# Vitamin D
## Recommendations during Pregnancy, Lactation and Early Infancy

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*Vitamin D recommendations are shifting. The Institute of Medicine recently revised the Estimated Average Requirement (EAR) from 200 to 400 international units (IU), the Recommended Dietary Allowance (RDA) from 400 to 600 international units (IU), and increased the Tolerable Upper Intake Level (UL) from 2,000 to 4,000 IU per day. What does this mean for the pregnant and lactating woman? To answer this question, current guidelines are described and adapted excerpts from a recent book on the subject are provided.*

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In November 2010, the Institute of Medicine (IOM) published their revised statement on vitamin D requirements (Food and Nutrition Board, 2010). Does the IOM's statement change how we should view vitamin D? Possibly. I believe that the IOM statement is closer to the truth. But like anything else in science, medicine and public policy, it is a work in progress. With our current understanding, how is IOM statement closer to the truth?

The Estimated Average Requirements (EAR), the daily amount expected to satisfy the needs of 50% of the people in that age group based on a review of the scientific literature, was increased from 200 to 400 IU/day and the Recommended Dietary Allowances (RDA; the daily dietary intake level of a nutrient considered sufficient by the Food and Nutrition Board to meet the requirements of nearly all (97–98%) healthy individuals in each life-stage and gender group) was raised to 600 IU/day (Food and Nutrition Board, 1997; 2010). The RDA is calculated based on the EAR and is usually approximately 20% higher than the EAR. Another important change made by the IOM was the increase of the Tolerable Upper Intake Levels (UL) from 2,000 to 4,000 IU/day (Food and Nutrition Board, 1997).

Are these increases adequate for the pregnant and lactating woman? In all fairness to the IOM, they had to review an inordinate amount of literature. They could not include data that had not been published. They also wanted to temper the exuberance that befalls Americans thinking that a little is good and more is better. Yet, the IOM did not extend itself to consider the overwhelming data that have emerged in the last five years that link vitamin D deficiency with immune dysfunction; rather, they restricted themselves to vitamin D and its role in maintaining bone health. As I described earlier, the IOM statement is a work in progress. With that understanding in mind, one has to reach a bit further and consider the big picture about vitamin D and how our understanding has emerged through the centuries–and it is *centuries* of inquiry.

Below is an excerpt and recent adaptation from the book *New Insights into Vitamin D during Pregnancy, Lactation and Early Infancy* (Wagner with Taylor & Hollis, 2010) that describes some of the issues surrounding vitamin D as well as the current recommendations. This excerpt is meant to give you a sense of vitamin D's history and encourage you to go to the primary source for more detail.

## An Overview of Vitamin D

Vitamin D is a preprohormone that has profound effects on metabolism and immune function that extend far beyond bone and calcium metabolism. We are only just beginning to understand its effects on various organ systems throughout the body—from epidemiological studies to its actions at the cellular level. Vitamin D (deficiency) has been linked to inflammatory and long-latency diseases, such as multiple sclerosis, rheumatoid

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arthritis, lupus, tuberculosis, diabetes, cardiovascular disease, and various cancers, to name a few. How can such a simple "vitamin" be involved in such diverse groups of diseases? What is the mechanism? What does it mean to you as an individual, practitioner, or public-policy maker?

There is a renewed interest in vitamin D today. With a rise in the prevalence of vitamin D deficiency in various populations across the globe, particularly in individuals of darker pigmentation or with limited access to sunlight, there has been an urgent need to understand why this has occurred and what effect such deficiency has across the lifespan. Long-standing vitamin D deficiency is linked to a myriad of disease states through its putative effect on the immune system.

How did we get to this place of widespread vitamin D deficiency (Wagner et al., 2008)? Is vitamin D the new vitamin E and vitamin C of the 21st century, the current fad "cure-all"? Health shows, magazine articles, and the lay press write reviews trying to decipher the plethora of emerging data that is published on a weekly basis about the benefits and potential dangers of vitamin D supplementation. The individual is inundated with a vast amount of information to decipher, and to ultimately decide, what should I do?

For pregnant or lactating women, the question becomes even more important, as it impacts women and their unborn children, developing newborns, and infants. Health care professionals must weigh the evidence and decades-old concern that if they supplement a woman with more than 400 IU vitamin D per day, they will make her vitamin D toxic and her unborn fetus will be at risk for birth defects. Public health officials are faced with the decision of recommending higher amounts of vitamin D in vitamins and revising the national recommendations of the upper limit of what is safe for various age groups, or erring on the side of caution in maintaining the *status quo* because it is what has happened for the last four decades, and it is "safe." There is always the underlying tenet of "Do no harm," which must be at the heart of every recommendation. The IOM statement suggests that vitamin D deficiency is overestimated, yet using their own guidelines of a circulating 25(OH)D level of less than 20 ng/mL, in our two pregnancy studies of over 700 women, more than 75% of African American women, 50% of Hispanic women, and 20% of Caucasian women met the criteria for vitamin D deficiency (Hamilton, McNeil et al., 2010).

## Dangers of Vitamin D

As early as the 1920s, reports of vitamin D toxicity surfaced. In an era when individual levels were not easily and reliably measured to document "deficiency" or "sufficiency," individuals were prescribed or given hundreds of thousands of IU's of vitamin D taken for weeks or months, which resulted in the classic symptomatology of toxicity. With careful, meticulous study, definitive "proof" of vitamin D's toxicity and teratogenicity surfaced in the early 1960s. In 1963, Black and Bonham-Carter recognized that elfin facies observed in patients with severe idiopathic infantile hypercalcemia resembled peculiar facies observed in patients with supravalvular aortic stenosis (SAS) syndrome. Shortly thereafter, Garcia et al. (1964) documented the occurrence of idiopathic hypercalcemia in an infant with SAS. The infant also had peripheral pulmonary stenosis, mental retardation, elfin facies, and an elevated blood concentration of vitamin D.

From the 1960s on, there was a rapid decline of rickets, and many believed that modern medicine and science had "cured" rickets. Unfortunately, nutritional rickets reemerged in the 1980s, particularly among African American and other darkly pigmented populations. The recurring characteristics of the reported cases were young age—particularly infants—darker pigmentation, often living at higher latitudes, and exclusive breastfeeding without vitamin D supplementation beyond 6 months of age (Rajakumar & Thomas, 2005). This finding led to a revised American Academy of Pediatrics (AAP) statement in 2003, recommending 200 IU of vitamin

**The question arises: If mom's serum levels are "normal," why would you give baby more oral vitamin D without checking baby's serum vitamin D levels to see if more is needed? The answer is that the amount of vitamin D to achieve the lower level of normal in the mother of 32 ng/mL or 80 nmol/L (in the absence of sunlight exposure: achieved with a daily prenatal vitamin containing 400 IU up to 4,000 IU/day in some women) does not translate into adequate levels in her milk, and thus, for her baby. In this scenario, the mother is replete but on the lower end so her infant is obligated to receive 400 IU/day vitamin D to ensure adequacy in that infant. [See Wagner et al. (2006) for more information.]**

D supplementation to all infants receiving less than 500 ml of fortified formula per day to begin within the first 2 months of life (Gartner, Greer et al., 2003).

Continued reports of rickets, limited dietary sources of vitamin D, inadequate sun exposure for vitamin D synthesis, and an enhanced understanding of vitamin D physiology and its actions have led to the most recent revision of the AAP statement in 2008 (Wagner, Greer, & American Academy of Pediatrics, 2008). The current recommendations are for all infants and children to be supplemented with a minimum of 400 IU per day of vitamin D, beginning in the first few days of life (Wagner, Greer et al., 2008). The issue today, however, is not too much vitamin D, but rather too little. In the past, the margin of safety of vitamin D was narrow.

There was an understandable reluctance to recommend supplementation for fear of causing toxicity. With careful study, it appears that daily vitamin D dosing of less 10,000 IU/day for extended periods is safe (Heaney et al., 2003; Vieth, 1999; Vieth & MacFarlane, 2001).

## Vitamin D Recommendations for Pregnant and Lactating Women and Children

As we discussed earlier, the recommendations for vitamin D requirements have changed during the past

**Table 1. Suggested Vitamin D Supplementation Regimen for Pregnant and Lactating Women, Infants, and Children**

| Age Group | Recommended Daily Vitamin D Intake (IU/day) | Caveats to Ponder |
|---|---|---|
| **Neonates** | 400 IU/day | This includes premature neonates and infants. More data are needed to determine what the IU/kg requirements are of preterm infants and neonates born to mothers with frank vitamin D deficiency. |
| **Infants < 1 year** | 400 IU/day up to 10 kg; then 25-50 IU/kg | |
| **Children 1-2 yrs** | 25-50 IU/kg | For example, a child weighing 20 kg would be given 500-1,000 IU/day. Another child weighing 25 kg would be given 625-1,250 IU/day. One could give the lower dose during summer months and the higher dose during winter months. |
| **Children 2-5 years** | 25-50 IU/kg up to 30 kg | |
| **Children 5-12 years** | 25 IU/kg up to 50 kg | |
| **Children 12-17 years** | >50 kg | 2,000-4,000 IU/day depending on BMI |
| **Pregnant Women** | >45 kg | 4,000 IU vitamin D/day<br>[This recommendation is based on our two RCT that were completed in 2009 (Wagner, Johnson et al., 2010; Wagner, McNeil et al., 2010).] |
| **Lactating Women** | | Likely 6,400 IU/day with refinement of recommendation once Lactation RCT vitamin D studies have been completed and analyzed. |

**This is a conservative guide. If an individual has an increased BMI or a history of malabsorption, then that individual may require higher daily vitamin D supplementation. It would be prudent to check levels if increasing intake beyond these recommendations. The ultimate goal is to attain circulating 25(OH)D levels in that individual that would mimic living in a sun-rich environment with daily sun exposure.*

century as the views of vitamin D's role in metabolism and toxicity have changed. It is a work in progress and each new study that helps us ascertain vitamin D's function within the body in various systems through the lifespan challenges our notion of what is required to reach optimal levels. There have been extensive data to suggest that vitamin D supplementation of 400 IU/day during the first year of life is adequate, but whether that amount is optimal remains to be proved.

**The American Academy of Pediatrics (AAP) statement in 2003, recommending 200 IU of vitamin D per day, was based on the IOM's recommendation at that time centered on preventing rickets in children. Continued reports of rickets, limited dietary sources of vitamin D, inadequate sun exposure for vitamin D synthesis, and an enhanced understanding of vitamin D physiology and its actions have led to the most-recent revision of the AAP statement in 2008. The current recommendations are for all infants and children to be supplemented with a minimum of 400 IU per day of vitamin D, beginning in the first few days of life (Wagner, Greer et al., 2008). (See Chapter 9 of Wagner, with Taylor & Hollis, 2010, for further discussion on the topic.)**

One size does *not*, nor will it ever, fit everyone. Variability in where one lives, one's diet, one's lifestyle, one's body composition (fat mass and lean body mass), and the season affect one's final vitamin D status. As the child grows, on a per kilogram basis, 400 IU/day is likely insufficient beyond a year, especially in those children with limited milk intake and sunlight exposure, in those with darker pigmentation, and who live at higher latitudes. With these caveats in mind, we can ask the question yet again: what should one do when it comes to vitamin D? The answer is found Table 1.

Children would receive incremental doses of vitamin D based on their weight and percent body fat to maintain circulating 25(OH)D levels, with a minimum of 32 ng/mL or 80 nmol/L (Holick, 2007; Hollis, 2005; Hollis et al., 2005; Vieth, 2009). Those children and teenagers with higher BMIs will require higher daily vitamin D intake to achieve a circulating 25(OH)D level of at least 32 ng/mL. Latitude, skin pigmentation, sunlight exposure and sunscreen use, and BMI are all factors that must be taken into account when making recommendations concerning vitamin D supplementation.

Pregnant women would be encouraged to take 4,000 IU/day[2] and lactating women at least 4,000 IU/day, with the expected increase in the recommendation once studies with lactating women and their infants have been completed. Our experience thus far has been that doses of 6,400 IU/day are necessary to raise maternal milk vitamin D levels in the adequate range, so that the infant is ingesting at least 400 IU/L breastmilk. While the efficacy of this dosing regimen has been tested (Wagner et al., 2006), **the safety of this regimen has not been fully tested on a large cohort of women.**

On an individual basis, if a health care professional prescribes higher doses to a lactating woman, it is recommended that the woman's breastfeeding infant have levels checked to ensure that the baby is vitamin D replete. The alternative? Give the lactating woman sufficient vitamin D to achieve a total circulating 25(OH)D level of at least 80 nmol/L or 32 ng/mL and to give her breastfeeding infant the time-honored 400 IU vitamin D/day. With the latter scenario, both mother and infant would have achieved normal vitamin D status. The downside is that both mother and baby would need to be supplemented.

Supplementing both the lactating mother and her baby is the standard of care at this time in the U.S., with 800 IU/day recommended by the Canadians for those [adults] living above latitude 45oN (Canadian Paediatric Society, 2007). In the end, it is not sufficient to accept marginal vitamin D status, just as one would not accept or support marginal status of other hormones, such as thyroxine in someone with hypothyroidism. As is the case with every hormone, we prescribe a regimen to correct the hormonal deficiency and we do not hesitate to check a follow-up level.

The measurement of the nutritional indicator of vitamin D—namely, total circulating 25(OH)D is a fastidious and exacting process. One must ensure that the laboratory that is used has independent validation of the levels reported. Once optimal vitamin D status and how to achieve it has been determined throughout the lifespan, there will be less need to check levels. We will "know" through experience that 4,000 IU vitamin D/day does the "trick" for the pregnant woman, just as we know today that 400 IU vitamin D/day does the "trick" in

[2] The recommendation of 4,000 IU/day during pregnancy comes from our recently completed randomized clinical trials previously presented at Pediatric Academic Societies meeting in Vancouver, May 2010, which will be published later this year.

preventing rickets and other health sequelae in young children.

Our learning curve is steep and we have come a long way since 1999 when Dr. Vieth first wowed the world with his "heretical" high-dose vitamin D safety trial (Vieth, 1999). We continue to build on the exacting rigors of scientific inquiry into the realm of vitamin D, and we should continue to demand nothing less. In the end, we must take the time to appreciate that the needs of our patients may not fit the schema that we have been taught, but rather here before us is a challenge that will help us to better understand and redefine what is really science and medicine at its finest—discovery. It is through such discovery and positive inquiry that we will redefine the vitamin D requirements during the 21st century.

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