### Mini Review

## Vitamin D status and food security in North-East Asia

Mark L Wahlqvist MD (Adelaide), MD (Uppsala) FRACP FAFPHM<sup>1,2,3</sup>

<sup>1</sup>Division of Preventive Medicine and Health Services Research, Institute of Population Health Sciences, National Health Research Institutes, Zhunan, Taiwan, ROC <sup>2</sup>School of Public Health, National Defense Medical Center, Taipei, Taiwan, ROC <sup>3</sup>Monash Asia Institute, Monash University, Melbourne, Victoria, Australia

The functions of vitamin D are pleiotropic affecting all body organs and systems in some way. Its adequacy depends principally on sunshine for UV light to stimulate its synthesis in skin and on foods which contain it, either animal-derived or obtained from fungi or mushrooms, with the UV-responsive substrates dehydrocholesterol for vitamin D-3 or ergosterol for vitamin D-2, respectively. Thus, vitamin D health is very environmentally dependent. With ecosytem degradation, whether by atmospheric pollution or food systems which do not derive UV irradiation, as with fish farming or mushroom processing, then this nutrient input into human biology may falter. Vitamin D deficiency is now common and widespread in North-East Asia as elsewhere. When discovered early in the 20<sup>th</sup> century it was linked to rickets in children and osteomalacia in adults and, for a generation or so, children were given fish, usually cod, liver oil to prevent bone disease. Now cod as a species and many edible fish are threatened. Over-exposure to sun-light increases the risk of skin cancer. We may tackle this problem by vitamin D supplementation with an alternative to fish liver. But the demographic pressures of population size and ageing (when the skin is less UV responsive) make the clinical and public health decisions and strategies demanding. Vitamin D health has become indicative of food security whose usual indicator is food diversity; such diversity may allow lesser concentrations to be more effective in organ and system function, but we have little evidence to support this at present.

Key Words: vitamin D, climate change, health, pleiotropic functions

### PLEOTROPIC FUNCTIONS OF VITAMIN D

Whereas once vitamin D was seen as a nutrient with actions principally in bone, its spectrum of activity is now known to be endocrine, autocrine and paracrine and to embrace probably every organ or tissue and every major body function<sup>1,2</sup> and throughout the life-cycle.<sup>3-6</sup> These actions range from cellular differentiation and risk for neoplastic disease,<sup>7,8</sup> to energy regulation and adiposity, locomotion (muscle and bone), cardiorespiratory,<sup>9,10</sup> renal,<sup>11</sup> gut,<sup>12</sup> integument (skin),<sup>13</sup> cognitive <sup>4</sup> and central nervous system,<sup>14</sup> the special senses,<sup>15,16</sup> male and female reproduction,<sup>17,18</sup> other endocrine (including pancreatic and diabetes),<sup>19</sup> immune system<sup>20-24</sup> and inflammatory responses.<sup>1,20</sup> The morbidity and threats to life of vitamin D deficiency extend well beyond the original recognition of its contribution to rickets in children <sup>25,26</sup> and to osteomalacia and osteoporosis in adult.<sup>1</sup>

### SOURCES

What is, therefore, most interesting is how dependent its status is on sun exposure and on food which was worked out by a number of investigators and eventually named vitamin D by McCollum in the 1920s.<sup>27</sup> The problem with foods as a source is that those that contain it are few, mainly animal-derived where dehydrocholesterol (cholesterol is only found in animals) is the precursor or fungi like mushrooms which contain the precursor ergosterol. In both cases, exposure to ultraviolet light is required to pro-

duce, respectively, vitamin D-3 or vitamin D-2. For most people, skin exposure to sunlight is the principal source unless the winters are long and dark and where seafood is abundant (as in the arctic regions).

#### Sunlight

Dependence on sunlight for vitamin D has become difficult for many since the risk of skin cancer through actinic damage has become a public health priority, especially where the ozone layer has been depleted through atmospheric contamination. Added to this is atmospheric pollution which obscures the sun, as in many urban precincts in North-East (NE) Asia, and where people spend more and more time indoors or in cars.

#### Food

In NE Asia, the main food sources of vitamin D are fish, meat, dairy (if fortified or irradiated with UV), eggs and mushrooms (where they have been dried in the sun). The

Manuscript received 4 December 2012.

doi: 10.6133/apjcn.2013.22.1.21

**Corresponding Author:** Prof Mark L Wahlqvist, Division of Preventive Medicine and Health Services Research, Institute of Population Health Sciences, National Health Research Institutes, No. 35 Keyan Road, Zhunan Town, Miaoli County, Taiwan 35053, ROC.

Tel: +88637246166 ext 36366; Fax: +88637586261 Email: profmlw@nhri.org.tw

skin of animals like chicken can be a source if the chickens have been raised with sunlight exposure.<sup>3</sup> Liver can be an important source, but its popularity is waning among younger people and because people fear that it might contain accumulated toxicants.

Increasing dependence on food which is vitamin D poor exacerbates the problem of limited sun exposure. This is occurring for several reasons. One is that there has been a concerted public health program in cardiovascular disease prevention to discourage animal-derived foods that happen to contain vitamin D because they are cholesterol-rich like eggs, organ meats (which include liver, brain, 'sweet-breads'). Another is that, for many, their dietary diversity is narrow, particularly through the workaday week when short-cuts to meal preparation and cheaper food choices are made.<sup>28</sup> Dairy is a useful source if fortified, but liquid milk itself is not a particularly good source of vitamin D.<sup>29</sup> In NE Asia, elderly people tend to use imported milk powder as a dairy source and this is usually fortified with vitamin D.<sup>3</sup> Food intake itself rarely provided the DRIs (Dietary Recommended Intakes) for vitamin D, and supplements are used to meet a gap which could be met with sun-light exposure, if it were not for the constraints mentioned above.<sup>4</sup>

### **RISK FACTORS FOR DEFICIENCY**

Environment, season, diet and skin pigmentation are major risk factors for vitamin D deficiency and its related health outcomes. Being male is a notable risk in Chinese men compared with women.<sup>30</sup> Physical activity and not smoking are favourable. There are also several other individual sociocultural and behavioural risk factors. These include hats and clothing, parasol usage, kind of recreation such as swimming, use of sunscreen use, occupational conditions, outdoor activities, travel by bicycle or car or public transport, and vitamin supplement usage.<sup>31</sup>

### EXTENT OF DEFICIENCY IN NE ASIA

With major gradients in sunlight exposure in NE Asia, it would be expected that those who live nearer to the equator would have the better vitamin D biochemical status whatever the intakes. This is probably the case as reports from sub-tropical and tropical Taiwan suggest.<sup>3,6</sup> Certainly, in the further north, Korea<sup>19,32</sup> exhibits extensive biochemical and functional deficiency. The same is the case for China.<sup>9,33,34</sup> Japanese elderly have been found to have acceptable vitamin D intakes in excess of 7 µg per day, but low 25-hydroxy vitamin D status;<sup>35</sup> this situation underscores the likely ongoing life-long need for sun exposure although its inadequacy might be compensated for by food fortification or supplementation. But that would overlook the companion value and eco-nutritional dimensions of being outdoors.<sup>36</sup>

Notwithstanding the relatively satisfactory vitamin D intakes in Taiwanese women, at the lower end of intake vitamin D have a protective effect against breast cancer in premenopausal women of normal weight in subtropical Taiwan. Intakes less than 5  $\mu$ g per day were a risk factor.<sup>8</sup> Lesser sunlight exposure was also a risk factor for breast cancer. A problem among Chinese women in this regard is sunlight avoidance with parasols and face masks in order to be pale (quite the reverse of European women in

Australia who seek the sun and suffer increased skin cancer as a consequence). In the Asia pacific region an example of apparently favourable vitamin D status is that of Fijian and Indian-Fijian women, while dark-skinned, as judged by serum 25-hydroxy vitamin D.<sup>37</sup>

While vitamin D deficiency is associated with increased mortality in a meta-analysis,<sup>38</sup> in Linxiang, china, noted for its micronutrient deficiencies and a link between vitamin D deficiency and oesophageal cancer,<sup>7</sup> mortality has not been found associated with vitamin D status.<sup>39</sup> It is possible that this incongruous finding is related to competing risks for mortality.

The question of optimal vitamin D intakes is clearly dependent on a number of behavioural and environmental considerations.<sup>40</sup> But the optimal serum concentrations of active forms of vitamin D are found to be higher than commonly encountered in surveys or clinical practice. Insofar as mortality is concerned, 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>38</sup>

# GENES AND ENVIRONMENT – ECOLOGICAL FACTORS AND SOLUTIONS

Genetic factors play a minor role in serum vitamin D variability although an exception may be Chinese men<sup>30</sup> and in winter with the residual serum concentrations after the more elevated summer values.<sup>31</sup>

Nevertheless, the expression of vitamin D related health outcomes for a particular intake and serum status may be considerably affected by vitamin D receptor polymorphisms.<sup>41</sup>

# OPTIMAL STATUS: IS IT POSSIBLE TO MANAGE WITH LESS?

Food intake and nutritional status may affect vitamin D function in a number of ways and these may extend back to fetal life and epigenetic effects on vitamin D absorption or cutaneous synthesis, transport, conversion to the active forms, 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D, as well as vitamin D receptor activity. Any of these considerations might allow people in some circumstances to have less sunlight exposure, consume safely or have lower serum status than otherwise possible.

Each of the fat soluble vitamins may interact with each other. Vitamins D and K both affect bone pathophysiology since osteocalcin is a vitamin K dependent bone protein.<sup>1,3,35</sup>

How much active vitamin D is required will also depend on the health outcome in question e.g., osteoporosis and fracture, CVD, and skin cancer where quite different associated risk profiles apply between them.

The environment to which an individual is exposed will also modulate the risk as previously enumerated.

### ENVIRONMENTAL MATCH AND VITAMIN D NUTRITION AS A FOOD SECURITY ISSUE

In human evolution various adaptations have enabled us to live with a wide range of climates, seasonal changes and food systems. Skin colour is an example which allows more or less cutaneous vitamin D synthesis dependent on sun exposure and which has allowed for restricted dietary vitamin D intakes. As sun exposure, whether for public health reasons or inadvertently, lessens, so dependence on the food supply will increase. Vitamin D fortification of foods or supplements appears to be part of the solution, but this approach is contextually novel for our species and its full risk analysis incomplete. This emerging scenario of food and environmental insecurity requires a more ecological approach.<sup>36,42-46</sup>

### AUTHOR DISCLOSURES

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

### REFERENCES

- 1. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357: 266-81.
- Verstuyf A, Carmeliet G, Bouillon R, Mathieu C. Vitamin D: a pleiotropic hormone. Kidney Int. 2010;78:140-5.
- Lee MS, Li HL, Hung TH, Chang HY, Yang FL, Wahlqvist ML. Vitamin D intake and its food sources in Taiwanese. Asia Pac J Clin Nutr. 2008;17:397-407.
- Llewellyn DJ, Lang IA, Langa KM, Melzer D. Vitamin D and cognitive impairment in the elderly U.S. population. J Gerontol A Biol Sci Med Sci. 2011;66:59-65.
- 5. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008;122:398-417.
- Wu SJ, Pan WH, Yeh NH, Chang HY. Trends in nutrient and dietary intake among adults and the elderly: from NAHSIT 1993-1996 to 2005-2008. Asia Pac J Clin Nutr. 2011;20:251-65.
- Abnet CC, Chen W, Dawsey SM, Wei WQ, Roth MJ, Liu B, Lu N, Taylor PR, Qiao YL. Serum 25(OH)-vitamin D concentration and risk of esophageal squamous dysplasia. Cancer Epidemiol Biomarkers Prev. 2007;16:1889-93.
- Lee MS, Huang YC, Wahlqvist ML, Wu TY, Chou YC, Wu MH, Yu JC, Sun CA. Vitamin D decreases risk of breast cancer in premenopausal women of normal weight in subtropical taiwan. J Epidemiol. 2011;21:87-94.
- Li F, Peng M, Jiang L, Sun Q, Zhang K, Lian F, Litonjua AA, Gao J, Gao X. Vitamin D deficiency is associated with decreased lung function in Chinese adults with asthma. Respiration. 2011;81:469-75.
- Zittermann A. Vitamin D and disease prevention with special reference to cardiovascular disease. Prog Biophys Mol Biol. 2006;92:39-48.
- Zhang Y, Kong J, Deb DK, Chang A, Li YC. Vitamin D receptor attenuates renal fibrosis by suppressing the reninangiotensin system. J Am Soc Nephrol. 2010;21:966-73.
- Wu S, Liao AP, Xia Y, Li YC, Li JD, Sartor RB, Sun J. Vitamin D receptor negatively regulates bacterial-stimulated NF-kappaB activity in intestine. Am J Pathol. 2010;177:686-97.
- 13. Eide MJ, Johnson DA, Jacobsen GR, Krajenta RJ, Rao DS, Lim HW, Johnson CC. Vitamin D and nonmelanoma skin cancer in a health maintenance organization cohort. Arch Dermatol. 2011;147:1379-84.
- Cantorna MT. Vitamin D and multiple sclerosis: an update. Nutr Rev. 2008;66:S135-8.
- Ikeda K, Kobayashi T, Itoh Z, Kusakari J, Takasaka T. Evaluation of vitamin D metabolism in patients with bilateral sensorineural hearing loss. Am J Otol. 1989;10:11-3.
- 16. Millen AE, Voland R, Sondel SA, Parekh N, Horst RL, Wallace RB, et al. Vitamin D status and early age-related macular degeneration in postmenopausal women. Arch Ophthalmol. 2011;129:481-9.

- Grundmann M, von Versen-Hoynck F. Vitamin D roles in women's reproductive health? Reprod Biol Endocrinol. 2011; 9:146.
- 18. Blomberg Jensen M, Bjerrum PJ, Jessen TE, Nielsen JE, Joensen UN, Olesen IA et al. Vitamin D is positively associated with sperm motility and increases intracellular calcium in human spermatozoa. Hum Reprod. 2011;26: 1307-17.
- 19. Lee BK, Park S, Kim Y. Age- and gender-specific associations between low serum 25-hydroxyvitamin D level and type 2 diabetes in the Korean general population: analysis of 2008-2009 Korean National Health and Nutrition Examination Survey data. Asia Pac J Clin Nutr. 2012;21: 536-46.
- 20. Coussens AK, Wilkinson RJ, Hanifa Y, Nikolayevskyy V, Elkington PT, Islam K et al. Vitamin D accelerates resolution of inflammatory responses during tuberculosis treatment. Proc Natl Acad Sci U S A. 2012;109:15449-54.
- 21. Fabri M, Stenger S, Shin DM, Yuk JM, Liu PT, Realegeno S, et al. Vitamin D is required for IFN-gamma-mediated antimicrobial activity of human macrophages. Sci Transl Med. 2011;3:104ra2.
- 22. Ginde AA, Mansbach JM, Camargo CA, Jr. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2009;169: 384-90.
- Grant WB. Vitamin D supplementation could reduce risk of sepsis in infants. World J Pediatr. 2010;6:185; author reply -6.
- 24. Sudfeld CR, Wang M, Aboud S, Giovannucci EL, Mugusi FM, Fawzi WW. Vitamin D and HIV progression among Tanzanian adults initiating antiretroviral therapy. PLoS One. 2012;7:e40036.
- Greer FR. 25-Hydroxyvitamin D: functional outcomes in infants and young children. Am J Clin Nutr. 2008;88:529S-33S.
- 26. Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. Prospective study of vitamin D supplementation and rickets in China. J Pediatr. 1992;120: 733-9.
- 27. The National Academy of Sciences. The National Academies: Beyond Discovery. The path from research to human benefit unraveling the enigma of vitamin DVersion. [cited 2012/12/2]; Available from: http:// www.beyonddiscovery.org/content/view.txt.asp?a=414.
- 28. Lo YT, Chang YH, Lee MS, Wahlqvist ML. Dietary diversity and food expenditure as indicators of food security in older Taiwanese. Appetite. 2012;58:180-7.
- Briggs D, Wahlqvist ML. Food facts. Melbourne: Penguin Books; 1984.
- 30. Arguelles LM, Langman CB, Ariza AJ, Ali FN, Dilley K, Price H et al. Heritability and environmental factors affecting vitamin D status in rural Chinese adolescent twins. J Clin Endocrinol Metab. 2009;94:3273-81.
- 31. Karohl C, Su S, Kumari M, Tangpricha V, Veledar E, Vaccarino V, Raggi P. Heritability and seasonal variability of vitamin D concentrations in male twins. Am J Clin Nutr. 2010;92:1393-8.
- Choi EY. 25(OH)D status and demographic and lifestyle determinants of 25(OH)D among Korean adults. Asia Pac J Clin Nutr. 2012;21:526-35.
- 33. Wat WZ, Leung JY, Tam S, Kung AW. Prevalence and impact of vitamin D insufficiency in southern Chinese adults. Ann Nutr Metab. 2007;51:59-64.
- 34. Zhu Z, Zhan J, Shao J, Chen W, Chen L, Li W, Ji C, Zhao Z. High prevalence of vitamin D deficiency among children

aged 1 month to 16 years in Hangzhou, China. BMC Public Health. 2012;12:126.

- 35. Kuwabara A, Himeno M, Tsugawa N, Kamao M, Fujii M, Kawai N et al. Hypovitaminosis D and K are highly prevalent and independent of overall malnutrition in the institutionalized elderly. Asia Pac J Clin Nutr. 2010;19:49-56.
- Wahlqvist ML. Eco-nutritional disease or nutrition and chronic disease. Asia Pac J Clin Nutr. 2002;11 Suppl 9: S753-5.
- Heere C, Skeaff CM, Waqatakirewa L, Vatucawaqa P, Khan AN, Green TJ. Serum 25-hydroxyvitamin D concentration of Indigenous-Fijian and Fijian-Indian women. Asia Pac J Clin Nutr. 2010;19:43-8.
- 38. Zittermann A, Iodice S, Pilz S, Grant WB, Bagnardi V, Gandini S. Vitamin D deficiency and mortality risk in the general population: a meta-analysis of prospective cohort studies. Am J Clin Nutr. 2012;95:91-100.
- 39. Lin SW, Chen W, Fan JH, Dawsey SM, Taylor PR, Qiao YL, Abnet CC. Prospective study of serum 25-hydroxyvitamin d concentration and mortality in a chinese population. Am J Epidemiol. 2012;176:1043-50.
- 40. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich

T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr. 2006;84:18-28.

- 41. Uitterlinden AG, Fang Y, Van Meurs JB, Pols HA, Van Leeuwen JP. Genetics and biology of vitamin D receptor polymorphisms. Gene. 2004;338:143-56.
- 42. Wahlqvist ML. Chronic disease prevention: A life-cycle approach which takesaccount of the environmental impact and opportunities of food, nutritionand public health policies
  the rationale for an eco-nutritional disease nomenclature. Asia Pac J Clin Nutr. 2002;11 Suppl 9: S759-62.
- 43. Wahlqvist ML. Why food in health security (FIHS)? Asia Pac J Clin Nutr. 2009;18:480-5.
- 44. Wahlqvist ML, Keatinge JD, Butler CD, Friel S, McKay J, Easdown W et al. A Food in Health Security (FIHS) platform in the Asia-Pacific Region: the way forward. Asia Pac J Clin Nutr. 2009;18:688-702.
- 45. Wahlqvist ML, McKay J, Chang YC, Chiu YW. Rethinking the food security debate in Asia: some missing ecological and health dimensions and solutions. Food Security. 2012;4: 657-70.
- 46. Li D, Wahlqvist ML. Securing food from field to table: what can we do? Asia Pac J Clin Nutr. 2011;20:149-50.

### Mini Review

## Vitamin D status and food security in North-East Asia

Mark L Wahlqvist MD (Adelaide), MD (Uppsala) FRACP FAFPHM<sup>1,2,3</sup>

<sup>1</sup>Division of Preventive Medicine and Health Services Research, Institute of Population Health Sciences, National Health Research Institutes, Zhunan, Taiwan, ROC <sup>2</sup>School of Public Health, National Defense Medical Center, Taipei, Taiwan, ROC <sup>3</sup>Monash Asia Institute, Monash University, Melbourne, Victoria, Australia

## 東北亞的維生素 D 狀況與糧食安全

維生素 D 的功能是透過某些途徑,多效地影響全身器官及系統。足量的維生素 D,主要靠陽光中的紫外線刺激皮膚合成,及含有維生素 D 的食物,如來 自動物或菇菌類中所含的維生素 D-3 與 D-2,分別由去氫膽固醇與麥角固醇合 成。因此,體內維生素 D 的狀況易受到環境影響。隨著生態系統的衰落,不 管是大氣污染或是因為養殖漁業、菇類加工,使這些食物無法保有經由紫外線 輻射而產生的維生素 D,可能讓此營養素進入人體的機會隨之減少。目前東北 亞維生素 D 缺乏的情形和他處一樣常見且普遍。在 20 世紀初,維生素 D 被發 現與孩童佝僂症和成人的軟骨症有關,當時那一輩的孩童藉由給與魚肝油(通 常是鱈魚)來防止骨疾病。然而現在,鱈魚及許多可食的魚類數量均銳減,過 度暴露於陽光下則會增加皮膚癌的風險。為了解決此問題,也許應以維生素 D 補充劑來取代魚肝。但是人口增加及老化(此時皮膚對紫外線的反應降低)的壓 力,使得臨床及公共衛生上的決策變得不可或缺。維生素 D 狀況已成為糧食 安全的代言,常用的指標為食物多樣性;多樣性或許使得以較少的濃度,就能 在器官和系統功能更有效率,但目前支持的證據尚不足。

關鍵字:維生素 D、氣候變遷、健康、多效作用