

Vitamin D: A review of the literature

CASE: 14-month-old Janine (not her real name) was referred for assessment of her “bowed legs.” X-rays showed cupping and fraying of the metaphysis and osteopenia. Further history revealed that Janine had been exclusively breastfed until 6 months of age but had not received vitamin D supplementation. Janine has vitamin D deficient rickets.

There has been an explosion of scientific and media attention related to the health effects of vitamin D supplementation. Vitamin D’s pivotal role in regulating calcium homeostasis and bone metabolism has long been recognized.¹ However, mounting evidence suggests that vitamin D may also influence cardiovascular disease, hypertension, diabetes, cancer, autoimmune disorders, and mortality. Claims that large segments of the population have inadequate vitamin D concentrations have prompted calls to increase vitamin D intake through supplementation or food fortification.

Ecological studies have reported higher rates of diabetes, hypertension, and coronary heart disease with increasing distance from the equator,² which suggests a possible association with vitamin D insufficiency in regions with less sun exposure to the skin (an important source of vitamin D).³ For instance, vitamin D intake is at the same low level in Denmark as in other Nordic countries with the exception of Iceland. The widespread use of cod liver oil in Iceland and previous lack of food fortification in Denmark may account for the lower levels.² Recent studies published in Canada corroborate this.⁴⁻⁶ Poor nutritional status found in circumstances of poverty and among indigenous and First Nations peoples place them at further risk.^{7,8} Australia has also reported low vitamin D levels in dark-skinned and

veiled women,⁹ as well as in mothers of children with rickets.¹⁰ The following is a brief summary of the current research.

Vitamin D metabolism

Vitamin D₃ (cholecalciferol) is taken in the diet (fortified dairy products and fish oils) or is synthesized in the skin from 7-dehydrocholesterol by ultraviolet irradiation. It is transported in the blood by the vitamin D binding protein (DBP) to the liver. In the liver it is hydroxylated, resulting in the formation of 25 hydroxyvitamin D₃ (25(OH)D₃). This is then transported to the kidney by DBP. In the proximal renal tubule 25(OH)D₃ is hydroxylated, resulting in the hormonally active form of vitamin D, 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃), which is responsible for most if not all of the biologic actions of vitamin D.¹¹

Immune modulation

Vitamin D acts on target cells in a steroid hormone-like manner, by binding to a specific nuclear receptor called the vitamin D receptor (VDR). A review of the literature reveals there is mounting evidence that the incidence and severity of autoimmune diseases, including rheumatoid arthritis, type 1 diabetes, inflammatory bowel disease, and MS may be reduced by increasing vitamin D levels.^{12,13} Observation that this happens only with adequate calcium intake underlines the importance of normal serum calcium in the regulation of autoimmune response.¹³ In pregnancy, the placenta regulates communication and transport between mother and

fetus. The immunosuppressive effects of 1,25(OH)₂D₃ are crucial for allowing proper trophoblast invasion of the uterus.¹¹ Impaired vitamin D status may also lead to aberrant response to infection.¹³

Cardiometabolic

Vitamin D has been documented as down-regulating the renin-angiotensin system and affecting BP positively.^{14,15} Two recent reviews found the association between vitamin D status and outcomes tenuously supportive but the studies, because of their design, were inconclusive.^{2,13} The limited data suggest that vitamin D supplements at moderate to high doses may reduce cardiovascular disease, but further research is needed.¹⁶

Neurological

Vitamin D activates receptors on neurons in regions implicated in the regulation of behavior, stimulates neurotrophin release, and protects the brain by buffering anti-oxidant and anti-inflammatory defence against vascular injury. There is growing evidence for a relationship between vitamin D receptors in the brain, hypovitaminosis D and abnormal cognitive executive functions, major depression bipolar disorder, and schizophrenia.¹⁷ Hypovitaminosis D has previously been connected to the autoimmune effects of multiple sclerosis.¹³

Canadian perspective

Studies quoted previously report low levels for vitamin D in Canada.^{6,7} Conference Proceedings of First Nations Nutrition and Health (2003) outline

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loss of traditional foods, which has a role. An example is the oolichan grease harvested from fish (*Thaleichthys pacificus*) referred to in Native culture as “liquid sunshine” since it is rich in fat-soluble vitamins including vitamin D.^{8,18-20} In addition, maternal vitamin D status is an important factor in determining the vitamin D status of infants and their risk of developing vitamin D deficiency and infantile nutritional rickets.²¹ In Canada the reality of vitamin D deficiency and rickets is real and significant, especially in First Nations populations. The Canadian Paediatric Surveillance Program reported 104 confirmed cases of rickets in Canada between 2002 and 2004; 13% were of First Nations descent and 12% of Inuit descent.²² As a result, the Canadian Pediatric Society has developed the position statement “Vitamin D supplementation: Recommendations for Canadian mothers and infants” to assist physicians in managing this important health issue (www.cps.ca/english/statements/ii/fnim07-01.htm).

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Key points

The health effects of vitamin D supplementation are significant. Vitamin D plays a major role in bone mineralization and bone strength and research suggests vitamin D also has immune-modulating properties affecting the severity of certain autoimmune diseases and neurological diseases. It also appears to have a positive effect on blood pressure. Vitamin D deficiency is an important health concern for Canadian mothers and their infants and appropriate supplementation is necessary. Further information regarding vitamin D supplementation can be found at the Health Canada and US National Institute of Health websites:

- www.hc-sc.gc.ca/fnan/nutrition/vitamin/vita-d-eng.php
- <http://ods.od.nih.gov/factsheets/vitamind/>

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