See corresponding article on page 860.

The urgent need to recommend an intake of vitamin D that is effective^{1,2}

Reinhold Vieth, Heike Bischoff-Ferrari, Barbara J Boucher, Bess Dawson-Hughes, Cedric F Garland, Robert P Heaney, Michael F Holick, Bruce W Hollis, Christel Lamberg-Allardt, John J McGrath, Anthony W Norman, Robert Scragg, Susan J Whiting, Walter C Willett, and Armin Zittermann

The report by Hyppönen and Power in this issue of the Journal (1) highlights a frustrating and regrettable situation for nutrition researchers. In the early 1970s, the same serum 25hydroxyvitamin D [25(OH)D] concentrations reported by Hyppönen and Power were thought to be indicative of "healthy" white adults in the United Kingdom (2). However, during those early years after the discovery of 25(OH)D, the adequacy of its serum concentration was based simply on whether the concentration was enough to prevent osteomalacia or rickets. Three decades later, we know that 25(OH)D concentrations relate to many other aspects of health, including fracture risk, bone density, colon cancer, and even tooth attachment (3); we also know that much higher concentrations of 25(OH)D are needed to prevent adverse outcomes. Indeed, in the 1958 British birth cohort, lower 25(OH)D is associated with a higher percentage of hemoglobin A_{1C} (a measure of long-term glucose concentration), which further emphasizes the need to maintain optimal 25(OH)D concentrations (4).

Randomized trials using the currently recommended intakes of 400 IU vitamin D/d have shown no appreciable reduction in fracture risk (3). In contrast, trials using 700–800 IU vitamin D/d found less fracture incidence, with and without supplemental calcium (3). The reduction in fracture incidence occurs when mean serum 25(OH)D concentrations exceed 72 nmol/L, and this change may result from both improved bone health and reduction in falls due to greater muscle strength (3). Although it is not yet proven through clinical trials, higher intakes may also reduce the incidence of colon and other cancers, and these relations indicate that the desirable 25(OH)D concentration is ≥75 nmol/L (3). One recent report associates greater 25(OH)D concentrations with lower risk of nursing home admission; the most desirable category of concentration starts at 75 nmol/L (5).

Human diets do not provide sufficient vitamin D; if they did, the abovementioned associations between health and serum 25(OH)D concentrations would not be so routinely observed. The vitamin D provided by foods and supplements is overwhelmed by the effect of skin exposure to ultraviolet B light. Geography, season, skin color, and sun-related behavior are the main predictors of vitamin D nutritional status (6–10). Correction of low 25(OH)D concentrations can happen only if some or all of the following are implemented: the encouragement of safe,

moderate exposure of skin to ultraviolet light; appropriate increases in food fortification with vitamin D; and the provision of higher doses of vitamin D in supplements for adults.

Evaluation of most relations of health and disease that involve vitamin D leads to the conclusion that a desirable 25(OH)D concentration is ≥75 nmol/L (30 ng/mL) (3–5). If a concentration of 75 nmol/L is the goal to be achieved by consumption of vitamin D, then why is it so rare for members of the population to accomplish this? One reason is that almost every time the public media report that vitamin D nutrition status is too low, or that higher vitamin D intakes may improve measures of health, the advice that accompanies the report is outdated and thus

Downloaded from www.ajcn.org at Univ of Calgary Med Lib Periodicals on March 7, 2007

¹ From the Departments of Nutritional Sciences and of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada (RV); the Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Canada (RV); the Department of Nutrition, Harvard School of Public Health, Boston, MA (HB-F and WCW); the Department of Rheumatology and the Institute of Physical Medicine, University Hospital Zurich, Zurich, Switzerland (HB-F); the Department of Epidemiology and the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Boston, MA (WCW); the Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA (BD-H); the School of Population Health, University of Auckland, Auckland, New Zealand (RS); the Vitamin D Laboratory, Section of Endocrinology, Nutrition and Diabetes, Department of Medicine, Boston University School of Medicine, Boston, MA (MFH); the Departments of Pediatrics, Biochemistry, and Molecular Biology, Medical University of South Carolina, Charleston, SC (BWH); the Department of Family and Preventive Medicine, University of California and the San Diego Naval Health Research Center, San Diego, CA (CFG); Creighton University, Omaha, NE (RPH); the Division of Biomedical Sciences, Department of Biochemistry, University of California-Riverside, CA (AWN); the College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, Canada (SJW); the Department of Cardio-Thoracic Surgery, Heart Center North-Rhine Westfalia, Ruhr University of Bochum, Bad Oeynhausen, Germany (AZ); The Centre for Diabetes and Metabolic Medicine, Queen Mary School of Medicine and Dentistry, University of London, London, United Kingdom (BJB); the Queensland Centre for Schizophrenia Research, The Park Centre for Mental Health, Brisbane, Australia (JJM); the Department of Psychiatry, The University of Queensland, Brisbane, Australia (JJM); and the Department of Applied Chemistry and Microbiology, University of Helsinki, Helsinki, Finland (CL-A).

² Reprints not available. Address correspondence to R Vieth, Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, 600 University Avenue, Toronto, ON, Canada M5G 1X5. E-mail: rvietha@mtsinai.on.ca.

misleading. Media reports to the public are typically accompanied by a paragraph that approximates the following: "Current recommendations from the Institute of Medicine call for 200 IU/d from birth through age 50 y, 400 IU for those aged 51–70 y, and 600 IU for those aged >70 y. Some experts say that optimal amounts are closer to 1000 IU daily. Until more is known, it is wise not to overdo it." The only conclusion that the public can draw from this is to do nothing different from what they have done in the past.

Supplemental intake of 400 IU vitamin D/d has only a modest effect on blood concentrations of 25(OH)D, raising them by 7–12 nmol/L, depending on the starting point. To raise 25(OH)D from 50 to 80 nmol/L requires an additional intake of $\approx \! 1700$ IU vitamin D/d (11). Safety is the first priority when giving advice to increase supplementation or fortification with any nutrient. A recent review in this Journal applied the risk assessment method used by the Food and Nutrition Board to update the safe tolerable upper intake level (UL) for vitamin D (12). The method focuses on the risk of hypercalcemia. The conclusion was that the UL for vitamin D consumption by adults should be 10 000 IU/d (12). This indicates that the margin of safety for vitamin D consumption for adults is >10 times any current recommended intakes.

The balance of the evidence leads to the conclusion that the public health is best served by a recommendation of higher daily intakes of vitamin D (3). Relatively simple and low-cost changes, such as increased food fortification or increasing the amount of vitamin D in vitamin supplement products, may very well bring about rapid and important reductions in the morbidity associated with low vitamin D status. The current UL is but one impediment to this action; another is the perpetuation of outdated intake recommendations.

It is important for major journals such as the AJCN to publish evidence of a widespread nutrient deficiency. Regrettably, we are now stuck in a revolving cycle of publications that are documenting the same vitamin D inadequacy (1-3, 5, 7-9, 13-17). This phenomenon has been referred to as "circular epidemiology" (18), and, for vitamin D, the phenomenon will continue for as long as the levels of vitamin D fortification and supplementation and the practical advice offered to the public remain essentially the same as they were in the era before we knew that 25(OH)D even existed. As scientists, the purpose of our work is to improve the health of the public. We know the realities of serum 25(OH)D concentrations in populations around the world, and we have come to the conclusion that public health will benefit from improved vitamin D nutritional status. We know the intakes of vitamin D needed to bring about desirable 25(OH)D concentrations, so why is the science not making a difference to public health? A major reason is that there is little public pressure on policy makers to support efforts to update recommendations about nutrition. Public pressure is generally rooted in the media, but we do not think that the public media present the vitamin D story in a complete and accurate manner. Reports about vitamin D inadequacies are presented straightforwardly, but, when it comes to discussing the intake of vitamin D needed to correct the situation, outdated official recommendations for vitamin D are propagated by the public media. This probably occurs because of restrictive editorial policies driven by concern about possible litigation if media were to advise a "toxic" intake greater than the UL. The unfortunate result is that there is minimal motivation for policy makers to implement the relatively simple steps that could correct this nutrient deficiency.

Because of the convincing evidence for benefit and the strong evidence of safety, we urge those who have the ability to support public health—the media, vitamin manufacturers, and policy makers—to undertake new initiatives that will have a realistic chance of making a difference in terms of vitamin D nutrition. We call for international agencies such as the Food and Nutrition Board and the European Commission's Health and Consumer Protection Directorate-General to reassess as a matter of high priority their dietary recommendations for vitamin D, because the formal nationwide advice from health agencies needs to be changed.

None of the authors had a personal or financial conflict of interest with respect to the topic under discussion or the report by Hyppönen and Power.

REFERENCES

- Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. Am J Clin Nutr 2007;85:860–8.
- Preece MA, McIntosh WB, Tomlinson S, Ford JA, Dunnigan MG, O'Riordan JL. Vitamin-D deficiency among Asian immigrants to Britain. Lancet 1973;1:907–10.
- Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006; 84:18–28.
- Hyppönen E, Power C. Vitamin D status and glucose homeostasis in the 1958 British birth cohort: the role of obesity. Diabetes Care 2006;29: 2244-6.
- Visser M, Deeg DJ, Puts MT, Seidell JC, Lips P. Low serum concentrations of 25-hydroxyvitamin D in older persons and the risk of nursing home admission. Am J Clin Nutr 2006;84:616–22.
- McKenna MJ. Differences in vitamin D status between countries in young adults and the elderly. Am J Med 1992;93:69–77.
- Falch JA, Steihaug S. Vitamin D deficiency in Pakistani premenopausal women living in Norway is not associated with evidence of reduced skeletal strength. Scand J Clin Lab Invest 2000;60:103–9.
- Vieth R, Cole DE, Hawker GA, Trang HM, Rubin LA. Wintertime vitamin D insufficiency is common in young Canadian women, and their vitamin D intake does not prevent it. Eur J Clin Nutr 2001;55:1091–7.
- van der Meer I, Karamali NS, Boeke AJ, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. Am J Clin Nutr 2006;84:350–3.
- Tangpricha V, Turner A, Spina C, Decastro S, Chen TC, Holick MF. Tanning is associated with optimal vitamin D status (serum 25hydroxyvitamin D concentration) and higher bone mineral density. Am J Clin Nutr 2004:80:1645–9
- Barger-Lux MJ, Heaney RP, Dowell S, Chen TC, Holick MF. Vitamin D and its major metabolites: serum levels after graded oral dosing in healthy men. Osteoporos Int 1998;8:222–30.
- Hathcock JN, Shao A, Vieth R, Heaney R. Risk assessment for vitamin D. Am J Clin Nutr 2007:85:6–18.
- Zadshir A, Tareen N, Pan D, Norris K, Martins D. The prevalence of hypovitaminosis D among US adults: data from the NHANES III. Ethn Dis 2005;15:S5–101.
- Rockell JE, Skeaff CM, Williams SM, Green TJ. Serum 25hydroxyvitamin D concentrations of New Zealanders aged 15 years and older. Osteoporos Int 2006:17:1382–9.
- Stein EM, Laing EM, Hall DB, et al. Serum 25-hydroxyvitamin D concentrations in girls aged 4–8 y living in the southeastern United States. Am J Clin Nutr 2006;83:75–81.
- Du X, Greenfield H, Fraser DR, Ge K, Trube A, Wang Y. Vitamin D deficiency and associated factors in adolescent girls in Beijing. Am J Clin Nutr 2001;74:494–500.
- 17. Nakamura K, Ueno K, Nishiwaki T, et al. Nutrition, mild hyperparathyroidism, and bone mineral density in young Japanese women. Am J Clin Nutr 2005;82:1127–33
- 18. Kuller LH. Circular epidemiology. Am J Epidemiol 1999;150:897–903.



The American Journal of Clinical Nutrition