

## Invited Commentary

### Vitamin D in the spotlight – time for urgent action?

There is no doubt that there is a real nutrition problem of low vitamin D status for populations living in the United Kingdom. For the immigrant population with darker skin such as South Asians, the situation could be more accurately described as a nutrition crisis. Safeguarding vitamin D levels seriously matters, since it is now recognised that almost every tissue and cell in the body has receptors for vitamin D, with studies suggesting that upwards of 200 different genes may be directly/indirectly regulated by vitamin D through the receptors for vitamin D<sup>(1)</sup>. For biological systems to function effectively, an adequate amount of vitamin D is required. While there is somewhat limited information available on whether the receptors are high-affinity receptors, it is predicted that low circulating concentrations of vitamin D are unlikely to be functionally adequate<sup>(2)</sup>.

There is a growing body of evidence from a combination of observational, clinical and experimental studies for the positive effects of vitamin D in reducing risk from diseases such as rickets, cancer, heart disease and osteoporosis, as well as all-cause mortality<sup>(3–7)</sup>, and there are some key data showing how critical maternal vitamin D status is to long-term bone health in growing children<sup>(8)</sup>. Interest in the vitamin D field has escalated hugely: at the 14th International Workshop on Vitamin D (held in Bruges, Belgium, 7–9 October 2009), it was highlighted that there has been a 40-fold increase in vitamin D-related publications in the last decade. The UK National Diet and Nutrition Surveys show an unacceptably high prevalence of vitamin D ‘deficiency’ (as defined by a 25-hydroxyvitamin D (25OHD) level below 25 nmol/l) in the UK Caucasian population in each of the key age groups: 4–18<sup>(9)</sup>; 19–64<sup>(10)</sup>; 65+ years<sup>(11)</sup>. Furthermore, in the largest study of 25OHD levels in the UK (*n* 7437), it has been shown that there are very high prevalence rates for hypovitaminosis D in Caucasian men and women. For example, during the winter/spring, 25OHD levels < 25, < 40 and < 75 nmol/l were found in 15.5, 46.6 and 87.1 % of the population, respectively<sup>(12)</sup>. Immigrant populations are not well represented in these studies, but in a recent Food Standards Agency-funded trial, premenopausal and postmenopausal South Asian women were found to be vitamin D deficient for the entire year, with little seasonal variation in comparison with their Caucasian counterparts living in Aberdeen<sup>(13)</sup> or Surrey<sup>(14)</sup>. Datta *et al.*<sup>(15)</sup> have shown in one of the few studies of pregnant women from ethnic minorities in the UK that more than 50 % of women had a plasma 25OHD level < 25 nmol/l.

In the present issue of the *British Journal of Nutrition*, Hyppönen & Boucher<sup>(16)</sup> make a very convincing case for the urgent need to address the widespread hypovitaminosis D in women of child-bearing age (and concomitantly in expectant mothers), with the proposal of universal vitamin D supplementation. They also identify, eloquently and succinctly, the lack of a clear and comprehensive message on vitamin D

supplementation in pregnant and breast-feeding mothers. Data presented in the paper from the Avon Longitudinal Study of Parents and Children showed that 90 % of white pregnant women had 25OHD concentrations below 50 nmol/l during the winter and spring (with 28 % below 25 nmol/l).

The term vitamin D itself is a misnomer, in that vitamin D is not a ‘vital-amine’ in the true sense of the ‘vitamine’ terminology, but rather it is a pro-hormone. Vitamin D is the generic term for two molecules, ergocalciferol (vitamin D<sub>2</sub>) and cholecalciferol (vitamin D<sub>3</sub>). Vitamin D<sub>2</sub> is derived by UV irradiation of the ergosterol that is widely distributed in plants and other fungi, whereas vitamin D<sub>3</sub> is formed from the action of UV irradiation on the skin. Mechanistically, the action of sunlight on the skin converts 7-dehydrocholesterol to pre-vitamin D, which is then converted to vitamin D by a temperature-dependent isomerisation. Vitamin D is then transported via the general circulation to the liver, where the enzyme 25-hydroxylase (CYP2R1) converts it to 25OHD. 25OHD is the main circulating vitamin D metabolite and is the best indicator of clinical status, whereas 1,25-(OH)<sub>2</sub>D (calcitriol) is the active form of the vitamin<sup>(17)</sup>. There remains controversy regarding the optimal range of plasma 25OHD concentrations and the threshold concentration of 25OHD below which an increased risk of inadequacy ensues, but there is an agreement from a number of vitamin D scientists across the globe that it is absolutely desirable for all population groups to have a plasma 25OHD level above 25 nmol/l<sup>(18)</sup>.

It is important to note the critical role that calcitriol plays in optimising Ca absorption through the production of Ca-binding protein. If calcitriol is limited, this is likely to result in reduced Ca absorption and hence Ca retention<sup>(19)</sup>. This is particularly critical for expectant and lactating mothers.

Natural dietary sources of vitamin D in the UK are extremely limited, and there are very few foods that are fortified. The main provider of vitamin D in the UK is oily fish, but eggs, fortified fat spreads (all yellow fats are fortified with vitamin D to bring them up to the level of vitamin D in butter), cereals and pastry products also contribute to dietary intake<sup>(20)</sup>. As shown in National Diet and Nutrition Surveys<sup>(9–11)</sup> and by findings from two of the recent Food Standards Agency-funded trials<sup>(13,14)</sup>, dietary intakes of vitamin D are consistently low (about 2–3 µg/d (80–120 IU/d)). Currently, there is controversy as to the effectiveness of vitamin D<sub>2</sub> v. D<sub>3</sub> in raising 25OHD levels in human subjects. It has been assumed, primarily on the strength of evidence from a number of trials published in the 1930s, that D<sub>2</sub> and D<sub>3</sub> were equally effective in human subjects<sup>(21)</sup>, but there is more recent debate on this issue with some studies showing that D<sub>3</sub> is superior to D<sub>2</sub> in raising 25OHD levels<sup>(22–24)</sup>, whereas other data suggest that D<sub>2</sub> and D<sub>3</sub> are equally effective<sup>(25,26)</sup>. This urgently needs to be clarified<sup>(27)</sup>, given that vitamin D<sub>3</sub> that is used in supplements/food fortification

is made by UVB irradiating 7-dehydrocholesterol obtained from lanolin from sheep's wool. This is key, as vitamin D<sub>3</sub> is thus hindered by perceptions that it is a product of 'animal origin', which is a problem for vegans and strict vegetarian communities (including Asian populations)<sup>(28)</sup>.

One of the factors that Hyppönen & Boucher<sup>(16)</sup> discuss as being contributory to low vitamin D levels is the recognition of a link between sunlight exposure and skin cancer risk and hence the public health advice for regular use of sunscreen and avoidance of the sun, which significantly influences the synthesis of vitamin D<sup>(29)</sup>.

Currently, there is no UK reference nutrient intake for vitamin D for people aged between 4 and 64 years in the general population except for those at specific risk of limited UVB skin exposure. For pregnant and lactating women, the recommendation is 10 µg/d. Initially derived by the Committee on Medical Aspects of Nutrition and Food Policy<sup>(30)</sup>, these recommendations have been endorsed by a Committee on Medical Aspects of Nutrition and Food Policy report on nutrition and bone health in 1998<sup>(31)</sup>, and then more recently, they have been reviewed by the Scientific Advisory Committee on Nutrition in their position statement on vitamin D in 2007<sup>(32)</sup>.

As Hyppönen & Boucher<sup>(16)</sup> highlight in their paper, advice on encouraging 10 µg/d of vitamin D intake during pregnancy and lactation is sporadic, while uptake of supplements is poor and there are conflicts in the advice being given by a number of organisations, and in particular, by the Department of Health and the National Institute for Health and Clinical Excellence on Antenatal Care. Furthermore, the UK remains only one out of a total of thirty-one countries in Europe with no recommended daily vitamin D intake for women of child-bearing age. This remains an extremely important concern, and a fundamental strategy for action is urgently required to address this.

### Declaration

The author is co-director of D3Tex Limited, and has acted in the past as a consultant to the following companies with respect to vitamin D: Dairy Crest Yoplait, GlaxoSmithKline, Nestlé and Danone.

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