

tant to continue advocating periconceptual folic acid supplementation and sound nutrition.

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#### Reference

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## Puzzling vitamin D results

I am puzzled by the seasonal mean values for 1,25-dihydroxy vitamin D [ $1,25-(\text{OH})_2\text{D}$ ] published in Table 2 of the article by Diana Rucker and colleagues.<sup>1</sup> They are about twice as high as those from a similar study done in Denmark,<sup>2</sup> which showed a mean of 29 pg/ml (75.4 pmol/L).

Two of the seasonal mean values (168.1, 148.9) are above the normal range quoted for the assay (45–145). This assay range seems to be correct, but the study data seem to be high.

I am particularly concerned that this study did not place much greater emphasis on the values of the active hormone  $1,25-(\text{OH})_2\text{D}$  than on the intermediate metabolite 25-hydroxy vitamin D [ $25(\text{OH})\text{D}$ ]. This is especially important in elderly populations, as extrarenal hydroxylase activity in inflammatory macrophages has been shown to generate a normal  $1,25-(\text{OH})_2\text{D}$  value from depressed levels of circulating  $25(\text{OH})\text{D}$ .

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#### References

1. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *CMAJ* 2002;166(12):1517-24.
2. Brot C, Jorgensen NR, Sorensen OH. The influence of smoking on vitamin D status and calcium metabolism. *Eur J Clin Nutr* 1999;53(12):920-6.

#### [One of the authors responds:]

I thank Trevor Marshall for paying such close attention to our article,<sup>1</sup> and I wish I had done the same in my proofreading. The normal range for the  $1,25-(\text{OH})_2\text{D}$ , or calcitriol, assay published in our paper was incorrect and was that for the earlier INCSTAR (later to become Diasorin) assay kit for calcitriol. This assay was in use at the Foot-hills Medical Centre when I submitted my grant proposal for this project. However, the current Diasorin calcitriol assay kit is currently used, in both my laboratory and the Calgary Health Region clinical laboratory, and the normal range (2 standard deviations above and below the mean for a group of healthy hospital workers) is 55–190 pmol/L. This is the range we should have included in Table 2, and our reported  $1,25-(\text{OH})_2\text{D}$  levels were within it.

Our  $1,25-(\text{OH})_2\text{D}$  assay still provided results consistent with known vitamin D physiology. The 2 seasons with the highest mean levels of  $1,25-(\text{OH})_2\text{D}$  were associated with the highest mean levels of parathyroid hormone and the lowest mean levels of serum inorganic phosphate, both known stimuli to conversion of  $25(\text{OH})\text{D}$  to  $1,25-(\text{OH})_2\text{D}$  by renal  $1\alpha$ -hydroxylase.

Although  $1,25-(\text{OH})_2\text{D}$  is the most biologically active form of vitamin D, it

is generally accepted that, when assessing patients' vitamin D stores, measurement of  $25(\text{OH})\text{D}$  in blood is much more clinically useful than that of  $1,25-(\text{OH})_2\text{D}$ .<sup>2,3</sup> Serum  $25(\text{OH})\text{D}$  levels are consistently low in malabsorption syndromes and clinical osteomalacia, although  $1,25-(\text{OH})_2\text{D}$  levels may be normal or high.<sup>4</sup> In osteomalacia due to vitamin D deficiency, the serum  $25(\text{OH})\text{D}$  level, not the  $1,25-(\text{OH})_2\text{D}$  level, correlates with the mineralization status of bone.<sup>5</sup> Recent identification of  $1\alpha$ -hydroxylase activity in nonrenal tissue provides a plausible explanation of how  $25(\text{OH})\text{D}$  may mediate vitamin D action at a cellular level,<sup>6,7</sup> and evidence also exists of direct effects of  $25(\text{OH})\text{D}$  on calcium absorption.<sup>8</sup>

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1. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *CMAJ* 2002;166(12):1517-24.
2. Holick MF. The use and interpretation of assays for vitamin D and its metabolites. *J Nutr* 1990;120(Suppl 11):1464-9.
3. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. *Am J Clin Nutr* 1999;69(5):842-56.

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