Perspective on the paper by Dijkstra et al (see page 750)

Mother-child vitamin D deficiency: an international perspective

Adekunle Dawodu, Carol L Wagner

Rickets is often considered a 19th century disease. However, despite the availability of vitamin D and demonstration of its efficacy in preventing rickets, vitamin D deficiency rickets still exists as a public health problem with significant morbidity in the Middle East and in many Asian countries, and has been reported with increasing prevalence in minority groups in North America and in immigrant populations in Europe, Australia and New Zealand. In many countries, there are reports of a high prevalence of subclinical vitamin D deficiency in children and adolescents and rickets may merely represent the tip of the iceberg.

With more studies, there are reports from many countries of a high prevalence of vitamin D deficiency in women of child-bearing age and during pregnancy and in nursing mothers, with likely adverse consequences for women, the fetus and growing infants and children. What seemed to be a rare entity has become so common that by the end of 2006 a lot of literature had been published that linked vitamin D deficiency with long-latency diseases, with vitamin D deficiency and childhood vitamin D deficiency and rickets are inter-related at least in populations where “sunshine deprivation” is very common? Further, are current recommended supplements for preventing vitamin D deficiency in women and children adequate if sun exposure is insufficient?

INSUFFICIENT SUN EXPOSURE AND VITAMIN D DEFICIENCY

The story of deficiency begins with vitamin D itself and its primary mode of synthesis, which is from sunlight. This chemical moiety forms from epidermal 7-dehydrocholesterol when UV-B at 290–310 nm hits the skin creating pre-vitamin D3 which is then transformed to vitamin D3. Subsequently, vitamin D is transferred via blood to the liver to become 25-hydroxyvitamin D (25(OH)D), an important prehormone whose active metabolite 1,25(OH)2D is involved in many metabolic processes beyond bone integrity and calcium homeostasis.

In comparison to sunlight, diet provides on average less than 10% of the body’s vitamin D requirements in the best of circumstances. However, a full body sunlight exposure during summer months for 10–15 min in a lighter pigmented adult individual will generate between 10 000 and 20 000 IU vitamin D3 within 24 h; darker pigmented individuals require up to 10 times more exposure to generate similar levels of vitamin D3. The amount of UV exposure available for the synthesis of vitamin D depends on many factors other than time spent outdoors, such as degree of skin pigmentation, body mass, latitude, season, the extent of air pollution blocking UV light, the amount of skin exposed and type of clothing, and the level of UV protection including sunscreens.

In the Middle East and other Arab countries, time spent outdoors is severely limited and for cultural and religious reasons, the dress style of women outdoors prevents exposure of skin to sunlight. In many other parts of the world lifestyle changes are resulting in a decrease in time spent outdoors. In the US and other Western countries, there has been a shift from outdoor activities to time spent indoors. In the US alone, Americans were found to spend an average of 93% of their time indoors.

Compounding the problem is the real concern that sunlight itself, the very entity that quickly creates vitamin D in our skin, has deleterious health effects when exposure occurs in high concentrations or for sustained periods, especially in individuals with lighter pigmentation. In order to limit exposure to ultraviolet light, the US Centers for Disease Control and Prevention, with the support of many organizations including the American Academy of Pediatrics and the American Cancer Society, have launched a major public health campaign to increase public awareness about sunlight exposure and the risks of various skin cancers. In many populations, there are conflicting concerns: on the one hand there are concerns about the hazards and consequences of excessive sun exposure and on the other there are concerns about current lifestyles with inadequate sun exposure increasing the risk of vitamin D deficiency.
and fetal (cord blood) circulating 25(OH)D levels, and is supported by recent studies from many countries, including the UAE, Iran, India, the United Kingdom, Greece and the US that have demonstrated a high prevalence of vitamin D deficiency in mother-infant pairs at birth. Even infants born to vitamin D replete mothers become vitamin D deficient after 8 weeks if not supplemented with vitamin D, while an unsupplemented infant born to a vitamin D deficient mother will reach a state of deficiency more quickly than an infant whose mother was replete during pregnancy. The significance of maternal deficiency during pregnancy is that the fetus is developing in a state of hypovitaminosis D, which likely has significant effects on innate immune function and fetal and childhood bone development. With severe maternal vitamin D deficiency, the fetus may rarely develop rickets in utero and manifest this deficiency at birth.

As one would predict, based on the physiology of vitamin D, the vitamin D content of human milk is related to the lactating mother’s vitamin D status. In lactating mothers supplemented with 400 IU/day vitamin D, the vitamin D content of milk ranges from 25 up to 78 IU/l. Based on the concentration of vitamin D in the milk of mothers who have marginal vitamin D status or who are deficient, infants who are exclusively breastfed but who do not receive supplemental vitamin D or adequate sunlight exposure have a high prevalence of vitamin D deficiency based on serum 25(OH)D levels and are therefore at increased risk of developing vitamin D deficiency rickets. In many populations where sunshine exposure is severely limited and vitamin D supplementation is not generally practiced, there is also a high prevalence of vitamin D deficiency in nursing mothers. From the above data it is clear that severe vitamin D deficiency is a growing concern internationally in pregnant and non-pregnant women and nursing mothers.

Childhood Vitamin D Deficiency and Rickets and Inter-Relationship with Maternal Vitamin D Deficiency

Vitamin D deficiency is the major cause of rickets around the world. Recent reviews indicate that vitamin D deficiency in childhood and rickets are public health problems in the Middle East and North Africa, some parts of Asia, and among immigrant populations in the UK, Netherlands, Denmark, Norway, Spain, Australia and New Zealand and have re-emerged as an important public health issue in minority groups in the US. Studies examining the vitamin D status of mothers of rachitic children have demonstrated a high prevalence of maternal vitamin D deficiency. Further, there is a higher prevalence of vitamin D deficiency in the mothers of rachitic than non-rachitic children; the authors of that study suggested that the vitamin D status of mothers of children with vitamin D deficiency rickets should be assessed. Taken together, the data from these studies indicate a link between maternal vitamin D deficiency and childhood rickets. The connection may be a combined effect of the positive relationship between maternal vitamin D nutritional status and vitamin D status in early infancy and a similar pattern of maternal and childhood sun exposure. In some populations at least, it is reasonable to view rickets and maternal vitamin D deficiency as inter-related, with important implications for a shift in the strategy for comprehensive prevention of vitamin D deficiency in women and children.

Current Recommendations of Vitamin D Requirements and Future Strategy

If sun exposure is insufficient, how adequate are the current recommendations to prevent vitamin D deficiency in mothers and children? Although vitamin D supplementation is effective in preventing vitamin D deficiency, the optimal vitamin D requirement in women and children is still unknown. In the past, studies by Delvin et al., Mallet et al. and Cockburn et al. showed that vitamin D supplements below 2000 IU/day did not effectively prevent deficiency. In pregnant women treated with 1000 IU vitamin D/day, maternal serum 25(OH)D levels ranged from a mean of 9.5 nmol/l at baseline to 25.3 nmol/l after receiving 1000 IU vitamin D/day during the last trimester. The post-supplementation value is consistent with the definition of deficiency. In a more recent study, supplementation of pregnant women belonging to minority groups in the UK with 800–1600 IU of vitamin D during pregnancy increased serum 25(OH)D levels from a mean of 14.5 nmol/l at baseline to only 28 nmol/l at term. In view of the complications of vitamin D deficiency, there is an urgent need to identify optimal vitamin D requirements in pregnancy. Recent studies indicate that vitamin D supplementation of >2000 IU/day is safe and effective in achieving vitamin D sufficiency in men and non-pregnant women. Studies are underway in the US to establish vitamin D requirements during pregnancy (http://clinicaltrials.gov/ct2/show/NCT0022263). There also are attempts to evaluate vitamin D requirements in lactating women. In a pilot study, vitamin D supplementation of 4000 IU/day of vitamin D2 was superior to 2000 IU/day in preventing hypovitaminosis D in lactating women. In another recent study from the UAE, vitamin D2 supplementation of 2000 IU/day or 60 000 IU/month in lactating women for 3 months was effective in achieving a serum 25(OH)D concentration >50 nmol/l in only 27% of the patients studied. In these studies, there were no reports of vitamin D toxicity. Given the results of these recent studies, higher doses of supplemental vitamin D than currently recommended appeared to be required to prevent vitamin D deficiency in lactating women, and should be investigated further.

The current accepted recommendation to prevent rickets in children includes supplementation of exclusively breastfeeding infants with 200–400 IU/day of vitamin D and ensuring adequate calcium intake. There are, however, not enough data to show that the recommended effective internationally. Although supplementation of the infant may prevent vitamin D deficiency in exclusively breastfeeding infants, it would not ensure the vitamin D sufficiency of the nursing mothers. Researchers, therefore, have begun to investigate the possibility of preventing vitamin D deficiency in lactating women and their breastfeeding infants through high-dose maternal vitamin D supplementation.

Studies in the 1980s showed that supplementation of nursing mothers with 2000 IU rather than 1000 IU of vitamin D had a significant effect on the breastfeeding infant’s vitamin D status as measured by infant serum 25(OH)D levels. Expanding on these findings, in two recent pilot studies involving lactating women supplemented with high-dose vitamin D of up to 6400 IU/day for 6 months, the vitamin D content of milk increased to levels as high as 873 IU/l without any evidence of maternal vitamin D toxicity. The serum 25(OH)D levels in the infants of mothers on 6400 IU/day increased from a mean of 32.5 nmol/l to 115 nmol/l and were similar to those of infants receiving 300–400 IU vitamin D/day whose 25(OH)D levels increased from a mean of 35 nmol/l to 108 nmol/l. Similarly, the vitamin D status of the mothers on high-dose supplementation increased from a mean serum 25(OH)D level of 85 nmol/l at baseline to 147 nmol/l after supplementation. Although vitamin D levels can be increased in the milk of lactating women taking large vitamin D supplements, such high dose supplementation in lactating women must be validated and demonstrated to be safe in larger, more representative populations of lactating women.

In summary, the shift from vitamin D sufficiency to deficiency has occurred in many populations as a result of insufficient
sun exposure and inadequate corrective vitamin D supplementation. Published data indicate that vitamin D deficiency may be an unrecognised public health problem in women, nursing mothers and children in many populations. At least in populations where sun exposure in women and children is severely limited, there is an inter-
relationship between maternal vitamin D deficiency and childhood rickets. There is an urgent need to determine the optimal dose of vitamin D to ensure vitamin D sufficiency45 in pregnant and lactating women when sun exposure is inadequate. A strategy to prevent vitamin D deficiency in infants through maternal supplemen-
tation which would achieve the double effect in infants through maternal supplementa-

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an urgent need to determine the optimal dose of vitamin D to ensure vitamin D sufficiency among African American and white women of reproductive age living in Detroit, Michigan and healthy western Canadians. CAMJ 2002;166:1517–24.


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tives. The time for action is now.
Vitamin D in pregnancy: an old problem still to be solved?

A F Williams

Perspective on the paper by Dijkstra et al (see page 750)

In this issue Dijkstra et al describe the high incidence of hypovitaminosis D (serum 25-hydroxyvitamin D <25 nmol/l) amongst infants born in Rotterdam, the Netherlands (latitude 52°N). Babies born to veiled or dark-skinned mothers were significantly more likely than those of white mothers to have a low 25-hydroxyvitamin D (250HD) concentration in umbilical cord blood. Similarly, a recent study of pregnant women in the Hague found that 56–66% of women in ethnic minority groups residing in the northern Netherlands (latitude 52°N) were most likely to be affected, with 8% of women of Western origin.1 Given that the vitamin D status of nursing women and their neonates is borne out by the National Diet and Nutrition Survey of British adults: 28% of women aged 19–24 and 13% of those aged 25–34 had plasma 25OHD concentrations <25 nmol/l. These findings suggest that infants who present clinically with vitamin D deficiency, either in the neonatal period or later with clinical rickets, represent only a small proportion of those with suboptimal vitamin D status.

How can the risk of vitamin D deficiency in pregnancy, and by implication in infancy, be reduced? In 1991 the Committee on Medical Aspects of Food and Nutrition Policy (COMA) set a reference nutrient intake (RNI) of 10 μg/day (400 IU/day) vitamin D for women who are pregnant or breast feeding.2 This amount was chosen as sufficient to maintain plasma 250HD >20 nmol/l during the winter months in Scotland and was endorsed by COMA as recently as 1998.3 Whilst sunlight exposure is generally of greater importance than diet in the maintenance of vitamin D status, there is no ambient ultraviolet light of the appropriate wavelength at UK latitudes during the winter months. For this reason maintenance of adequate vitamin D status in pregnancy is best achieved through dietary means. However, the average vitamin D intake of young women in the UK approximates 3 μg/day and fewer than 1% consume more than the 10 μg RNI.4 Achieving the RNI therefore necessitates supplementation. The advice applies to all women and not merely those in ethnic minority groups, yet very few women take a vitamin D supplement during pregnancy and an individual woman’s risk of deficiency in pregnancy seems rarely to be assessed.

Unfortunately there have been many barriers to policy implementation. These

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