data demonstrating long-term benefits to early calcium or phosphorus supplementation of human milk–fed healthy infants. However, supplementation with 400 international units (IU) of vitamin D per day has been recommended (36). Although controlled trials to evaluate the lifelong effects of infant supplementation with minerals and vitamin D are not available, it is reasonable to consider the available evidence and the benefits and potential risks to different levels of the bone minerals and vitamin D in the diets of infants and small children.

In this review, we consider normal and abnormal patterns of bone mineralization in infants and the sources of calcium, phosphorus, and vitamin D in infants and small children. We further consider long-term effects of potential interventions related to these vitamins and minerals. New guidelines [Dietary Reference Intakes (DRIs)] for calcium and vitamin D intake for the United States and Canada were released recently by the National Academy of Sciences, Institute of Medicine (IOM) (29). As the DRI process uses a life-stage approach, considering small children to be those 12 to 48 months of age, we discuss children from 0 to 48 months in this review (**Table 1**).

DRIs: Dietary Reference Intakes

IOM: Institute of Medicine

FETAL BONE MINERALIZATION

In identifying normal patterns of bone mineral accretion, it is worthwhile to start by defining terms and considering in utero physiology of bone mineral. The commonly used term for the accretion of bone mineral to the skeleton is "bone mineralization." However, this term has been challenged (30) based on the idea that bone mineral accretion is dependent on both bone growth and the addition of mineral to the bone, whereas "mineralization" may be seen as the "accumulation of mineral by the osteoid." In practical terms, however, this is not a useful distinction for most clinicians, and the total increment of bone mineral, determined by dual-emission X-ray absorptiometry, is referred to as bone mineralization. We use that term herein, recognizing some ambiguity in its meaning, especially in children.

Table 1 Selected calcium and vitamin D Dietary Reference Intake values for children and adolescents (29)

Age	Calcium (mg/day)			Vitamin D (IU/day)		
	Estimated average requirement	Recommended dietary allowance[a]	Tolerable upper intake level	Estimated average requirement	Recommended dietary allowance[a]	Tolerable upper intake level
0–6 months	–	200	1000	–	400	1000
6–12 months	–	260	1500	–	400	1500
1–3 years	500	700	2500	400	600	2500
4–8 years	800	1000	2500	400	600	3000
9–18 years	1100	1300	3000	400	600	4000

[a]Adequate intake used for 0–6 months and 6–12 months. IU, international unit.

Most data related to bone mineralization during fetal development have looked at the total accretion of calcium during a full-term pregnancy. The skeleton of the full-term fetus accumulates a total of 30 g of calcium, approximately two-thirds of this during the third trimester. The calcium concentration in the third-trimester fetus is greater than in the maternal plasma, indicating the need for active transport across the placenta (3).

Recent animal data regarding the factors affecting fetal calcium transport have been reviewed by Belkacemi et al. (10). Multiple calcium-binding proteins involved in this process have been identified. Much less clear are the roles of vitamin D, estrogen, and parathyroid hormone. Maternal 1,25-dihydroxyvitamin-D levels increase during the third trimester, and vitamin D is synthesized in the placenta. Furthermore, it is possible that vitamin D increases the synthesis of various calcium-binding proteins.

However, several studies suggest that very low maternal calcium intakes may be a risk for lower bone mass in the neonate. These data include a study in India in which bone mineral density in babies was significantly related to maternal bone mass (32). In a controlled trial of calcium supplementation during pregnancy in the United States, mothers with a low habitual calcium intake (less than 600 mg/day) who were provided calcium supplementation delivered babies with a greater bone mineral mass than that of babies whose mothers were not supplemented (21). In a group of African American pregnant adolescents with a mean age of 16 years, nutrition was significantly related to fetal femur growth during pregnancy such that dairy intakes of less than two servings per day were associated with lower fetal bone development than were greater intakes of dairy (12).

Data relating to vitamin D and fetal bone growth are very limited. A study of 198 children born in the United Kingdom indicated that the maternal use of any vitamin D supplement was significantly associated with greater childhood bone mineral mass (18). In particular, very low maternal levels of serum 25-hydroxyvitamin-D (25-OHD) were associated with lower bone mineral mass in the offspring at 9 years of age. The implications of this finding for prenatal nutritional care are uncertain. Of note is that there are no convincing data to support a relationship between infant feeding (breast milk versus formula) and long-term bone mineral mass (34), although total calcium absorption is generally lower in breast- compared with formula-fed infants. It is possible that in utero events are more important in this regard than infant feeding practices, but this is not clear from studies in animal models or premature infants (15–17).

An additional line of evidence suggestive of a relationship between maternal vitamin D status and infant bone metabolism is derived from studies of the effect of season at delivery on infant bone mineral mass. Namgung & Tsang (27) described results from a study of Caucasian babies delivered in Cincinnati, Ohio, which

25-OHD: 25-hydroxyvitamin-D

demonstrated greater neonatal bone mineral mass in the winter but not the summer. In contrast, in the same report, infants in Korea born during the summer showed a greater bone mass than those born during the winter. The authors speculate that the different effects found in these two locations may be due to a high frequency of very low maternal vitamin D status during the winter in Korea that may lead to frank vitamin D deficiency in the mother and baby. However, controlled trials of vitamin D supplementation do not currently exist to support this hypothesis.

APPROACHES TO ASSURING ADEQUATE BONE MINERALIZATION IN INFANTS

The normal pattern of bone mineralization in infants has historically been identified using a combination of anthropometric, radiological, densitometric, and balance approaches. Each of these approaches has strengths and limitations that are briefly considered.

Historically, body weight growth curves were used to determine likely normal skeletal growth patterns. Based on the time-dependent change in body weight, total body calcium increased by approximately 140 mg/day during the first year of life (16, 28, 29). This greatly exceeds the accretion rate of approximately 30 to 35 mg per day from 0 through 4 months of age and 50 to 55 mg per day from 4 through 12 months of age derived from cadaveric sources (14, 16, 28, 29). A mean accretion rate of approximately 80 mg/day during the first year of life was derived using metacarpal morphometry data (22,14). Resolution of these different values for usual accretion rate is not currently possible, but a best assessment of both these data and the metabolic balance data suggests that a mean calcium accretion rate of about 100 mg/day overall during the first year of life is typical for human milk-fed infants (14, 28, 29).

Even fewer data are available for children after the first year of life. The methods applied for infants have generally yielded values suggesting an increment of about 100 to 150 mg per day in the second, third, and fourth years of life (29).

It is important to consider the limitations in these data for determining both usual and optimal rates of calcium accretion. First, much of the older data were based on small sample sizes and questionably accurate measurements of total body calcium or bone mineral content (BMC). Second and equally important is that the overwhelming majority of data exists based primarily on infants fed a high-mineral-containing formula or in which the proportion of breast-feeding and formula feeding was not identified. This provides challenges in defining what is "normal" or "optimal" in these age groups when comparisons of human milk with formula or even comparisons between infant formulas are done (20).

CALCIUM INTAKE IN INFANTS

The standard by which calcium intake is determined for infants is the intake of the breast-fed infant. In reviewing the literature, the 1997 IOM DRI committee determined that the average milk intake for human milk-fed infants in the first six months of life was 780 ml, with a mean calcium concentration of 259 mg/ml (28). This led to a calculated calcium intake just over 200 mg/day, which was rounded up to 210 mg/day. In reviewing these data, the 2011 IOM committee (29) chose to use a value of 200 mg/day. This distinction (210 versus 200 mg/day) is not meaningful biologically. In reality, the breast-fed full-term infant is assumed to have a sufficient calcium intake regardless of what that intake is exactly (**Table 2**). In choosing to use the human milk-fed infant as a standard, the committee noted that there are no reports of full-term, vitamin D–replete infants developing calcium deficiency, clinical bone mineral deficiency, or rickets when fed exclusively human milk.

Calcium balance data further support the adequacy of human milk as a calcium source for healthy full-term infants. For human milk-fed infants with a calcium intake of 200 mg/day,

Table 2 Mineral content of common feedings provided to infants

Milk/formula	Ca	Phos
Human milk	28	14
Cow milk	120	95
Goat milk	136	112
Cow milk formulas	42–52	24–35
Preterm formulas	132–146	66–81

Ca, calcium; phos, phosphorus.

a reasonable estimate is 65% net absorption. Combining this with an estimated total urinary excretion of 20 to 30 mg/day would lead to a retention average of about 80 to 100 mg/day (1, 2, 13, 14).

In considering formula-fed babies, it is often assumed that calcium is less bioavailable from infant formula compared to human milk. In fact, there is little evidence for a fundamental difference in bioavailability of calcium from lactose-containing cow milk–based infant formulas and human milk. Statutory guidance in the United States, and common practice throughout the world, is to provide 30% to 100% more calcium in infant formula than in human milk (**Tables 1** and **2**). Therefore, the fractional absorption of calcium, likely primarily driven by passive, nonvitamin D–related forces at high calcium intakes, will be lower from most formulas than that of human milk due to the higher calcium concentration of the infant formulas (2).

Several recent studies support the suggestion that the bioavailability of calcium in human milk is unlikely to be markedly higher than the bioavailability of calcium in lactose containing cow milk–based infant formula (3, 4, 6, 23). Overall, for lactose-containing cow milk–based infant formula, net absorption of 40% to 50% from an intake of 400 mg/day would lead to a net calcium retention of about 120 to 150 mg/day compared to the 80 to 90 mg/day expected for breast-fed infants. Although bioavailability from noncow milk– and nonlactose-containing infant formulas is likely to be lower, these often provide higher concentrations of calcium, leading to net calcium retention comparable to cow milk–based and lactose-containing formulas (**Table 3**). However, there are virtually no data using modern isotope techniques regarding the calcium absorption of increasingly commonly used protein hydrolysate– and amino acid–based formulas. This is an area requiring further investigation, especially as babies who receive these formulas may have abnormal gastrointestinal tract length or function.

Taken together, there is little doubt that the net calcium retention from most if not all lactose-containing cow milk–based formulas in the United States exceeds that of human milk due to the higher concentration of calcium in these formulas. The difference is difficult to quantify and highly variable but is probably about 40 to 60 mg/day on the average or about 30% above that of human milk (**Table 1**).

INFANTS 6 TO 12 MONTHS OF AGE

In considering older infants, the intake of calcium from solid foods needs to be taken into account. During the 7- through 12-month age period, the intake of solid foods becomes more significant, and calcium intakes may increase substantially from these sources. Few data are available for typical calcium intakes

Table 3 Balance data in infants fed human milk or formula (4, 6, 14, 23)

Feeding type	Calcium concentration (mg/100 mL)	Fractional absorption (%)	Approximate calcium retention (mg/d)
Human milk	28	65	90
Infant formula	48	45	150

Based on 780 mL/d intake milk or formula. Includes estimates for endogenous excretion and urinary calcium.

AI: adequate intake

EAR: estimated average requirement

RDA: recommended dietary allowance

from foods by human milk–fed older infants, and these data must be interpreted cautiously. The marketing practice recently of supplementing weaning foods with extra calcium may not reflect any real necessity for this practice.

The 2011 IOM committee used data suggesting mean calcium intakes from solid foods of 120 to 140 mg/day during the second six months of life (29). Combined with a somewhat lower intake of breast milk during this time period, the adequate intake was set at 260 mg/day, virtually the same as in 1997 (270 mg/day) (28). Of note is that there is little evidence for a marked increase in calcium requirements from 7 to 12 months of age compared with earlier in infancy, and the bioavailability of the calcium from the solid foods is likely to be lower than from breast milk but has not been specifically quantified. Furthermore, infants fed a commercial formula will likely greatly exceed this intake of calcium. Nonetheless, it is prudent to ensure that solid foods given to 7- to 12-month-old infants who are breast-fed contain some calcium and phosphorus to meet bone mineral needs.

QUESTIONS RELATED TO INFANT CALCIUM REQUIREMENTS

In considering these values, a few questions can be raised. First, why should an adequate intake (AI) be used rather than an estimated average requirement (EAR) and/or recommended dietary allowance (RDA) for infant calcium intake (**Table 3**)? Second, how can clinicians interpret the AI for babies receiving a wide range of feeding types? Finally, is using the breast-fed infant as a standard truly optimal?

The use of the AI relates to the inability to provide meaningful variances in the intake of the breast-fed infant and, more importantly, to identify any physiological outcomes of variance in intake by the breast-fed infant. It further represents the fact that vitamin D–sufficient breast-fed infants are not deficient in bone mineral accretion nor do they develop rickets or clinically evident bone demineralization. It is not appropriate to use formula-fed babies for setting the DRI values because this would represent a separate standard, not a variation in nutrient metabolism or requirement. In other words, establishing an average requirement based on any clinical outcome was not possible in infants, and only the usual dietary intake from breast-fed infants could be used as a guide.

Remarkably, no studies have directly compared the changes over a prolonged period of time, such as into adulthood, in total body BMC in breast- and formula-fed babies in a single cohort. A recent study in Korea showed the expected greater bone density at 12 months in formula-fed compared to breast-fed infants, with no effect of 200 IU/day vitamin D supplementation on this difference (21). On a theoretical basis, it is worth considering whether an increase in calcium retention by the skeleton of 30% in the first year of life is likely to have long-term benefits or even some risks.

The skeleton increases from about 30 g of calcium at birth to about 90 to 100 g of calcium at one year of age (14, 16, 18). Augmenting the rate of skeletal mineralization (60 to 70 g/year) by 30% using formula instead of breast milk might lead to a net increase of about 20 g of calcium in the skeleton by one year of age. During adolescence, the skeleton increases by about 600 g of calcium. The variability of this increase is about 30% within a defined population (2, 15, 16, 29). Therefore, the difference in effect of increasing the skeleton by 20 g in the first year of life is only about 10% of the natural biological variability of adolescent calcium accretion. The natural variability in bone mineralization is likely controlled primarily by genetic factors, not by calcium absorption during early childhood. In an individual, it is unlikely that the addition of a small amount of calcium to the skeleton in the first year of life will be maintained against natural genetic programming and the variability associated with pubertal growth (11, 31).

These ideas about the effects of infant mineralization on long-term BMC or fractures are speculative. Both human and animal research studies provide little compelling information in this regard. There is no suggestion in the

peer-reviewed literature that being breast-fed as an infant is a risk factor for osteoporosis or fracture later in life (2, 19, 20). It is possible that the natural programming of lower bone mass in infancy is beneficial, but the subject has been inadequately studied.

A final topic related to infant calcium intake is the tolerable upper intake level (UL). A value for the UL was not set for infants in 1997, but was set in the 2011 IOM report as 1,000 mg/day for 0 to 6 months and 1,500 mg/day for 7 to 12 months (29). These values were chosen on the basis of limited available safety data and suggest that calcium toxicity is extremely unlikely to occur in healthy infants unless high-dose supplementation would be provided.

CALCIUM INTAKE IN TODDLERS AND SMALL CHILDREN

Extremely few research studies have evaluated bone mineral development and dietary mineral requirements of children 1 to 4 years of age. Due to the transition from breast milk or infant formula to cow milk and a relatively high intake of dairy, most children this age do well clinically, and there are few clinical outcome data on which to identify calcium requirements. However, a small group of infants has been reported to develop rickets, commonly late in the first year or early in the second year of life and associated with extended breast-feeding, lack of vitamin D supplementation, and minimal solid-food calcium and vitamin D intake (1). The combination of these three factors represents a high risk for rickets in any population in the world of infants or small children.

One approach used to assess calcium requirements is to calculate average rates of increase of BMC from a typical diet and then evaluate, on the basis of available balance data, the amount of calcium needed in the diet to achieve this intake and the variability of this intake. Using this approach, Lynch et al. (24) calculated a usual rate of calcium accretion of 140 mg/day. A daily calcium intake of about 500 mg would be needed to achieve this intake. Variability of absorption and retention of about 30% led to a value of 700 mg/day intake to achieve this accretion in nearly all children. The 2011 DRI panel used this rationale to establish an EAR of 500 mg/day and an RDA of 700 mg/day for children in this age group (29).

UL: tolerable upper intake level

Benefits of High Doses of Calcium and Other Issues

Questions about this age group would include the following. First, is there any likely benefit (or risk) to providing much higher calcium intakes in small children? Second, do other dietary components, such as phytic acid, affect the calcium requirement? Third, does extended breast-feeding into the second year of life affect calcium requirements?

In considering the first question, it is likely that at dietary intakes substantially above the RDA of 700 mg/day, small children accrete minimal additional calcium to the skeleton. Although a specific value at which no further calcium is accreted cannot be identified from the literature, it is unlikely that intakes greater than 1,000 mg/day lead to any biologically meaningful increase in skeletal mineralization in small children due to the natural decrease in absorption at higher intakes and increased urinary and endogenous fecal excretion. Although competition between calcium and iron or calcium and zinc is not likely a major effect at usual calcium intakes, owing to concern about these nutrient interactions, it is not prudent to markedly increase calcium intake in this age group (29). One potential benefit of very high calcium intakes is inhibition of lead absorption, but this is not relevant to most children and not a basis for determining calcium intakes.

With regard to the second question, inhibitors of calcium absorption may exist in the diet of small children, especially in developing countries. When combined with low calcium intakes, a high risk for rickets exists even in the presence of an adequate vitamin D intake. It is not known exactly how low calcium intake needs to be in this circumstance, but it is likely that daily calcium intake of less than

200 to 250 mg leads to an increased risk of rickets (35).

With regard to the question of calcium requirements during extended breast-feeding, it is true that some cases of rickets are reported in the second year of life in babies still being breast-fed (1). This is much more likely with dark-skinned children who are not taking vitamin D supplements. No special precautions are needed in this circumstance, but attention should be given to achieving an appropriate vitamin D intake and adequate calcium from solid foods. The appropriate use of solid foods that contain calcium (e.g., yogurt, calcium-fortified infant foods) should also be emphasized for families practicing breast-feeding in the second year of life as well as those breast-feeding infants who are 6 to 12 months of age.

Calcium supplements should seldom be needed in infants or small children. Usual milk and dairy intakes provide adequate calcium intake in this age group. For those who avoid cow milk protein or lactose, calcium-fortified soy milk, low-lactose milks, and other calcium sources are available and should be considered. Although minimal intake of juices is recommended in this age group, the use of calcium-fortified orange or other juices can be considered after one year of age.

PHOSPHORUS INTAKE IN INFANTS AND SMALL CHILDREN

Although most attention in the literature related to mineral requirements for bone health relate to calcium requirements, it is important also to consider the other primary bone mineral, phosphorus (28). Of note is that phosphorus was not included in the mandate for the 2011 IOM report (29). Furthermore, policy statements related to bone health in infants and children have focused on calcium and vitamin D and not on phosphorus.

However, despite this lack of attention, there is no doubt that phosphorus can be limiting in the newborn period, especially in very premature infants. Premature infants have a high urinary calcium excretion due to relative phosphorus depletion; phosphorus supplementation decreases urinary calcium excretion (8).

The marginal phosphorus status of newborns and their sensitivity to supplementation come into consideration in two situations. First is the provision of calcium supplementation without phosphorus. Although few data specifically speak to this practice, it is not well advised for infants, especially premature infants. Infants given parenteral nutrition without phosphorus demonstrate a rapid rise in serum calcium and, more relevant to this situation, a drop in serum phosphorus with inadequate phosphorus intake. In infants, any attempt to increase calcium intake, via supplement or in infant formulas, needs to additionally evaluate and consider the effects of phosphorus balance. This is not easily done, however, because phosphorus has no usable (minor) stable isotopes and thus assessment of phosphorus absorption is difficult and requires mass balance techniques that are rarely used and are of limited accuracy.

A second and more common concern is the consequence of relatively high intakes of phosphorus in infant formulas on serum calcium in the first week of life. A condition often referred to as late-hypocalcemic tetany exists in which infants, usually 3 and 6 days of age, present with seizures and evidence of severe hypocalcemia and hyperphosphatemia (7). The etiology is not completely determined but is certainly related to, at least in part, a higher level of phosphorus in the diet than is tolerated by the infant. Of note is that this condition does not occur in exclusively breast-fed infants, suggesting a biological rationale for the low phosphorus content of human milk.

VITAMIN D REQUIREMENTS IN INFANTS AND SMALL CHILDREN

The role of different intake levels and serum levels of vitamin D in both maintaining bone health and in decreasing the risk of a wide range of illnesses is a vigorously debated nutritional issue. The 2011 IOM committee established an AI of 400 IU/day of vitamin D for infants to

one year of age and an EAR of 400 IU/day and RDA of 600 IU/day for older children (**Table 1**). The rationale for these values is fully described in the IOM report (29), but several key issues are discussed here.

For the most part, discussions of the role of vitamin D beyond bone health in the 2011 IOM report (29) have centered on outcomes primarily relevant to adults, such as breast and colon cancer and cardiovascular outcomes. However, some nonbone issues do relate to children in this age group, including a potential effect on asthma, influenza, autism, and Type 1 diabetes. No convincing evidence was found to support establishing a dietary requirement for vitamin D in children on the basis of these nonbone outcomes. Nor were the data sufficient to support any particular level of vitamin D intake or serum 25-OHD level to prevent nonbone-related disorders in infants and children. Future research in the form of well-controlled trials will need to consider these issues.

In establishing dietary vitamin D requirements, a fundamental issue is to identify the serum 25-OHD needed in infants to prevent hypocalcemia, rickets, or other bone diseases in early life or to improve bone mineral outcomes later in life. Although many values have been discussed in the literature for adults, no consensus exists in children. Both the American Academy of Pediatrics (AAP), the Pediatric Endocrine Society and the 2011 IOM report support a 25-OHD concentration of at least 50 nmol/L (20 ng/ml) as likely to be consistent with the physiological needs of infants and children (26, 29, 36). This value is lower than that suggested by some authorities, especially for adults, although the DRI report did not support higher target levels in adults either. The recommended level is one that is achieved by most infants and children in the United States at the present time, although an important portion of the population, in particular African American children, have serum 25-OHD concentrations below 20 ng/ml (25).

Translating the target serum 25-OHD concentration to dietary intake recommendations is difficult in part owing to the variable effect on 25-OHD of sunshine exposure of the skin. It is recognized that sunshine provides a substantial proportion of vitamin D via photoconversion from UVB radiation. However, it is important to provide infants and children vitamin D from dietary sources. Due to a variety of factors, including the use of sunblocks, the lack of sunshine in northern areas for much of the year, and social influences, it is not appropriate to expect solar exposure to provide the UVB needed for vitamin D formation in children. Although vitamin D–related cutaneous photoconversion occurs before more dangerous erythematous exposure, timing such exposure in infants is nearly impossible. Providing 10 to 15 minutes solar exposure without sunblock, then putting sunblock on the baby, allowing it to take effect, and returning for additional outdoor time is impractical. It is not an approach that is recommended for achieving adequate vitamin D exposure for infants and small children (29, 36).

Once it is accepted that dietary or supplement sources must be used to provide vitamin D, then the question becomes what sources and what level should be provided. For infants, both the AAP (36) and the 2011 IOM panel (29) concluded that 400 IU/day vitamin D intake would be the goal for infants, using the AI by the DRI panel. The AAP and 2011 IOM statements differ in that the AAP targeted 400 IU from shortly after birth, and the DRI panel's AI reflects an average over the first six months of life. The DRI panel's statement specifically notes that it is recognized, especially in formula-fed babies, that formula intake and thus vitamin D intake would not reach 400 IU/day in the early newborn period because of a lower volume of formula intake in the first few months of life.

Therefore, formula-fed infants who, for example, at an age of 2 to 4 weeks, may be receiving only 600 to 700 mL/day of infant formula have little need for a vitamin D supplement. In theory, almost all routine infant formulas marketed as of July 2010 in the United States and Canada provide 400 IU/liter vitamin D, according to the nutrition label. Infant formulas as consumed by the infant frequently contain a substantial overage of

vitamin D (29). This would place almost all infants at 300 IU/day by about 4 weeks of age and near 400 IU/day by 6 to 8 weeks of age. Furthermore, the recommended intake of 400 IU daily vitamin D provides a considerable safety margin, as 300 IU/day will provide for a 25-OHD level above 50 nmol/L in almost all young infants (9, 28, 29). A recent study in breast-fed infants in Germany, showing that 250 IU/day led to relatively high 25-OHD levels similar to those achieved with 500 IU/day (33), supports the idea that 400 IU/day, although a reasonable goal, is not an exact daily target for most infants, even those with minimal sun exposure.

Regarding breast-fed infants, it is usually recommended to provide a supplement of vitamin D3 or a multivitamin drop providing 400 IU. Traditionally, this has been the volume of one milliliter or one dropper of vitamin D3–containing drops designed for this purpose. Recently, however, very concentrated drops have appeared on the market, causing concern and a safety warning from both the AAP and the U.S. Food and Drug Administration. Health care practitioners should also be aware that extremely high-dose vitamin D in liquid form is marketed in the United States. Drops marketed for infants can contain up to 400 IU/drop and those for adults up to 2,000 IU/drop. It is possible for families to confuse recommendations or to provide multiple drops to each infant or small child. Provision of a full milliliter of these drops over a relatively brief period could provide a dose of over 100,000 IU of vitamin D, resulting in a potentially serious risk for clinical vitamin D toxicity in small infants.

A common question is what to do about babies who in the initial days of life receive both human milk and infant formula. This practice is common among some ethnic groups and may lead to rapid weaning to formula or increased breast-feeding and decreased use or stoppage of formula. It can be impossible to assess in the first week of life when breast-fed infants should begin their supplementation. In this case, it is appropriate to provide 400 IU/day of vitamin D as a supplement. If the baby is fully weaned on to infant formula, the vitamin D can be stopped at any time. There is no harm in having a baby receive 600 to 800 IU/day of vitamin D total from formula and a supplement during the weaning process if this occurs before the pediatrician can advise the mother to stop the supplement. The upper limit of 1,000 IU/day for infants less than six months of age was maintained by the 2011 IOM committee and would not be exceeded by that practice.

BENEFITS OF HIGH DOSES OF VITAMIN D FOR MOTHER OR INFANTS

Recent studies have demonstrated that the provision of usual amounts of vitamin D to lactating women has little effect on the vitamin D content of milk. Doses to the mother of at least 4,000 IU/day and up to 6,400 IU/day are needed to increase milk vitamin D content such that 300 to 400 IU of vitamin D are present in a 24-hour supply of breast milk (9). At the present time, this approach is not routinely recommended. More research is needed into the risks and benefits of high doses of vitamin D for lactating women. Nonetheless, this approach, although not specifically recommended by the AAP or IOM (29, 34), may appeal to some women who do not wish to give their infants anything orally in the initial weeks of life other than breast milk. In an individual situation such as this, the possibility of using high-dose maternal supplementation, of approximately 6,000 IU/day can be considered and discussed with the family.

In older children, adolescents, and even adults, serum 25-OHD is not closely related to calcium absorption efficiency when the 25-OHD is greater than 30 to 40 nmol/L (5). The need to provide a safety margin led to the 2011 IOM target for the RDA of 50 nmol/L (20 ng/ml) (29). It is unlikely that there is some unique sensitivity of calcium absorption in infants or small children requiring levels above 50 nmol/L to be effective, although this has not been evaluated. Therefore, the new RDA

of 600 IU should provide for adequate vitamin D for this purpose in small children.

Intakes of vitamin D above 600 IU/day may be considered by some practitioners for use in small children for the potential prevention or treatment of a condition that is nonbone related, such as asthma or influenza. The possibility of using vitamin D in these disorders deserves careful examination in controlled trials in which both safety and efficacy are assessed in multicenter, multiseasonal, and multiethnic studies. Small trials should be evaluated with extreme caution, as should trials conducted in very northern latitudes or among specialized populations. The new upper level of vitamin D intake of 2,500 units for 1- to 3-year-old children should provide an adequate basis for most such investigations (29). It is important to note, however, that the UL is not designed as a maximum related to research studies. Vitamin D doses higher than the UL can and should be used in clinical trials with appropriate monitoring of serum and urine calcium levels and other potential adverse outcomes.

CONCLUSIONS

Despite the widespread enthusiasm for providing high levels of bone minerals and vitamin D to infants and small children, there are inadequate controlled trials to evaluate such therapy. Calcium and phosphorus are adequate in human milk for healthy full-term infants, and modest intakes are needed from weaning foods. Supplemental vitamin D, at about 400 IU/day, should be provided to all infants, with intakes of 400 to 600 IU/day provided after one year of age. Further controlled vitamin D trials with both short- and long-term outcomes are needed, particularly in relation to vitamin D requirements in small children with chronic illnesses, to determine whether higher-dose vitamin D supplementation might be beneficial during infancy and early childhood.

SUMMARY POINTS

1. Human milk provides adequate calcium and phosphorus to meet the needs of all full-term (but not preterm) infants.
2. In contrast, supplemental vitamin D must be provided as drops to human milk–fed infants or as part of infant formulas.
3. Maximizing bone mineral content in infants by providing high levels of calcium and vitamin D to infants has not been shown to have any long-term beneficial effects.
4. The safety of providing high-dose vitamin D to any group of children must be evaluated before it can be recommended.

FUTURE ISSUES

1. What is the risk/benefit to increasing current intakes of calcium or vitamin D to infants via infant formula, other solid foods, or dietary supplements providing more than 400 IU/day of vitamin D?
2. What is the risk of toxic effects from achieving levels of 25-hydroxyvitamin-D greater than 30 to 40 ng/ml in infants and small children?
3. Should young children with chronic illnesses be provided additional minerals or vitamin D?

DISCLOSURE STATEMENT

The author was a member of both the 1997 and 2011 DRI committees related to calcium and vitamin D and is a current member of the American Academy of Pediatrics Committee on Nutrition. The author serves as a scientific consultant to the Milk Processors Education Program.

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