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Invited Commentary

Invited commentary in response to: Serum 25-hydroxyvitamin D, calcium and parathyroid hormone in Native and European populations in Greenland

Inuit populations in nutrition transition are at risk of compromised nutritional status

Inuit populations in the Arctic are undergoing nutrition transition and there are concerns that a shift from the traditional diet, rich in seal, whale, wild fowl, reindeer, musk ox and hare, towards an imported, highly processed diet, is compromising food security and nutritional status by undermining a core component of the Inuit adaptation to life in the Arctic. Using data from the International Polar Year Inuit Health Survey (2007–2008) of thirty-six Inuit communities in Northern Canada, Egeland *et al.*[1] reported higher intakes of protein and micronutrients among traditional food consumers and higher carbohydrate, saturated fat, dietary fibre and Na:K intakes among non-consumers. Several nutritional biomarkers, including serum concentrations of 25-hydroxyvitamin D (25(OH)D), indicating vitamin D exposure, were higher among traditional food consumers. Older adults consumed more traditional foods and had higher vitamin D intakes than younger adults. Among 2207 individuals[2], more than 40 % overall had low vitamin D status, indicated by having a 25(OH)D concentration below 50 nmol/l – the target specified by the Institutes of Medicine[3], the European Food Safety Authority[4] and Norden[5] to meet the vitamin D requirements of almost all healthy persons. The strongest determinants of 25(OH)D were older age and healthy waist circumference[2].

The Inuit Health in Transition study in West and East Greenland, conducted from 2005 to 2010, told a similar story. Among 2877 randomly selected Inuit adults, Nielsen *et al.*[6] reported that serum 25(OH)D concentrations were lowest among 18–29-year-olds, at approximately 31 nmol/l, and increased with age. The other important determinants of vitamin D status were consumption of a traditional diet and female sex. This study analysed bio-banked samples collected in 1987 from a sub-group of 330, allowing analysis of trends over time. Among all ages, 25(OH)D decreased by one-third to a half over the 30-year time frame. The authors suggested that a change away from a traditional diet may explain this decline[6], although there were no dietary data to support this suggestion.

Beyond vitamin D – calcium homoeostasis in Inuit and non-Inuit adults in Greenland

In their study among 50–69-year-old Inuit and non-Inuit adults in Greenland, Andersen *et al.*[7] have extended their previous work on vitamin D status in Greenland residents by considering Ca homoeostasis and reporting analysis of serum parathyroid hormone (PTH) and Ca, as well as 25(OH)D concentrations and dietary habits. Previously, this team described determinants of circulating 25(OH)D among the 50–69-year-old adult demographic in the capital, Nuuk, and a town and remote settlement in East Greenland (both at approximately 65°N)[8]. With a median 25(OH)D of 41 nmol/l, non-Inuit people had lower vitamin D status than Inuit individuals, at 64 nmol/l. Consumption of a traditional diet, particularly seal and whale, was an important determinant of circulating 25(OH)D, particularly for the prevention of very low vitamin D status; among participants with Inuit food scores below 40 %, 25(OH)D was <20 nmol/l in 14 % and <50 nmol/l in 60 %, whereas among those who scored above 40 % 25(OH)D was <20 nmol/l in only 0·2 % and <50 nmol/l in 25 %[8].

Andersen *et al.*[9] also studied younger Inuit and non-Inuit adults aged 30–50 years living in two different regions of Greenland further North (70°N). Consumption of an Inuit diet was again associated with higher 25(OH)D concentrations all year round, further emphasising the role of vitamin D from food for maintaining vitamin D status above very low thresholds. This study demonstrated seasonal variation in 25(OH)D concentrations among both Inuit and non-Inuit adults, but the data also emphasised the effect of vitamin D supplied by the traditional diet in preventing deficiency, particularly during the extended winter. On the basis of the data in both of these earlier studies[8,9], the authors concluded that the risk of vitamin D deficiency increases with the dietary transition of societies in Greenland.

Although the current study by Andersen *et al.*[7] has documented higher 25(OH)D among Inuit than non-Inuit participants, as before[8], the investigators have also found significantly lower serum Ca and PTH. Among the non-Inuit participants, as expected, PTH increased as 25(OH)D decreased, with an inflection between approximately 40 and 50 nmol/l, whereas there was no such trend among the Inuit participants. On the basis of this racial difference, as well as associations among diet, serum 25(OH)D and PTH, the investigators concluded that Inuit people in Greenland may have adapted to their low-Ca environment by increasing capacity for 1,25-dihydroxyvitamin D (1,25(OH)$_2$D) production, with increased intestinal absorption and renal resorption of Ca, thus providing some protection for the skeleton[7]. In an earlier study, Rejnmark *et al.*[10] reported that, compared with Danes in Greenland, Inuit had higher 1,25(OH)$_2$D, lower PTH and low plasma Ca concentrations and suggested that Inuit may have an inherent lower 'set-point' for Ca-regulated PTH release or enhanced renal 1,25(OH)$_2$D production. Certainly, racial

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differences are apparent in the relative proportions of calcitropic hormones and the relationships between them. The health implications of these differences need further investigation.

Although many observational studies have reported associations between low vitamin D status and adverse skeletal and non-skeletal health outcomes, including mortality[11], the Inuit Health in Transition study in Greenland did not observe significant associations of serum 25(OH)D concentrations with subclinical CVD, indicated by carotid intima–media thickness[12]. In a larger sample from the same study, this group also reported no association between 25(OH)D and impaired glucose tolerance or type 2 diabetes[13]. In contrast, weak positive associations between 25(OH)D and elevated plasma glucose levels and HbA1c and a negative association with β-cell function were found[13]. Elsewhere, longitudinal cohort studies have presented associations of elevated PTH with mortality[14]. In the US National Health and Nutrition Examination Surveys (NHANES, 2003–2006), associations between 25(OH)D and hypertension were attenuated following adjustment for PTH[15]. Similarly, using the Korean NHANES (2010–2011), serum PTH, but not 25(OH)D, was associated with hypertension in middle-aged and older adults[16]. The inverse association between vitamin D and PTH is well described and vitamin D supplementation often reduces PTH. This can be confounded by obesity, which is associated with low vitamin D status and secondary hyperparathyroidism, as well as cardiovascular risk. Lotito *et al.*[17] showed in a recent systematic review and meta-analysis of eighteen randomised controlled trials that 25 μg/d (1000 IU) of vitamin D_3 was effective at suppressing serum PTH levels in overweight/obese adults. The role of sufficient vitamin D status in modifying pathways of disease risk linked to interactions with PTH deserves further study.

Racial differences in the relationship between vitamin D, bone mineral density and PTH in NHANES have been described[18], where Blacks and Mexican-Americans had significantly lower 25(OH)D and higher PTH concentrations than Whites. Bone mineral density significantly decreased as serum 25(OH)D and Ca intake decreased among Whites and Mexican-Americans, but this effect was not seen in Blacks. In addition, the impact on PTH of having a 25(OH)D concentration <50 nmol/l was modified by race; whereas 25(OH)D and PTH were inversely related both above and below the 50 nmol/l threshold in Whites and Mexican-Americans, an inverse relation in Blacks was only present when 25(OH)D was below 50 nmol/l. This suggests that PTH may be maximally suppressed at lower 25(OH)D levels in Blacks than in Whites or Mexican-Americans.

In conclusion, there are important implications from the study by Andersen *et al.*[7]. Exploring effects of ethnicity on the 25(OH)D–PTH relationship and its impact on Ca homoeostasis in the context of health and disease risk is a significant avenue for exploration. Inclusion of serum phosphate analysis and fibroblast growth factor 23 may provide additional insights. Within Inuit communities in nutrition transition, extension of these analyses into the young adult cohort described earlier[8], as well as adolescents and children, would be extremely valuable given the marked shift in consumption of imported foods among the younger Inuit population and children[19]. A close analysis of the nutritional impacts of departing from traditional foods may help to provide evidence for development of public health strategies to counteract emerging nutritional deficiencies.

With regard to vitamin D, an additional concern in the Arctic is the predicted reduction of the monthly noon UV index and the effective dose for skin synthesis of vitamin D, which has been simulated across past, present and future time frames. Models predict the greatest reductions in northern Asia, Greenland and the north-east shores of Canada and Alaska, locally reaching approximately 30 % for the noon UV index and approximately 50 % for the noon effective UV dose for vitamin D synthesis[20]. A deeper understanding of the role of vitamin D in the food supply in these regions will be critical to develop strategies to offset this disruptive environmental challenge.

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