# **Editorial >> Robert L. Barbieri, MD** Editor in Chief



# How did we arrive at a worldwide epidemic of vitamin D deficiency?

Our levels of 25-hydroxyvitamin D are distressingly low, putting pregnant women and newborns, among others, at risk

he news is troubling: Humans are, today, absolutely deficient in vitamin D, and evidence is accumulating that this deficiency is damaging the health of our patients and their children. How did we arrive at such a state?

# Sources are numerous but lifestyle and miscalculation confound intake

We have several main sources of vitamin D:

- fatty fish (e.g., salmon, which contains 500 IU in 3 oz)
- eggs (25 IU in one yolk)
- vitamin D-enriched milk products (cow's milk, 100 IU in every 8 oz)
- vitamin D supplements
- exposure to sunlight.

On the whole, we've markedly reduced our exposure to sunlight as we've changed from living outdoors in rural agrarian communities to an indoor urban lifestyle. Dermatologists have long crusaded against

What do you know about vitamin D deficiency?

exposure to sunlight as a way to reduce our risk of skin cancer. And milk intake has dropped significantly over the past decade.

To those shifts, add the fact that the US government and its advisory councils have, historically, recommended an intake of vitamin D—200 IU/d for children and 400 IU/d for adults—that is too low to prevent vitamin D deficiency.

In short, our low exposure to sunlight and our low intake of vitamin D have caused an epidemic of vitamin D deficiency. Here is a look at key facets of the problem; the benefits of maintaining adequate stores of vitamin D; and recommendations for ending the epidemic.

### Pregnant women are vitamin D deficient, most studies show

Measurement of circulating 25hydroxyvitamin D (25OH vitamin D) is an accepted method of assessing vitamin D physiologic status. Many authorities believe that **1**) a 25OH vitamin D concentration >30 ng/mL indicates adequate vitamin D stores and that **2**) a level <20 ng/mL clearly represents vitamin D deficiency. In a recent study of pregnant women from Finland, more than 70% of subjects were vitamin D deficient.<sup>1</sup> In turn, many of the newborns of subjects in the Finnish study were also vitamin D deficient.<sup>1</sup>

**Preventing preeclampsia.** Does vitamin D supplementation in pregnant women reduce their risk of preeclampsia? We don't know—no randomized clinical trial has demonstrated such an effect. But investigators in several observational studies have reported that a low maternal serum concentration of 25OH vitamin D is associated with an increased risk of preeclampsia.<sup>2,3</sup>

In one such study, an imputed total vitamin D intake of 600 to 800 IU/d was associated with a 24% reduction in the risk of preeclampsia from what was seen when total vitamin D intake was 200 IU/d.<sup>4</sup>

## Many infants are vitamin D deficient

Bone mass is reduced in children who are vitamin D deficient.<sup>1</sup> Historically, the American Academy of Pediatrics (AAP) has asserted that vitamin D intake of 200 IU/d was adequate for infants,<sup>5</sup> but the Academy recently changed its recommendation to daily supplementation with 400 IU/d for infants, beginning soon after birth.<sup>6</sup>

A recent survey showed that the majority of children do not receive

#### How much vitamin D is too much?

#### Vitamin D supplements and toxicity

The two commonly available forms of supplemental vitamin D are ergocalciferol ( $D_2$ ) and cholecalciferol ( $D_3$ ). Both are effective supplements,<sup>1</sup> although some authorities contend that cholecalciferol may be slightly better absorbed.<sup>2</sup>

Commercial laboratories typically measure and report **1**) total 25OH vitamin D as a single value, or **2**) two values, one for 25OH vitamin  $D_2$  and one for 25OH vitamin  $D_3$ . If two values are reported, you should add them together to assess the total concentration of 25OH vitamin D. Most authorities believe that a 25OH vitamin D level >30 ng/mL is normal and a value <20 ng/mL is clearly abnormally low.

For **nonpregnant women** who have a 25OH vitamin D level <20 ng/mL, some authorities recommend a weekly dosage of 50,000 IU of vitamin D for 8 weeks followed by a repeat measurement of 25OH vitamin D. If the post-treatment 25OH vitamin D level is >30 ng/mL, a daily dosage of 800 IU is initiated. If the vitamin D level is still very low, the 8-week course of high-dose vitamin D may be repeated.

For **pregnant women**, some authorities recommend a daily dose of 2,000 IU of vitamin D. This can be achieved by taking a prenatal vitamin (vitamin D, 400 IU) and two capsules of vitamin D, 800 IU per capsule, daily. **Toxicity is poorly understood.** The dose of vitamin D that is toxic is not well defined. In 1997, the Institute of Medicine of the National Academy of Sciences concluded that the "tolerable upper intake level" for vitamin D was 2,000 IU daily.<sup>3</sup> Recent data suggest that dosages as high as 10,000 IU/d taken for as long as 5 months are not toxic.<sup>4,5</sup>

Excessive vitamin D intake, especially when combined with calcium supplementation, may be associated with hypercalcemia, hypercalciuria, and kidney stones.

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adequate vitamin D supplementation.<sup>7</sup> Lactation and vitamin D deficiency. The concentration of 25OH vitamin D in breast milk correlates with maternal vitamin D stores. Because most pregnant women are vitamin D deficient, their infants are, when breast-fed, also at higher risk of vitamin D deficiency.<sup>8,9</sup>

Authorities recommend that

all infants who are being breast-fed receive vitamin D supplementation with 400 IU/d.

### Which women are at high risk of vitamin D deficiency?

Women whose skin is darkly pigmented are at high risk of vitamin D deficiency; they require approximately three times the amount of exposure to sunlight as women with lightly pigmented skin to generate the same amount of vitamin D.<sup>10</sup> In one study of pregnant adolescent African-American women, 46% had a 25OH vitamin D level <20 ng/mL.<sup>11</sup>

Women who wear concealing clothes, such as a burka, are also at increased risk of vitamin D deficiency.<sup>12,13</sup>

Women living in poverty may have dietary and lifestyle patterns that limit vitamin D intake and exposure to sun. In a study conducted in Camden, New Jersey, total vitamin D intake was reported to be low in African-American and Hispanic women.<sup>14</sup>

**Musculoskeletal health in women.** Many young women are deficient in vitamin D. In a recent study of 16- to 22-year-old women living in sun-drenched California, 59% of subjects had, surprisingly, a 25OH vitamin D level <30 ng/mL; 41% had a level <20 ng/mL.<sup>15</sup>

Of interest, women in this study who had a low vitamin D level tended to have increased fat infiltration in muscle at the mid-thigh (detected by computed tomographic scanning). Based on other studies, it is now thought that fat infiltration reduces muscle strength and undermines physical performance, including athletic performance. In a study of young adolescents, a positive relationship was detected between the vitamin D level and enhanced muscle function, including muscle power, velocity, and jump height.<sup>16</sup>

**Osteoporosis.** Many postmenopausal women are vitamin D deficient. A low level of vitamin D is associated with decreased intestinal calcium absorption, a negative calcium balance, and a rise in the parathyroid hormone level, which accelerates bone resorption.

A total calcium intake of approximately 1,500 mg/d in postmenopausal women is associated with positive calcium balance. A serum 25OH vitamin D level of about 20 to 40 ng/mL maximally suppresses PTH secretion.

A low 25OH vitamin D level is associated with an increased risk of hip fracture<sup>17</sup>; adequate calcium and vitamin D supplementation reduces the risk of osteoporotic fractures in the elderly. The authors of a metaanalysis of seven randomized trials reported that the risk of fracture was reduced about 35% when women were given vitamin D supplementation at 700 to 800 IU/d—but that risk was *not* reduced at a dosage of 400 IU/d.<sup>18</sup> Similar findings have been reported in other meta-analyses.<sup>19</sup>

A note of caution: In one randomized trial, supplementation with vitamin D and calcium was associated with a 17% increase in the risk of kidney stones.<sup>20</sup>

**Colon cancer.** In prospective observational studies, a strong inverse relationship has been observed between levels of 25OH vitamin D and the risk of colon cancer.

For example, in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, the vitamin D level was measured in health study participants, and analysis of the relationship between this level and new, incident cases of colon cancer revealed that 25OH vitamin D levels >30 ng/mL were associated with a 12% decrease in the risk of colon cancer, compared to subjects with levels of 20 to 30 ng/mL.<sup>21</sup> For subjects who had a 25OH vitamin D level >40 ng/mL, the risk of colon cancer was reduced by 23%.

A prospective randomized trial would be required, however, to prove that vitamin D has a protective effect on the risk of colon cancer.

#### A taste one doesn't soon forget-forgotten

Throughout the 1950s, I remember the mandatory weekly dose of natural cod liver oil, a rich source of vitamin D. Somehow, with a movement away from that weekly regimen, and miscalculation of what constitutes optimal vitamin D supplementation, we've entered a period of worldwide vitamin D deficiency.

It is clear that for most women, vitamin D supplementation at 400 IU/d is inadequate to prevent deficiency. **Most women should consider a vitamin D dosage of 800 to 1,000 IU/d.** Measuring the 25OH vitamin D level, with the aim of providing supplemental vitamin D to achieve a value >30 ng/mL, will help end the epidemic.<sup>22</sup> **@** 

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