I. INTRODUCTION

Significant changes in maternal calcium metabolism occur during pregnancy, lactation, and after weaning to provide the calcium needed for fetal bone mineral accretion, for the synthesis of breast milk, and for the restoration of the maternal skeleton. Multiple factors are involved in regulating these processes so that maternal blood calcium concentrations are maintained within a narrow range despite the large changes in calcium fluxes that occur. Primary strategies include changes in the efficiency of absorption of calcium from the intestinal tract, alterations in renal calcium reabsorption and thus urinary calcium excretion, and the flux of calcium in and out of bone. Reproductive hormones have important effects on calcium homeostasis and bone metabolism, and during pregnancy and lactation their actions work in concert with the vitamin D endocrine system to ensure that calcium needs are met for fetal bone mineral accretion, for breast milk production, and to maintain circulating maternal calcium concentrations.

II. ADAPTATIONS IN VITAMIN D AND CALCIUM METABOLISM DURING PREGNANCY

A. Vitamin D and Calcium Metabolism

Approximately 25 to 30 g of calcium is transferred to the fetal skeleton by the end of pregnancy, the most of which is transferred during the last trimester. The fetus accumulates 2 to 3 mg/d during the first trimester, but 250 mg/d during the third trimester [1]. Maternal serum calcium concentrations decrease in the first half of pregnancy, reaching a nadir at mid-gestation due to plasma volume expansion and decreased albumin concentrations [2,3]. Serum concentrations of ionized calcium or calcium adjusted for albumin concentrations show less fluctuation and remain relatively stable throughout pregnancy [2,4,5]. Serum concentrations of intact parathyroid hormone (PTH) have been reported to decrease [2,4,6] or not change [3] over the course of pregnancy. In contrast, circulating concentrations of the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D), are increased during pregnancy. By the second trimester serum concentrations of 1,25(OH)2D increase by 50–100% over pre-pregnant values, and in the third trimester they increase by 100% [3,7] (Fig. 1). The signal to increase 1,25(OH)2D synthesis is not clear, as PTH concentrations are not elevated. Vitamin D binding protein (DBP) concentrations increase in pregnancy possibly due to increased concentrations of estrogen. Although some of the increase in serum 1,25(OH)2D concentrations may be due to the increase in the amount bound to its binding protein, the amount of free 1,25(OH)2D is still elevated [3,8]. Some of the circulating 1,25(OH)2D may be of extrarenal origin as the decidua has been shown to synthesize 1,25(OH)2D [9] (see Chapter 79). Consistent with this is the fact that maternal 1,25(OH)2D concentrations rapidly decrease within a few days after delivery [10]. The increase in 1,25(OH)2D concentrations during pregnancy is accompanied by an increase in intestinal calcium absorption (Fig. 1). Fractional calcium absorption increases by 50–56% over prepregnant
levels in the second trimester and by 54–62% in the third trimester [3,7]. Thus increased maternal intestinal absorption of calcium is an important physiologic adaptation to secure sufficient amounts of this mineral for the fetus. Despite the increased need for calcium, urinary calcium excretion increases by 40–50% over the course of pregnancy. This is most likely due to the marked increase in glomerular filtration rate and increased absorptive load [2,3,11].

Several studies report increased concentrations of biochemical markers of bone turnover during pregnancy. Serum concentrations of biochemical markers of bone formation, namely bone specific alkaline phosphatase and the propeptide of type 1 collagen (PICP), are elevated in the third trimester with a steep peak in the last month of pregnancy [2,6]. It is not clear whether there are changes in the first two trimesters of pregnancy as an increase, decrease or no change in the concentration of these bone formation markers have been reported [2,6]. Osteocalcin concentrations have been found to decrease [6], decrease then increase [3], or not change during pregnancy [10]. Markers of bone resorption, namely the breakdown products of collagen such as pyridinoline, deoxypyridinoline, and NTx, increase throughout pregnancy reaching a peak at the end of pregnancy [2,3,6]. Although it appears that there is a dissociation of bone resorption and bone formation in the first two trimesters with elevated bone resorption predominating, it is difficult to predict whether there is a net loss of maternal bone during pregnancy using biochemical markers alone. Other factors confound the interpretation of biochemical markers of bone turnover during pregnancy such as whether they are of maternal, placental, or fetal origin, and the effects of pregnancy on the metabolic clearance of these proteins by the liver and kidney. It also has been suggested that some of the increase in bone turnover markers is due to increased turnover of soft tissue collagen of the uterus and skin [6,12].

Increases in circulating concentrations of insulin-like growth factor-1 (IGF-1) and placental lactogen have been suggested as the possible mechanisms behind increased bone turnover during pregnancy [2,6]. Increases in IGF-1 concentrations precede the increase in bone formation markers, and IGF-1 concentrations correlated more strongly with markers of bone formation than bone resorption. A recent study investigated changes in calcium-regulating hormones and osteoprotegerin (OPG) during pregnancy and found that maternal serum OPG concentrations steadily increased with gestational age [10]. Receptor activator of nuclear factor-κB ligand (RANKL) is important in osteoclast differentiation [13], and OPG acts as a decoy receptor for RANKL, thereby preventing the differentiation of osteoclast precursors into mature osteoclasts and decreasing bone resorption. The authors speculated that higher OPG concentrations during pregnancy, possibly of placental origin, might play a role in the control of bone metabolism throughout gestation.

B. Changes in Bone Mineral Content and Density during Pregnancy

Few studies have included bone mineral density measurements during pregnancy because of the potential risks to the fetus associated with radiation exposure. There is conflicting evidence as to whether there is a net change in bone density during pregnancy. Several different approaches have been used to evaluate the impact of pregnancy on maternal bone. Some longitudinal studies have measured bone density by dual energy X-ray absorptiometry (DXA) before conception and shortly after delivery and have found no significant loss of bone density [3,7,14,15]. However, other studies report losses of 2 to 2.6% at the ultradistal radius [16,17], 2 to 4% at the spine [2,6,18], and 2.4 to 3.6% at the hip [2,19]. In some of these studies bone density was measured as far as 6 weeks postpartum, and significant losses of bone may occur within the immediate postpartum period thereby making it hard to interpret these results. Naylor and co-workers found that the changes in bone density during pregnancy varied according to skeletal site. Bone density at trabecular-rich sites (pelvis and spine) decreased by 3 to 4%, whereas bone density at cortical sites (arms and legs) increased by 2% [6].

Many investigators have investigated changes in bone density by use of ultrasound as it does not involve
radiation exposure. Speed of sound (SOS) and bone ultrasound attenuation (BUA) are strongly correlated with bone density measured at the same skeletal site. Longitudinal studies over the course of pregnancy have documented a decrease in SOS and BUA measured at the os calcis or phalanges in the latter half of pregnancy, particularly in the third trimester [20–23]. These data are consistent with a loss of maternal bone mineral toward the end of pregnancy when the fetus is accreting bone mineral most rapidly. Longitudinal studies of bone density in women who do not lactate after delivery show that bone density at the spine and hip increase by about 2% in the first year postpartum [24–26]. It is possible that this increase in bone may compensate for bone lost during pregnancy. If so, this may explain why studies comparing bone density of women with different pregnancy histories have found no differences in bone density measured many years later [27–30]. Henderson et al. found that even grand multiparous women having six or more pregnancies and long lactations did not have lower bone density of the lumbar spine, femoral neck, or mid-radius than nulliparous women later in life [31].

In summary, several adaptations in the maternal calcium economy occur in order to provide sufficient calcium for fetal bone mineral accretion (Fig. 2). The primary adaptive strategy is an increase in intestinal calcium absorption. Additional calcium may come from demineralization of maternal bone. The increased concentrations of \(1,25(\text{OH})_2\text{D}\), estrogen, IGF-1, placental lactogen, and OPG interact to facilitate these changes. Despite the increased need for calcium during pregnancy, urinary calcium losses are increased due to increased glomerular filtration rate and an increased absorptive calcium load.

III. EFFECTS OF LOW MATERNAL VITAMIN D AND CALCIUM INTAKE DURING PREGNANCY ON THE FETUS AND NEONATE

A. Vitamin D

Maternal vitamin D deficiency is more likely to occur in winter months, in countries that do not routinely fortify dairy or other food products with vitamin D, among members of ethnic groups who cover most of their skin, or among individuals with heavily pigmented skin. Few randomized nutritional vitamin D and calcium interventions have been conducted during pregnancy, and the importance of maternal vitamin D and calcium intake is best illustrated from observational studies of women with poor calcium and/or vitamin D intake. These observational studies, along with the results of the few clinical trials that have been conducted, indicate that maternal vitamin D and calcium status are important in neonatal handling of calcium, and possibly in fetal growth and bone maturation and mineralization.

Maternal vitamin D deficiency during pregnancy can affect neonatal calcium metabolism. Maternal vitamin D deficiency is associated with secondary hyperparathyroidism, and maternal hyperparathyroidism during pregnancy may lead to neonatal hypocalcemia or tetany [32,33]. In the early 1970s, Purvis and co-workers noted that the occurrence of neonatal tetany among 112 infants was inversely related to the amount of sunlight exposure the mothers had during the last trimester of pregnancy [34]. The authors speculated that the mothers developed hyperparathyroidism secondary to vitamin D deficiency leading to a transitory hypoparathyroidism and hypocalcemia in the neonate. Several investigators subsequently reported that infants of mothers with low vitamin D intake during pregnancy had low serum calcium concentrations in cord blood or during the first week of life [35–37]. Several randomized trials of vitamin D supplementation during pregnancy were later reported.

Cockburn and co-workers randomized two obstetric wards, one with 506 women who received 400 IU vitamin D/day from the 12th week of gestation and another with 633 women who did not receive vitamin D [38]. They reported higher maternal, cord and, infant 25-hydroxyvitamin D (25OHD) concentrations with vitamin D supplementation. They also found that the incidence of neonatal hypocalcemia was less with
vitamin D supplementation, although this was modified by the infant’s feeding (hypocalcemia greater with formula feeding vs breast-feeding) (Fig. 3) [38]. Several randomized trials of vitamin D supplementation (1000 IU/d) during pregnancy subsequently found that infants of mothers receiving vitamin D had higher serum calcium concentrations within the first week of life than infants of mothers receiving placebo [39]. Brooke and co-workers conducted a randomized, double-blind trial of vitamin D supplementation (1000 IU/d from 28 to 32 weeks gestation) and found that infants of mothers receiving vitamin D had higher serum calcium on days 3 and 6 and a lower incidence of symptomatic hypocalcemia than infants of mothers receiving placebo [39–41]. These studies were completed in populations that are at increased risk for vitamin D deficiency, and the results indicate that adequate maternal vitamin D status during pregnancy may be necessary to ensure appropriate neonatal calcium homeostasis.

Maternal vitamin D deficiency during pregnancy also may lead to impaired fetal growth and bone development. The occurrence of vitamin D deficiency is high among Asians from the Indian subcontinent living in Britain [33]. A trial of vitamin D supplementation (1000 IU/d) among pregnant Asian women found that a higher percent of the infants randomized to the placebo group (28.6%) were small-for-gestational-age compared to infants in the supplemented group (15.3%) [39]. Some investigators [37,42], but not all [41], have reported lower birth weights of infants born to mothers with low vs adequate vitamin D status. Decreased skeletal mineralization in utero may be manifested as rickets or osteopenia in the newborn infant. However, fetal or congenital rickets of the newborn are rare. Case reports of congenital rickets in newborn infants of mothers with severe nutritional osteomalacia associated with vitamin D or calcium deficiency have been reported [43–45]. Reif and co-workers, in a case-control study, reported an association between cranioptades, or delayed ossification of the cranial vertex, and maternal and neonatal 25OHD concentrations. However, these findings have not been replicated in other observational studies or trials [36,39]. Although Brooke and co-workers did not find an association between cranioptades and vitamin D status, they did find that infants of mothers who received placebo had larger fontanelles than infants of mothers supplemented with vitamin D, which is consistent with impaired skull ossification [39]. A study conducted in China also found possible evidence for a relationship between maternal vitamin D deficiency and impaired fetal bone ossification [46]. The presence of wrist ossification centers in neonates was associated with cord serum 25OHD concentrations. A higher rate of ossification centers in newborn infants of mothers with adequate vitamin D status was apparent when compared to infants of mothers with low vitamin D status.

Few studies have investigated the role of maternal vitamin D status on infant bone mineralization.Congdon et al. measured forearm BMC using single photon absorptiometry and found that BMC did not differ by history of vitamin D supplementation during pregnancy and was not correlated with cord serum 25OHD concentrations [36]. The majority of the vitamin D supplementation trials reported to date began supplements late in gestation. There are observational studies suggesting that maternal vitamin D status early in gestation may be important in fetal bone development. Seasonal differences in adult bone density have been reported by some [47,48] but not all investigators [49] and may be attributed to seasonal variations in vitamin D status. Studies that have examined seasonal differences in newborn BMC have had conflicting findings. Two studies conducted in the United States found that infants born in the summer have lower BMC compared to infants born in the winter months [50,51]. These findings are opposite to what is seen in adults. However, Namgung and co-workers examined this association in infants born in Korea and also found that winter-born infants had lower BMC than summer-born infants in Korea [52]. One explanation for these contradictory findings is that many United States women take prenatal vitamins containing vitamin D beginning in the second trimester of pregnancy. Thus the observed seasonal effects on infant BMC in the United States may reflect vitamin D status in the first trimester of pregnancy. Because there is minimal fetal calcium accretion in the first trimester,
this would indicate some other function of vitamin D on fetal bone development.

In summary, maternal vitamin D status during pregnancy has been shown to be associated with neonatal calcium homeostasis. There are conflicting reports indicating a possible role of maternal vitamin D status in fetal growth and bone development.

**B. Calcium**

Few studies have evaluated the effects of maternal calcium intakes on fetal bone mineral accretion. A study by Raman and co-workers in India found that undernourished pregnant mothers who were supplemented with 300 or 600 mg calcium/d had similar maternal metacarpal bone density compared to mothers not supplemented, but the bone density of their newborns was greater [53]. Similar results have been reported in a large randomized trial of maternal calcium supplementation for the prevention of preeclampsia [54]. A total of 256 women were enrolled in the randomized, double-blind, placebo-controlled trial. Newborn infants of mothers in the lowest quintile of calcium intake (<600 mg/d) who were randomized to calcium supplementation had higher BMC compared to newborns in the lowest quintile whose mothers were randomized to placebo (Fig. 4). There was no difference in neonatal BMC between placebo and supplemented maternal groups in the upper four quintiles of maternal calcium intake. These studies suggest that there is a lower limit to the mother's calcium regulatory capacity to buffer the fetus from variations in her calcium intake. This intake of approximately 600 mg/d is below the current recommended calcium intakes for pregnant women.

**IV. ADAPTATIONS IN VITAMIN D AND CALCIUM METABOLISM DURING LACTATION AND AFTER WEANING**

**A. Vitamin D and Calcium Metabolism during Lactation**

Lactating women secrete approximately 200–240 mg of calcium daily in breast milk [55]. Over 6 months of lactation this is equivalent to approximately 6% of her total skeletal calcium reserve. Despite this large transfer of calcium from the maternal circulation, maternal serum calcium concentrations are unchanged [3,56] or slightly elevated [57,58]. There is no increase in PTH concentrations during lactation. In fact, serum concentrations of PTH are lower in lactating as compared to nonlactating women in the first 3 months postpartum [56,59,60].

The lower PTH concentrations during lactation are likely to be a consequence of the rapid bone resorption that occurs especially early in lactation and the resultant increase in serum calcium concentrations. Two potential causes of bone resorption are hypoestrogenemia and elevated circulating concentrations of parathyroid hormone related peptide (PTHrP) [61–63]. Lactation results in prolonged postpartum amenorrhea and hypoestrogenemia due to suppression of the hypothalamic–pituitary–gonadal axis. Hypoestrogenemia is known to result in bone resorption in a variety of clinical and experimental situations. PTHrP also stimulates bone resorption (see Chapter 43). PTHrP is made in the mammary gland and is present in very high concentrations in breast milk [64]. Presumably some of the PTHrP synthesized by the mammary gland may gain access to the maternal circulation. Circulating PTHrP has actions similar to PTH and acts through the PTH receptor [65]. PTHrP is a potent stimulator of bone resorption, and administration of PTHrP results in an immediate increase in serum calcium concentrations [66]. In lactating women, serum concentrations of calcium are more highly correlated with PTHrP than with PTH [62], suggesting that the decrease in PTH also may be secondary to elevated PTHrP concentrations and subsequently increased serum calcium concentrations. Whether or not there is a decrease in urinary calcium excretion during lactation is unclear. Some studies have found a 20 to 50% decrease in urinary calcium excretion in lactating women [3,57,67–70]. However, some of this decrease may be a postpartum phenomenon and not just a result of lactation. Studies that compared urinary calcium excretion in lactating women to that of nonlactating postpartum controls have not found urinary calcium excretion to be lower in lactating women [56,59,60,71].
Unlike during pregnancy, there is no increase in circulating concentrations of 1,25(OH)₂D in lactating as compared to nonlactating postpartum women [56,59]. Commensurate with this finding is that there is no difference in intestinal calcium absorption in lactating as compared to nonlactating women [3,71–73]. Intestinal calcium absorption is increased in lactating rats that are suckling multiple pups, but this does not occur in women nursing one infant. Greer et al. found that women nursing twins had elevated concentrations of PTH and 1,25(OH)₂D [74]. Urinary calcium excretion and intestinal calcium absorption were not measured, but presumably elevations in PTH and 1,25(OH)₂D concentrations resulted in changes in urinary calcium excretion and intestinal calcium absorption. Although bone demineralization, and not improved efficiency of intestinal calcium absorption, is the primary compensatory response to secure calcium in lactating women, it can be hypothesized that increased absorption efficiency may occur in situations of greater calcium demand such as women nursing multiple infants.

B. Changes in Bone Mineral during Lactation

One of the primary changes in calcium homeostasis during lactation is the marked decrease in bone mineral content and density. Decreases of 3% to 9% at the lumbar spine and femoral neck have been reported [3,17,24,25,60,75–78]. The decreases in bone density of the spine and hip occur rapidly within the first 3 to 6 months of lactation, and bone density remains lower with continued lactation [75,76]. The rate of bone loss at these sites in the first 6 months of lactation is significant as it approaches 1% per month. In comparison, menopausal and early postmenopausal women lose bone at the rate of 1% to 2% per year [79].

The amount of bone lost during lactation is variable among women. Women who breast-feed longer, or who have a greater breast milk volume, have greater bone loss compared to women who breast-feed for shorter periods of time [17,55,75,80]. In addition, the length of postpartum amenorrhea is an important determinant of bone loss during lactation. Women who resume menses early have less bone loss than women who have longer periods of postpartum amenorrhea [17,25,76]. Although the length of postpartum amenorrhea and length of lactation are related, some women resume menses while still breastfeeding. Kalkwarf et al. found that the net change in bone density at the lumbar spine at 6 months postpartum was only −1.8% in women who had resumed menses whereas it was −4.4% in women who had not resumed menses despite the fact that both groups were breast-feeding five times a day [81]. Polatti et al. also found less of a deficit in bone density in lactating women who resumed menses by 5 months postpartum as compared to those who were remained amenorrheic (−3.0% vs −5.8%) [25]. These findings underscore the importance of ovarian hormones in regulating bone loss during lactation.

Dietary calcium intake does not appear to affect the amount of bone lost during lactation in women. Bone loss during lactation has been observed in women with high calcium intakes (>1500 mg/d) [17,60,75], and dietary calcium intake has not been shown to be a significant predictor of bone loss during lactation [55,59,75,80]. Furthermore, three randomized calcium supplementation trials have demonstrated that provision of supplemental calcium does not affect bone loss during lactation. Prentice et al. studied 60 lactating women in the Gambia who had a very low calcium intake (274 mg/d). Half of the women received an average of 714 mg of supplemental calcium per day, and half received a placebo. Overall there was a significant loss (1.1%) of bone mineral at the radial shaft by 13 weeks postpartum, but there was no difference in the amount of bone lost between supplemented and unsupplemented lactating women [67]. Kalkwarf et al. randomized 83 lactating women and 81 nonlactating postpartum women whose dietary calcium intake averaged 735 mg/d, to receive a calcium supplement (1 g/d) or placebo for 6 months. There was a small effect (+1.2%) of calcium supplementation on bone density of the lumbar spine when considering all women [24]. However, bone loss did not differ between lactating women who received the calcium supplement and those that received placebo (4.2% vs 4.9%) (Fig. 5). In a supplementation trial conducted in 274 Italian women, Polatti et al. found no difference in the amount of bone lost at the lumbar spine (4.0% vs 4.4%) or the ultradistal radius (2.0% vs 2.2%) between supplemented

![Figure 5](image-url)

**Figure 5** Effects of lactation and calcium supplementation (1 g/d) on percent change in bone density of the lumbar spine during the first 6 months postpartum. Reproduced from Kalkwarf et al. [24].
(1 g calcium/d) and unsupplemented women over 6 months of lactation [25].

The primary adaptive strategy to secure calcium to support breast milk production is demineralization of maternal bone (Fig. 6). Lactation also may result in urinary calcium conservation, although the results from studies are conflicting as to whether this is a lactation effect or a postpartum effect. Bone loss during lactation is related to postpartum amenorrhea and hypoestrogenemia. Elevated circulating concentrations of PTHrP also may have a role in bone loss during lactation.

C. Vitamin D and Calcium Metabolism after Weaning

Additional adjustments in calcium metabolism occur shortly after lactation has stopped as the maternal physiologic system switches from mobilizing calcium from the skeleton and secreting calcium into breast milk to restoring maternal calcium reserves. Some studies have found an increase in serum concentrations of PTH shortly after weaning and decreased urinary calcium excretion, presumably in response to increased PTH concentrations [7,57]. However, these changes have not been found in all studies [56]. Kalkwarf et al. found that serum concentrations of 1,25(OH)2D were higher in women shortly after weaning [72], and this was accompanied by a higher intestinal calcium absorption (37% vs 31%). Ritchie et al. did not find a significant increase in intestinal calcium absorption after weaning, but the smaller sample size in that study may have limited their ability to detect a small increase [3].

D. Changes in Bone Mineral after Weaning

Maternal bone density increases rapidly after weaning. Much of the bone density lost during lactation is recovered within the first 6 months after weaning. Laskey and co-workers demonstrated that the resumption of menses was as good a predictor of bone changes as was the length of lactation [76]. Increases in bone density after weaning occur earlier for the spine than for the femoral neck, which may be a consequence of the greater amount of trabecular bone at the spine [17,75,76,78]. Although most studies show a complete recovery of bone density at the spine after weaning, it is not clear that the recovery of bone at the femoral neck is complete, as deficits in bone density at this site were still evident at the end of the study follow-up in most of these studies [17,75,78]. It is possible that a complete recovery of bone may have occurred with a longer follow-up period. Consistent with this are the results of studies in postmenopausal women that have found that lactation history is not a significant predictor of bone density [27–30] and is not associated with increased risk of hip fracture [82–84].

Kalkwarf et al. conducted a calcium supplementation trial in 76 women who had lactated for 6 months and then weaned their infants and 82 nonlactating postpartum controls to determine whether provision of supplemental calcium could enhance bone recovery after weaning [24]. By 6 months after the initiation of weaning (4 months after complete weaning), lactating women who had received 1 g/d of supplemental calcium had a significantly greater increase in spinal BMD compared to women who received the placebo (5.9% vs 4.4%) (Fig. 7).

The restoration of bone mass after lactation has ceased is important in maintaining maternal bone health.
Bone mass and density increase in parallel with the return of menstruation and presumably normalization of circulating estrogen concentrations. The recovery of bone mass may be facilitated by an increase in intestinal calcium absorption efficiency and a decrease in urinary calcium excretion, but these alterations have not been found consistently across studies (Fig. 8).

V. EFFECTS OF LOW MATERNAL VITAMIN D AND CALCIUM INTAKES ON BREAST MILK VITAMIN D AND CALCIUM CONCENTRATIONS

A. Vitamin D

Vitamin D deficiency leads to rickets in children. Infant formula is routinely fortified with vitamin D, but very low vitamin D concentrations have been found in human milk [85]. Infant serum 25OHD is correlated with maternal vitamin D status early in the neonatal period and is probably a result of placental vitamin D transfer and fetal stores. Beyond the neonatal period, the breast-fed infant’s serum 25OHD concentrations are correlated with neither breast milk vitamin D nor maternal serum 25OHD concentrations [86], and the infant is dependent upon endogenous synthesis or other dietary sources for vitamin D.

Most reported cases of rickets have been of black infants, supporting the premise that persons with dark skin have difficulty synthesizing adequate amounts of vitamin D due to the relative inability of sunlight to penetrate heavily pigmented skin. In addition, the diet of mothers of rachitic infants appears to be low in vitamin D and the mothers may be vitamin D deficient themselves.

Although some investigators have found breast milk vitamin D or 25OHD concentrations to be correlated with maternal intake of vitamin D, mothers who consume 600–700 IU vitamin D/d still have low concentrations of vitamin D in breast milk ranging from only 5 to 136 IU/liter. The biological activity of vitamin D in human milk averages 13 IU/liter, while the 25OHD concentrations represent 38 IU/liter. The average biological activity of vitamin D in human milk is less than 50 IU per day, assuming an average intake of 0.75 liter/d [87].

Investigators recently found that consumption of cod liver oil supplements among Icelandic women increased milk vitamin D concentrations, but the milk concentrations were still below the current Nordic recommendations [88]. Ala-Houhala and co-workers from Finland, in a series of vitamin D supplementation trials, found that supplementing lactating mothers with up to 1000 IU vitamin D/d in northern latitudes during winter months increased maternal serum 25OHD concentrations, but did not stabilize infant serum 25OHD concentrations (Fig. 9) [89]. Maternal supplementation with 2000 IU/d was found to normalize infant serum 25OHD concentrations [90]. There were no differences in infant serum calcium or alkaline phosphatase concentrations when mothers were supplemented with...
either 1000 or 2000 IU vitamin D/d or when infants were supplemented with 400 IU/d.

Specker and co-workers found based on conservative estimates, that exclusively breast-fed infants residing in Cincinnati could maintain serum 25OHD concentrations above the lower limit of normal (11 ng/ml) with 2 hr of sunshine exposure per week if fully clothed except for the face [86]. The cutoff for defining low 25OHD is based on the concentration at which nutritional rickets has been observed. Other factors such as latitude, season, weather conditions, and use of sunscreens may affect vitamin D status. Large seasonal differences in sunlight exposure and serum 25OHD concentrations over the first year of life have been observed in infants followed longitudinally [91]. These findings indicate that the infant’s sunlight exposure plays a more dominant role in determining his or her vitamin D status than the mother’s vitamin D status or milk vitamin D concentrations.

B. Calcium

Two of the randomized trials described earlier that investigated the effect of supplemental calcium on maternal bone changes during lactation also measured milk calcium concentrations. Kalkwarf and co-workers found that women with habitually low calcium intake (<800 mg/d) who were supplemented with calcium (1 g/d) had breast milk calcium concentrations similar to that of women who received the placebo [24] (Fig. 10). Prentice and co-workers also conducted a randomized calcium supplementation trial among Gambian women and found no effect of calcium intake on breast milk calcium concentrations [67]. These results are consistent with older observational studies showing that milk calcium concentrations are not associated with maternal calcium intake [92,93].

VI. CONCLUSIONS

Multiple changes in the maternal calcium economy occur during pregnancy, lactation, and after weaning to protect maternal calcium concentrations while providing sufficient calcium for fetal bone mineral accretion, breast milk production and maternal bone recovery. The strategies to secure calcium during these physiologic states differ. During pregnancy, the primary strategy to secure additional calcium is by increases in serum concentrations of 1,25(OH)2D and intestinal calcium absorption. During lactation, maternal bone is demineralized, possibly because of the lactation-induced amenorrhea, in order to secure adequate availability of calcium for breast milk production. After weaning and the return of menses, maternal bone density increases. Lactation does not appear to have a long-term negative effect on maternal bone density nor does it increase osteoporotic fracture risk. The maternal calcium regulatory system is able to provide sufficient calcium to the fetus and for breast milk even when calcium intake is low. However, there is some evidence that neonatal calcium homeostasis and fetal bone mineral accretion may be compromised when maternal vitamin D status is low or calcium intake is below 600 mg/d.

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