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Skeletal and Non-Skeletal Role of Vitamin D: Are We Getting Enough?

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Introduction

From the standpoint of public perception, vitamin D only relates to bone health, because of the notion that vitamin D is only needed to help in the absorption of calcium. Vitamin D is also perceived as potentially toxic. It is believed that great caution should be exercised in considering or promoting its consumption. Based on recent evidence these perceptions need to be evaluated.

Recommendations for vitamin D intake were initially intended to prevent rickets in infants. In essence, the infant dose of 400 IU/day was selected because it approximated what was in a teaspoon-full of cod-liver oil. Cod-liver oil had been a folk remedy for almost 200 years, for the vague purpose of helping babies to thrive[1]. The dose happens to be appropriate for preventing rickets. Until recently, there has been no objective measure of the quality of vitamin D nutrition in adults. During the past 25 years, the criteria of vitamin D nutritional adequacy for adults has progressed from a vitamin D intake ensuring protection against osteomalacia (adult rickets), to an intake that suppresses parathyroid hormone secretion, and more recently, to prevent osteoporosis[2,3]. To achieve these latter targets, specific blood levels of 25-hydroxyvitamin D [25(OH)D] must be maintained.

Based on the serum 25(OH)D concentrations of Canadians, there is strong evidence that vitamin D is the one nutrient that we are most deficient in during winter. Despite this fact, supplementing with vitamin D particularly during winter is rarely promoted.

The past decade has seen a rapid growth in knowledge about vitamin D. In 1997, North American nutritional recommendations for calcium and vitamin D were revised[2]. For adults over age 70 years, the recommended intake for vitamin D was tripled, in what is still regarded as the largest ever increase for any nutrient recommendation. Even with that, the amounts of vitamin D consumed by North American adults remain inconsequential in terms of ensuring that circulating 25(OH)D levels are in the desirable range.

The first part of this review summarizes vitamin D nutrition consistent with current guidelines[2]; the second part presents evidence of how specific vitamin D intakes affect circulating 25(OH)D concentrations and summarizes the effects of vitamin D nutrition that are not related to bone.

PART I
Adult Bone Health

On average adults resorb (dissolve away) just under 1% of the skeleton every month, and at the same time put almost that much back. After about age 35, we only put back about nine tenths of what we take out of the skeleton. The calcium in our bones could be thought of like a retirement bank account where withdrawals exceed deposits. With this analogy, osteoporosis is a form of bankruptcy that pertains to the amount of calcium stored in the skeleton. Here, depletion results in bones that might no longer withstand some of the normal stresses of everyday living. Consequently, minor falls or unusual movements can result in a fracture. Current treatments for osteoporosis restore bone density by a few percentage points, hence stabilizing the condition.

Bone mass falls faster during the winter months, and during the summer bone density remains fairly stable. The group headed by Bess Dawson-Hughes showed that vitamin D supplements eliminate the faster fall in bone density during winter[4]. And when vitamin D is used along with calcium supplements, it is difficult to tell which is doing more good at the bone, the vitamin D or the calcium[5,6]. They probably act together by providing calcium, and by suppressing the secretion of parathyroid hormone [PTH].

For the elderly starting to take calcium and vitamin D, the risk of fracture is reduced fairly quickly, even though bone density is not increased by enough to account for the fewer fractures[6]. What is not yet common knowledge, is that vitamin D improves muscle strength and balance -- it is thought that this is what reduces the occurrence of falls that cause fractures[7].

Vitamin D does not necessarily have to be at the stomach at the same time as the calcium. Vitamin D is the raw material needed to make a hormone, through a 2-step process. After vitamin D enters the blood via the skin or the diet, the liver automatically converts it to 25(OH)D within a day or two[8]. This compound has a half-life of about two months, and conventional dogma regards 25(OH)D as having no activity by itself. However, 25(OH)D is the best measure of vitamin D nutritional status, and it is the main criterion for diagnosing nutritional rickets or osteomalacia. The kidney functions as an endocrine gland, using 25(OH)D to make the hormone 1,25-dihydroxyvitamin D [1,25(OH)2D, or calcitriol]. Synthesis of 1,25(OH)2D is greatest when calcium supplies are lowest. The hormone induces the active transport of calcium through intestinal mucosa. The minimal supplies of vitamin D needed to normalize 1,25(OH)2D synthesis are not enough to prevent rickets or osteomalacia. Further increases in vitamin D will not increase 1,25(OH)2D levels[9-12]. As kidney function deteriorates, its endocrine capability also declines, and thus a low 1,25(OH)2D level reflects impaired renal function, not poor nutrition[13].

Current Nutritional Recommendations

Nutritional recommendations specify 200 IU of vitamin D per day for infants and for adults under age 50. For those between 51 - 70 years age, the recommended intake is 400 IU of vitamin D per day; and for adults over 70 years, 600 IU per day[2].

In Canada, it is a legal requirement that dairy milk for drinking must contain vitamin D. Other products produced from milk, like butter, ice cream, and yogurt cannot contain vitamin D. Conventional, milk-containing North American diets provide about 200 IU per day (100 IU per glass), but close to half of the population does not drink milk at all. There is some vitamin D in ocean fish like cod and salmon, but since we do not eat these regularly, their contribution to vitamin D intake of Canadians is limited. Nutritional legislation assumes that we get at least 200 units from the sun, and that occasional exposure of the face and hands to sunlight is enough.

PART II
The RDA for Vitamin D

The working definition of recommended dietary allowance [RDA] is to ensure "levels of intake of essential nutrients considered... to be adequate to meet the known nutritional needs of practically all healthy persons"[14]. From this, one should assume that if the recommended intakes of vitamin D are maintained, they will protect adults from vitamin D insufficiency, the definition of which now involves suppression of PTH[15,16]. Our own data, based on nutritional questionnaires and measurement of 25(OH)D show no connection between the biochemical measurement, and subjects' stated vitamin D intake. Likewise, two recent studies cast doubt on the current RDA value for vitamin D beyond childhood. In immigrant women in Denmark, Glerup et al could not uncover any prevention of 25(OH)D < 40 nmol/L when 5-15 µg/d (200–600 IU) was taken[17]. In Finland, 10 µg/d (400 IU) vitamin D was given to 9 to 15-year-old girls to test whether this would protect from developing 25(OH)D concentrations below 37.5 nmol/L during winter. There was no protective effect[18].

Non-bone Effects of Vitamin D

The level of evidence needed to make a health claim involves direct intervention, the controlled administration of the agent to many healthy people, and showing an effect that stands up to statistical analysis. The evidence for following is based on cross-sectional studies. Although the effects described here are statistically significant, the cross-sectional nature of such studies would regard the quality of evidence implicating vitamin D as still

circumstantial. Epidemiological studies show that higher serum 25(OH)D, or environmental ultraviolet exposure is associated with lower rates of cancer, particularly of the breast, ovary, prostate, and colon[19-26]. Multiple sclerosis is more prevalent in populations having lower levels of vitamin D nutrition or ultraviolet exposure[24,27], and it has been proposed that vitamin D intake, ranging from 1,300 to 3,800 IU per day, helps prevent the disease[27]. Established osteoarthritis progresses more slowly (i.e less severe) in adults with higher vitamin D nutritional status; McAlindon recommends serum 25(OH)D exceed 75 nmol/L for adults with osteoarthritis[28,29]. Hypertension is more prevalent with distance, north or south, from the equator[30]. Blood pressure goes down in subjects whose 25(OH)D levels are raised to over 100 nmol/L by tanning[31]. Vitamin D deficiency impairs immune function in animals[32]. In children there is a strong association between pneumonia and nutritional rickets[33]. If any of these non-traditional effects of vitamin D were taken into account, they would result in a substantial upward revision of the RDA for vitamin D.

Vitamin D Toxicity

Like anything that has an effect on living things, vitamin D can be harmful if it is taken in excess. It is probable that the reason vitamin D is thought of as toxic, is that daily ingestion in the milligram range has caused harm. This toxic intake exceeds by four times the amount of vitamin D adults acquire naturally through sunshine. Conversely, the current RDA for adults under age 50 represents only about 2% of what they could be making if they regularly spent 20 min with skin exposed to summer sun.

Lifeguards and farmers acquire the equivalent of at least 10 000 IU/day (250 micrograms, or 0.25 milligrams per day)[1]. The current safety limit for vitamin D supplements is 2000 IU/day[2], but review of the literature shows that the lowest dose of vitamin D proven to cause toxicity is 40,000 IU/day[1]. This translates to 1000 micrograms, or 1 milligram, taken daily for many months. If a Canadian consumer wanted to achieve the toxic dose, he or she would need to take forty of the 1000 IU pills (the highest dose available without a prescription) every day for many months.

Concluding Comments

The adult recommended dietary intake for vitamin D was based on an educated guess made in the 1960's, before there were objective criteria for adequacy. Furthermore, the dietary recommendations were aimed at preventing rickets in children with no consideration for its requirement in adults. Long-standing, mild insufficiency of vitamin D is now regarded as a cause of osteoporosis. We can now quantify vitamin D nutrition by testing circulating 25(OH)D concentrations. The blind guesses about vitamin D requirements, made almost 40 years ago are turning out to be so inadequate particularly for adults. Our current dietary and nondietary vitamin D intake is inadequate in predicting a person's 25(OH)D status. Another complication entering the vitamin D picture is our cultural response toward sunlight. We are avoiding the sun more because of fear of skin cancer, and for many Canadians there is a cultural preference to prevent skin from tanning. For older adults, sunlight is more harmful than for the young. For older adults, less vitamin D is produced when skin is exposed to the sun.

The solution to the problem of diminished vitamin D nutrition from sunshine, is to supplement with more vitamin D than we have been - with at least 1000 IU (25 µg)/day not just during winter, but all year. Vitamin D is safe, inexpensive, it is effective in terms of bone disease. In addition, there is growing evidence that Vitamin D intake is beneficial for other conditions.

Table 1. Clinical interpretation of serum 25(OH)D levels and the estimated intakes of vitamin D needed to ensure these levels (1 µg = 40 IU)

	Deficiency (rickets and Osteomalacia)	**Insufficiency** (increased PTH secretion, osteoporosis)	**Sufficiency**	**Desirable** (suppress PTH)	**Toxic/Therapy** (could increase urine and serum calcium)
Serum 25(OH)D nmol/L	0-25	25-40	40-100	75-160	>220
Vitamin D3 µg/day needed to reach the 25(OH)D above:					
Dietary guidelines	0 µg/d	5-10	5-20	not stated	≥95
From evidence reviewed	0-5 µg/d	10-15	25-100	100-250	>1000 (> 40000 IU)

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