

## Clinical Commentary

# Vitamin D in North-East Asian clinical nutrition practice

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Sound clinical nutrition practice is grounded in evidence and stimulated by research. Yet, there are unanswered questions about food-health relationships. Clinical nutrition involves the identification of nutritional disorders and the motivation to rectify them with all required care. Vitamin D health exemplifies the biomedical, societal and environmental dimensions of clinical nutrition, its science and practice. It depends most of all on access to sunshine and food and probably represents a paradigm in human health which is still at its beginning. Nevertheless, the problem of its deficiency is much more widespread and common than has been thought since it was first identified as a cause of rickets and osteomalacia. It is now known to spare no body organ or system. The problem in North-East Asia is comparable to much of the rest of the world, but the risk profile for it is exaggerated by atmospheric pollution, cultures with sun-avoidance on account of skin colour and potentially mitigated by food-stuffs like fish, eggs, organ meats and mushrooms which can partially offset sunshine-deficiency. Diagnosis requires a high index of suspicion and confirmation by biochemistry which may not be affordable. Therefore a close working relationship between public health and clinical nutritionist is essential.

**Key Words:** vitamin D deficiency, ethnicity, atmospheric pollution, food, sunlight, diagnosis, food sources

## HISTORICAL CONSIDERATIONS

For many years after its discovery in the early part of the 20<sup>th</sup> century, the endocrine, autocrine and paracrine vitamin D was thought to have functions largely related to bone, manifesting in children as rickets and in adults as osteomalacia and osteoporosis. The widespread use of fish liver oil in the mid-20<sup>th</sup> century and emphasis on sun exposure led to a marked decline in rickets and osteomalacia, while osteoporosis became a major problem in ageing populations. With time, reports have grown which indicate that vitamin D deficiency remains common throughout the life-cycle and that this applies to North-East Asia as it does elsewhere.<sup>1,2</sup> Its manifestations are pleiotropic which is to say that, on account of its many functions, its health effects are diverse and complex.<sup>3</sup> It is a good example of why 'clinical nutrition' needs a wide embrace and to be multidisciplinary.<sup>4</sup>

Here we consider how the problem of vitamin D deficiency can be identified, prevented and managed by clinicians.

## EVIDENCE BASED NUTRITION AND VITAMIN D

Contemporary health care practice aims to operate in accordance with scientific evidence, so-called 'evidence-based medicine'. Its nutrition counterpart is 'evidence-based nutrition' (EBN).<sup>5</sup> It has been argued that EBN is best served by 'portfolios of evidence' including clinical trials, observational studies, experimental studies on animals along with ex vivo, in vivo and in vitro investigations, rather than 'hierarchies of evidence' with clinical trials as the best evidence.<sup>6</sup> The limitations of nutrient

trials with calcium and vitamin D have been reviewed by Lappe and Heaney.<sup>7</sup>

## Clinical Nutrition Epidemiology and Vitamin D

There are several major studies in North-East Asia, from greater China,<sup>8-16</sup> Korea<sup>17,18</sup> and Japan<sup>19</sup> which demonstrate the considerable prevalence of biochemical vitamin D deficiency in the region. This is not always accompanied by population-wide low intakes as in Taiwan,<sup>15</sup> which indicates that environmental (especially sun-exposure), behavioural (e.g., sun-avoidance by women, outdoor or indoor recreation or employment, smoking) or other clinical factors (e.g., malabsorption; drug interactions; obesity and weight management; dietary restrictions) play a role as determinants of vitamin D deficiency. The seasons vary from north to south in sunshine and vitamin D status and health vary accordingly, as can be seen with the multiple sclerosis gradients where vitamin D is involved.

Public health strategies to reduce the incidence of skin cancer now contribute to vitamin D deficiency and pose a health system dilemma exacerbated by climate change

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with loss of the protective ozone layer and confounded by atmospheric pollution.

Few foods provide vitamin D. In North-East Asia it comes mainly as vitamin D-3 from fish, meats especially organ meats like liver, eggs, animal skin like chicken skin and dairy if fortified; and as vitamin D-2 from fungi or mushrooms which have been dried in the sun or exposed to UV irradiation.<sup>14,15</sup> Ultimately, vitamin D is made from dehydrocholesterol in animals or from ergosterol in fungi or mushrooms under UV irradiation. Unfortunately, because of fear of cholesterol in the diet, many of these foods were discouraged, even though dietary cholesterol is not the main determinant of blood cholesterol. In turn, the prevention of diseases which was intended, like obesity, diabetes and cardiovascular disease may have been compromised in this way. This underscores the relative safety (and sustainability) of small amounts of diverse foods rather than large amounts of a few.

## CLINICAL RELEVANCE

### *Preventive opportunities*

Given the extensive biological effects of vitamin D, throughout the life-cycle from conception, during pregnancy and lactation, growth and development, adulthood and later life, there are substantial opportunities for clinicians and those in public health to minimise deficiency in the interests of healthy life expectancies.

### *Organ, System and Ecological Dysfunction*

There is probably no branch of health care where vitamin D deficiency is not relevant. No organ or system is spared. Vitamin D is indicative of our links with the ecosystems of which we are part, through our diurnal and seasonal biorhythms, the food we eat and the health of our microbiomic interface with nature.<sup>20, 21</sup>

### *Mortality*

While vitamin D deficiency is associated with increased mortality in a meta-analysis,<sup>22</sup> in Linxiang, China, noted for its micronutrient deficiencies and a link between vitamin D deficiency and oesophageal cancer,<sup>8</sup> mortality has not been found associated with vitamin D status.<sup>12</sup> It is possible that this incongruous finding is related to competing risks for mortality.

## DIAGNOSIS

### *Index of suspicion*

The likelihood of vitamin D deficiency should be suspected in precarious ecological situations which affect sun exposure or the food supply, as winter approaches and exits, where occupation or activities are mainly indoor, with a family history of osteoporosis or fracture, cancer (perhaps related to vitamin D receptor polymorphisms), where diet or dietary patterns are restricted as in vegans where animal food derived vitamin is absent or with very low fat intakes also low in other fat-soluble vitamins A, E and K (the co-operativity of these vitamins is also relevant). Other diseases (e.g., with malabsorption) may also be causes of secondary vitamin D deficiency. With practice most health care professionals will develop efficient "Clinical Repertoires".<sup>23</sup>

### *Institutionalisation, indoor employment*

At considerable risk of vitamin D deficiency are those who have the twin problems of lack of sunshine and dependency on others for their food supply. Where biochemical assessment is available it is not uncommon to find very low or even unmeasurable vitamin D concentrations. Examples are institutionalised elders and computer scientists.

### *Constellation of symptoms and signs*

In patients with a constellation of bone disease, muscle dysfunction or weakness, body compositional disorders (e.g., overfatness, sarcopenia), diabetes, reproductive dysfunction, recurrent or persistent infection (especially respiratory tract, tuberculosis and HIV positivity), autoimmune disease, neoplastic disease, malabsorption, cognitive impairment or other neurodegenerative disease, or multiple sclerosis, vitamin D deficiency is a possibility. In some the deficiency will be a pathogenetic factor in the disorder or disease; in others it will be a secondary deficiency. It may also serve to create a spiral of increasing morbidity involving an array of organs and systems.<sup>1,2</sup>

### *Biochemical and endocrine function*

Serum 25 OH vitamin D: 1,25OH vitamin D may be measured depending on the clinical picture, especially whether there is hepatic or renal disease which could impair, respectively, 25-hydroxy or 1,25-dihydroxy vitamin D synthesis. To be confident that there is functional deficiency, the presence of secondary hyperparathyroidism can be established by measurement of serum PTH (parathyroid hormone). The PTH response to treatment is also helpful in judging progress. A steady state urinary calcium excretion will reflect calcium balance, and, for comparison, usual intake can be estimated by asking about calcium-rich foods consumed. Its response to treatment can also be reassuring or otherwise. These investigations may be out of financial and pathology services reach for many. In these circumstances, the clinician must depend on quality history-taking

### *Early and delayed recognition*

Without clinical alertness to the problem of vitamin D deficiency when symptoms are non-specific, delayed recognition can lead to considerable accumulated pathology and frailty. On the other hand, early recognition can allow rapid resolution of related health problems and reduced health costs. The nutritional economics of these different scenarios requires analysis.<sup>24</sup>

## MANAGEMENT

Clearly the most important aspects of management of Vitamin D deficiency are to deal with the underlying causes. But these may themselves be complex especially insofar as the likely multifactorial pathogenesis which will usually obtain involving environmental (place of abode, occupation, recreation) behavioural (diet, physical activity and habits like smoking), gender and bio-medical considerations. Time and commitment to facilitatory counselling, perhaps with a team, is to be encouraged.

Optimal vitamin D intakes are dependent on behavioural and environmental considerations.<sup>25</sup> But the opti-

mal serum concentrations of active forms of vitamin D are generally higher than commonly encountered in surveys or clinical practice. Zittermann et al found that there was “a nonlinear decrease in mortality risk as circulating 25(OH) D increases, with optimal concentrations ~75–87.5 nmol/L”.<sup>22</sup> Although DRIs (Dietary Recommended Intakes) in the USA as from 2010 are 15 µg for most but the elderly, with estimated average requirement 10 µg and an upper limit of 100 µg, it is not uncommon in clinical practice to be able to achieve the optimal serum 25-hydroxy vitamin D without pushing towards the upper limit, especially in older people. That there may be vitamin D resistance is suggested by a PTH which remains high.

#### AUTHOR DISCLOSURES

The author has no conflict of interest in regard to this paper.

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## 東北亞的維生素 D 臨床營養施行

良好的臨床營養是建立在證據的基礎上並受到研究的啟發。然而，關於食物-健康之關聯仍有許多未解的問題，包含對營養失調的確認，及運用應有之照護來改正營養失調的動力。以維生素 D 為例，在臨床營養的科學及治療上就包含了生物醫學、社會與環境這幾個面向。維生素 D 主要受到日照的機會及食物所影響；也許它亦是人類健康狀況的指標，但此觀點仍在萌芽階段。然而，自從確認維生素 D 缺乏造成佝僂症和軟骨症以來，其缺乏的層面比我們所想的還要普遍且常見。現在已知幾乎沒有身體器官或系統不會受其影響。東北亞的問題不比世界其他地方小，但其風險會受到大氣污染、因不喜深膚色而避免曬到太陽的文化而增高；同時可能因攝取某些食物，如魚、蛋、內臟和菇類，部分彌補日照缺乏而減輕風險。維生素 D 缺乏的診斷需要高度懷疑的警覺且配合昂貴的生化檢驗確認。因此，公共衛生與臨床營養學家在工作上密切的合作是不可或缺的。

**關鍵字：**維生素 D 缺乏、種族、大氣污染、食物、日照、診斷、食物來源