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Vitamin D

A Canadian response to the 2010 Institute of Medicine vitamin D and calcium guidelines

Madam

The new Institute of Medicine (IOM) guidelines[1] for vitamin D are a step in the right direction to indicate a greater amount of vitamin D is needed than previously thought; however, there are a number of shortcomings and unanswered questions.

First, the minimum daily requirement has tripled from 5 to 15 μg/d for bone health. This information is welcome. This would bring most people in the general population to a 25-hydroxyvitamin D (25(OH)D; the metabolite measured for status) level >50 nmol/l, according to this report. However, this is not an adequate cut-off since maximum absorption of Ca improves up to about 80 nmol/l[2], which would in turn improve bone health. Parathyroid hormone (PTH) levels increase rapidly with 25(OH)D levels <50 nmol/l, but there are clinical studies that show a gradual rise in PTH with levels of 25(OH)D <78 nmol/l[3]. Thus, the cut-off should be 80 nmol/l, not 50 nmol/l, and many researchers across the world would agree with this. The Canadian Osteoporosis Society recommends achieving >75 nmol/l with 20 μg of vitamin D daily but acknowledges that intakes up to 50 μg/d are required[4]. Dental health would be improved in all people with levels above 20 μg/d, as 10 or 15 μg/d did not show any benefit[5]. This has been known since the 1930s and 1940s but has not been addressed.

Second, to say that most people have adequate levels from diet, even for bone health, using the conservative cut-off of 50 nmol/l is certainly not true. This is especially so in Canada where the latitude and long winters contribute to the low vitamin D levels. Two studies show that many population groups in Canada have very low levels of vitamin D and about 18% of Canadians have levels below 40 nmol/l[6,7]. In the Canadian Health Measures Survey, respondents who were not white had 25(OH)D levels 20 nmol/l lower than those of white European origin[4]. Supplementation with vitamin D at 50 μg/d in a nursing home setting, where levels average about 35–40 nmol/l because of little or no sun exposure, did not achieve levels over 80 nmol/l in 6% of the population studied and did not result in any toxic levels or elevation of Ca[8].

Third, the IOM did not address the needs in pregnancy. The Canadian Pediatric Society recommends all pregnant women take 50 μg/d, which is only reasonable since this group has very low vitamin D levels and consequences are grave if vitamin D levels are not adequate[9]. Low vitamin D levels have been associated with pre-eclampsia[10] and bacterial vaginosis in pregnancy[11]. The use

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of 50 μg/d in the first year of life has been shown to reduce the development of type 1 diabetes by 80% over the next 30 years[12]. The dose recommended for pregnant women in the IOM report is only 15 μg/d, which would be inadequate.

Finally, the increase of the upper tolerable level of vitamin D from 50 to 100 μg/d is very welcome and will result in the ability to perform studies that use appropriate doses of vitamin D for the bone and for some, but not all, non-bone effects. However much of the rhetoric surrounding the release of the report concerned risk of taking vitamin D supplements, a risk that is not based on good evidence. The IOM committee had some concerns about the U-shaped curve in a number of studies where levels above 100–125 nmol/l showed a possible increase in cardiovascular deaths[13,14]. Many researchers question this effect, believing that high levels of Ca as well as high levels of vitamin D get us into trouble. With adequate levels of vitamin D, the need for more than 800 mg Ca daily for bone health is really questionable[15].

What should physicians do? The Canadian Cancer Society has already suggested the use of 25 μg vitamin D daily for all Canadian adults for the prevention of cancer[16]. This should be expanded to include all Canadian children over the age of 1 year. Those 12 months and younger should take only the 10 μg/d dose recommended. Will vitamin D at this level have an impact on cancer prevention? The effect of vitamin D on reducing risk of bowel cancer is well established in the literature and it is surprising that this was totally ignored by the IOM. Even the WHO's ultra conservative body, the International Agency for Research on Cancer, has recently accepted that insufficiency of vitamin D increases colon cancer[17].

But physicians should not fall victim to 'more is better' or use inappropriately high doses of vitamin D. The use of 12 500 μg yearly for osteoporosis resulted in an increase in falls/fractures[18]. This dose makes no physiological sense; such a high level of vitamin D would result in some displacement from the vitamin D-binding receptor of the active hormone, causing a rise in the free active hormone to a degree that the body would actively degrade the hormone, resulting in a transient lowering of 1,25-dihydroxyvitamin D_3 and thus give the opposite result. This kind of dosing should never be recommended again. However, the use of 250 μg/d, which is physiological, has been shown to improve outcomes when used as an adjunct for tuberculosis therapy[5]. One should remember that sanatoriums were considered part of therapy for tuberculosis only 50 years ago.

The recommendations that seem to make the most sense and which come from both ends of the life cycle are between 20 and 50 μg of vitamin D daily. It seems Canadians need to lead the way. How much longer do we need to see needless morbidity and mortality? In looking at the North American continent as a whole the Canadian average blood levels may provide a better model for northern US states than US averages, which must be weighted by the large southern population. The savings in health-care dollars each year in Canada[19] and the USA[20] have been estimated in the billions and would save many lives.

Gerry K. Schwalfenberg
Assistant Clinical Professor
Department of Family Medicine, University of Alberta
#301, 9509-156 Street, Edmonton, Alberta
Canada, T5P 4J5
Email: schwalfe@ualberta.ca

Susan J. Whiting
Professor of Nutrition and Dietetics
College of Pharmacy and Nutrition
University of Saskatchewan
110 Science Place, Saskatoon, Saskatchewan
Canada, S79 5C9
Email: susan.whiting@usask.ca
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Vitamin D

The vitamin D requirement during human lactation: the facts and IOM's 'utter' failure

Madam

The new Institute of Medicine (IOM) recommendation for vitamin D intake is stated to be 10 and 10–15 μg/d for the newborn infant and lactating mother, respectively[1], and represents only a marginal change from its previous recommendations[2]. We have no issue with respect to the infant recommendations; however, the lactating woman's recommendation is another matter. Our lab has been investigating this area for more than three decades and was the first to actually quantify the vitamin D compounds in human milk[3]. Surprisingly, most of our data have been ignored in favour of the original recommendation – or, more appropriately, 'the estimation' – by Blumberg, Forbes and Fraser in 1963[4].

As a graduate student in human nutrition in the 1970s (B.W.H.), the senior investigator in our lab Dr Hollis was struck by the teaching that human milk was the 'perfect' food for the human neonate with one exception: it was inadequate with respect to vitamin D content, and rickets could result in the nursing infant if not provided with exogenous vitamin D supplementation. How could this be? What did these infants do prior to the discovery of vitamin D and how could nature have allowed this to happen? Actually, the answer is quite simple: we in medicine believed our own dogma instead of actually following the science, and thus we tried to 'fit' our 10 μg/d recommendation to the physiology instead of applying the physiology to discover the true recommendation.

First, it was said that milk had plenty of vitamin D due to the presence of vitamin D-sulfate. In fact, research 'conveniently' demonstrated that vitamin D-sulfate provided activity of about 10 μg/d in human milk[5]. The problem was that this research was faulty: vitamin D-sulfate did not exist in milk at all[6], so we were back to the drawing board. Accurate assessment had shown the vitamin D content of human milk in 'normal' lactating women to be less than 2.5 μg/l[3,7]. We had shown that lactating women exposed to UV light or given high oral doses of vitamin D to control hypoparathyroidism could produce milk that contained extremely high levels of antirachitic activity of up to 200 μg/l[8,9]. This increase in activity was almost totally due to the parent compound, vitamin D, gaining access to the milk and not the major circulating form, 25-hydroxyvitamin D (25(OH)D)[8,9]. But, how could this knowledge be applied to 'normal' women since it was 'well known' that intakes of vitamin D in excess of 50 μg/d would result in toxicity?[2] Because of this belief, this area of research lay dormant for nearly two decades; our laboratory being as guilty as anyone else's for believing it. Fortunately, our view on this matter changed when Vieth *et al.*[10] published a seminal paper in 2001 that demonstrated oral intakes of vitamin D_2 up to 100 μg/d were safe.

Let us piece together the physiology for vitamin D metabolism in the human female. The parent compound, vitamin D_3, is mostly derived from human skin following exposure to UV light, which can result in the release of several thousand IU/d into the circulation[11]. This vitamin D_3 is 'loosely' bound to the vitamin D-binding protein (DBP) with a circulating half-life of approximately 1 d[12]. A portion of this parent compound is metabolized to 25(OH)D, which is 'tightly' bound to the DBP with a circulating half-life of approximately 3 weeks[12]. Here is where one has to pay attention to the physiology. While 25(OH)D is the major circulating form of vitamin D, it is poorly transferred into human milk while the parent vitamin D is readily transferred[8,9,13]. The problem is that because the half-life of vitamin D is so fast, it has to be replenished daily to be effective and this replenishment has to be substantially greater than the 'artificial' requirement of 10 μg/d, which does nothing to raise the circulating parent vitamin D_3 levels in the mother. In fact, one can use all this data and simply calculate that for each 25 μg intake of vitamin D by the mother daily she will deposit approximately 2.5 μg of antirachitic activity into a litre of her milk. Thus, one can supplement the lactating women with vitamin D at 150 μg/d or let her obtain significant sun exposure and she will not only replete herself but also supply her nursing infant with vitamin D in her milk at 12.5 μg/l or so. The sun exposure part does not