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## Vitamin D deficiency in the 21st century: a persistent problem among Canadian infants and mothers

## Leanne M. Ward

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Titamin D deficiency is an age-old public health problem. It was first described, as rickets, in the mid-17th century by Francis Glisson and other fellows of the Royal College of Physicians in London. Although there has long been a folk understanding of the therapeutic benefit of cod-liver oil (such as is speculated to have been given to Dickens' Tiny Tim), discovery of the biochemical structure of vitamin D in the 1930s led to a scientific understanding of the importance of sunshine and dietary sources to prevent vitamin D deficiency. In recent years, despite this understanding and the numerous preventive and therapeutic strategies now available, vitamin D deficiency has resurfaced as a global health problem among infants and children.

Vitamin D plays a key role in bone development by promoting calcium absorption in the gut. Its main source is synthesis in the skin after cutaneous exposure to ultraviolet B rays. When northern latitudes, darker skin, sun blocks or lifestyle choices limit our exposure to sunshine, vitamin D levels can be maintained through the intake of supplements and of foods that contain natural or added vitamin D. Adequate vitamin D concentrations during pregnancy are crucial to provide the calcium needed for fetal bone mineral accretion, most of which occurs in the final trimester. A severe deficiency in vitamin D takes a heavy toll on the growing skeleton by causing impaired mineralization of bone tissue (leading to osteomalacia) and of the growth plate (which manifests as rickets). Profound vitamin D deficiency during pregnancy can result in neonatal rickets.<sup>1,2</sup>

The consequences of milder vitamin D deficiency during fetal development — that is, deficiency less severe than that which causes rickets — are less well understood. It is known that vitamin D deficient mothers and their babies have lower serum calcium and higher parathyroid hormone levels.<sup>3-5</sup> Only 1 study has investigated the effect of vitamin D status on newborn skeletal mineralization; over 20 years ago, Congdon and colleagues<sup>6</sup> measured forearm bone mineral content (BMC) in infants born to Asian and white mothers and found that infant BMC was independent of vitamin D supplementation during pregnancy and had no relation to umbilical cord 25-hydroxyvitamin D levels.

The study by Weiler and colleagues reported in this issue<sup>7</sup> (see page 757) adds new data to the picture. Plasma vitamin D levels were measured in 50 mother–newborn pairs from the Winnipeg area, and the results were related to the BMC of the newborns. Almost half of the mothers and

over one-third of the newborns had plasma 25-hydroxyvitamin D levels in what the authors considered to be the deficient range. As expected, vitamin D deficiency was more common in non-white mothers and their infants. BMC values were similar in infants with vitamin D deficiency and sufficiency, but the vitamin D deficient newborns were, on average, heavier and longer than those with adequate vitamin D levels. As the authors note, heavier newborns are expected to have a heavier skeleton. The finding of similar BMC values in the presence of a larger body weight in the vitamin D deficient group therefore may be indicative of a relative paucity of bone mineral.

The authors draw 3 main conclusions from their report: (1) newborn vitamin D deficiency has a positive impact on birth weight and length; (2) infant (but not maternal) vitamin D deficiency leads to lower infant bone mass relative to body weight; (3) women and newborns in the Winnipeg area are at risk for vitamin D deficiency.

The first conclusion is inconsistent with earlier studies, which have found maternal vitamin D deficiency to have either a negative or no effect on offspring birth weight.<sup>6,8-10</sup> In a double-blind, controlled study, Maxwell and colleagues showed that supplemental vitamin D given to women in the third trimester of pregnancy did not affect birth weight or length.<sup>11</sup> In the Weiler and colleagues' study, sample size or unmeasured differences between the vitamin D deficient versus sufficient groups may have contributed to their unexpected finding.

The second conclusion is also in contrast to the (scant) literature. As discussed, Congdon and colleagues found no relation between umbilical cord blood 25-hydroxyvitamin D levels and infant BMC.<sup>6</sup> It is possible that the improved sensitivity of newer densitometric methods has led to this difference in results. Weiler and colleagues also note that, in their Winnipeg cohort, mothers with vitamin D deficiency were significantly younger and more likely to be non-white than mothers with adequate vitamin D. Untested differences resulting from maternal age, ethnicity or both may have affected the BMC results in the infants. These discrepancies merit further study.

The third conclusion highlights an important care gap in this country: vitamin D deficiency among Canadian mother–infant pairs is a persistent problem despite existing recommendations for its prevention and despite ready access to vitamin D supplementation. This is consistent with observations worldwide; even in developed countries with plenty of sunshine, vitamin D deficiency remains an issue.<sup>12</sup> Recent reports through the Canadian Paediatric Surveillance Program have highlighted the fact that the prevention of vitamin D deficiency rickets is frequently overlooked in Canada, and that breast-fed, darker skinned infants are at greatest risk (although fair-skinned infants are not exempt).<sup>13,14</sup> Additional risk factors for rickets, as discussed in these reports, include maternal lack of vitamin D supplementation during pregnancy and lactation.

Breast milk is indisputably the ideal food source for infants. However, it is not a rich source of vitamin D, a fact that becomes relevant at our northern latitude. The current recommendation for prevention of vitamin D deficiency rickets is for breast-fed infants to receive a daily oral supplement of vitamin D (400 IU/day). For breast-fed infants residing above the 55th parallel or at lower latitudes with a high incidence of vitamin D deficiency, 800 IU/day are recommended during the winter months.<sup>17</sup> Bottle-fed infants on standard infant formula, and infants who have "graduated" to commercially produced cow's milk, receive appropriate amounts of vitamin D by way of fluid fortification. Although the American Academy of Pediatrics has recently recommended a decrease in the amount of vitamin D required for rickets prevention from 400 to 200 IU/day, 18 preliminary results suggest that in the northern United States this quantity may not be adequate to prevent a vitamin D deficient state. 19 Given Canada's more northern latitude, multi-ethnicity resulting in variable skin colour, and the fact that 400 IU/day of vitamin D has long-standing safety and effectiveness for rickets prevention, 400 IU/day remains a sound recommendation for Canadian infants.

The need for attention to maternal vitamin D intake during pregnancy and lactation is suggested by observational studies and vitamin D supplementation trials involving pregnant women, most of which show improved neonatal calcium metabolism when maternal vitamin D status is optimized. 6,8-10,20,21 The current recommendation for prevention of vitamin D deficiency in pregnancy is 400 IU/day.<sup>22</sup> For pregnant and nursing mothers above the 55th parallel, the Indian and Inuit Health Committee of the Canadian Paediatric Society recommends that vitamin D intake be increased to 800 IU/day from October to April.<sup>17</sup> To date, the balance of evidence does not support supplementation during pregnancy above amounts typically required to prevent vitamin D deficiency.23 Until more data are available on the safety and efficacy of higher daily dose and pulse vitamin D therapy (for pregnant and nursing mothers and their infants, alike), it is not recommended that such therapy be administered routinely.

The impact of vitamin D deficiency during fetal development and the growing years may well prove to extend beyond rickets. It is now recognized that attention to bone development during the years when the skeleton is "under construction" is key to the optimization of bone health throughout the lifespan. To this end, the long-term impact of vitamin D deficiency during fetal and childhood skeletal development,

and the most appropriate dose and timing for vitamin D supplementation, remain important areas for study.

Leanne Ward is a Canadian Institutes of Health Research New Investigator, Assistant Professor of Pediatrics, University of Ottawa, and Pediatric Endocrinologist, Children's Hospital of Eastern Ontario, Ottawa, Ont.

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Correspondence to: Leanne M. Ward, 401 Smyth Rd., Ottawa ON K1H 8L1; fax: 613 738-4236; ward\_L@cheo.on.ca