

Vitamin D Deficiency in Pregnancy: Bringing the Issues to Light

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In this issue of *The Journal of Nutrition*, Bodnar et al. (1) provide compelling evidence that 1) pregnant women and their neonates living in the northern U.S. are at risk of vitamin D deficiency, 2) this problem is worse for blacks than whites, 3) seasonal variation contributes little to vitamin D status among black women and their neonates, and 4) current formulations of prenatal vitamin supplements may be inadequate to achieve desired serum 25 hydroxy vitamin D [25(OH) D] (storage form of vitamin D) concentrations. The authors analyzed a random subsample of banked maternal and cord serum from 200 white and 200 black participants in the Pregnancy Exposures and Pre-eclampsia Prevention Study, conducted through Pittsburgh clinics. Early in pregnancy, 45% of black mothers (compared with 2% of white mothers) were classified as vitamin D deficient, and insufficiency was common among women of both racial and ethnic groups. By the time of delivery, mothers' vitamin D status improved, but only slightly. The prevalence of vitamin D deficiency for neonates was even greater than that of their mothers. This is particularly striking given that the vast majority of all women reported taking prenatal vitamins by the end of the study period.

Why is this study timely? First, rickets has reemerged in the U.S., particularly among black infants (2). Maternal vitamin D insufficiency was also recently associated with reduced bone mineral accrual in offspring followed for 9 y (3). But apart from vitamin D's well-established role in maintaining proper bone mineralization, vitamin D insufficiency has also been associated in some studies with a host of other health outcomes, including certain cancers, asthma, autoimmune diseases, and diabetes (4,5). Several of these outcomes are linked to early life exposures, and many are more common among black individuals. Ironically, while evidence supporting the many health benefits of vitamin D grows exponentially, evidence is also building that vitamin D deficiency is a common public health problem (6,7). Those most at risk include darkly pigmented individuals (in whom cutaneous vitamin D synthesis is blunted), the elderly, those who, for medical or cultural reasons, avoid sun exposure, and solely breast-fed infants.

This study addressed 2 probable causes of vitamin D insufficiency in this population: inadequate skin synthesis and supplementation. Vitamin D is found naturally in few foods (e.g., fatty fish), so major dietary sources include fortified foods

(primarily milk and some ready-to-eat cereals in the U.S.) and vitamin supplements. However, sun exposure is the most important source, except in the winter among people living at $\geq 37^\circ$ latitude, when UVB rays do not reach the earth surface and cannot form vitamin D precursors in the skin. The authors of this study observed disparate changes in serum 25(OH) D levels between white and black women from winter to summer months: in white women, 25(OH) D levels rose in the summer (although still not enough to eliminate insufficiency), but in black women and their neonates, negligible increases in 25(OH) D levels were observed during warmer months. Although differences in efficiency of cutaneous vitamin D synthesis by race or ethnicity are well-known (6), this study is among the largest to examine these questions in this at-risk population. Information on specific sun exposure practices in both groups would have been informative, but was unavailable, presumably because this was not the primary hypothesis of the parent study.

Perhaps more remarkable was that, by the end of the pregnancy, 90% of all women were taking prenatal vitamins, and yet deficiency was still common. From the study, it is not clear how diligently the women were taking prenatal vitamins (insofar as the regular use of prenatal vitamins was defined as "at least once per week") or whether supplement-use patterns varied by race or ethnicity. A subanalysis of 25(OH) D levels among daily users would have helped clarify the efficacy of prenatal vitamins, which, although they contain 400 international units (IU) of vitamin D, twice the Dietary Reference Intake (DRI) (8) for pregnancy and lactation, may not contain enough vitamin D to raise levels sufficiently (2). Another unknown variable is the form of vitamin D ingested by these women: both ergocalciferol (vitamin D-2) and cholecalciferol (vitamin D-3) are found in vitamin supplements, but D-3 is believed to more effectively raise 25(OH) D. In a national survey, black women of reproductive age who consumed "adequate" vitamin D intakes (200 IU) from diet and supplements still had a high prevalence of low 25(OH) D blood concentrations (7). Moreover, NHANES data show that only half of teenage girls and women consume 200 IU of vitamin D daily (from food and supplements), and the percentages are lower among black women (9). Fortified milk is the largest source of dietary vitamin D in the U.S., but intakes are lower among blacks, presumably due to greater occurrence of lactose intolerance (9).

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Considering these findings, why not raise the DRI for vitamin D? Most experts agree that the current DRI of 200–600 IU (8) is too low, and that, based on current evidence, daily requirements may be closer to 1000 IU (4) or higher (2). Recent reviews and consensus panels on vitamin D and health also conclude that more research is needed on optimal vitamin D doses and blood concentrations for several health outcomes, and on the safety of long-term higher-dose vitamin D supplementation in all populations (2,4,10). However, as noted recently, the official Upper Tolerable Level (UL) of 2000 IU/d makes it difficult to study the efficacy and safety of higher levels (11), and perhaps creates a fear of recommending higher doses. Vitamin D toxicity can occur at much higher intake levels (11) but is rare. Developing expert recommendations is a complex task, because vitamin D needs vary depending on sun exposure (season, latitude, skin pigmentation, and sun exposure practices). Consideration of sun exposure as a source requires weighing the benefits with the risks of UV exposure on the development of melanoma and cataracts (12). To minimize health risks from UV exposure and maximize vitamin D status, a balanced diet, supplementation, and limited amounts of sun exposure are the preferred methods for obtaining vitamin D (10,13). Momentum is building for an updated review of the DRI by the Institute of Medicine. Such an authoritative review would shed light on the gaps in research and practice and provide needed guidance to professionals, health organizations, food manufacturers, and the public, in order to move research forward and improve public health.

The study in this issue illuminates the danger of assuming that prenatal vitamins in their present form are ensuring vitamin D sufficiency in pregnant women and their newborns. Whereas more studies are needed to determine precise vitamin D requirements in all populations, we do have enough evidence to show that current practices are not serving at-risk groups. Because pregnant women are already under medical care and taking a prenatal vitamin, the benefits of a higher dose of vitamin D supplementation and perhaps 25(OH) D screening (in high-risk groups) is worthy of further investigation.

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