

# VITAMIN D PART II: CLINICAL IMPLICATIONS

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## INTRODUCTION

Vitamin D is critical for the development, growth, and maintenance of a healthy body, from birth until death. *'The Focus on Vitamin D'* in the February/March issue of San Doctor, gave a practical update on vitamin D. Here we provide a brief review of the literature, and summarise the clinical importance of vitamin D.

## AUTISM

Low maternal vitamin D3 has important ramifications for the developing brain. Vitamin D is a steroid hormone with many important functions in the brain, mediated through the nuclear vitamin D receptor (VDR). Disfunctional VDR demonstrate altered emotional behavior and specific motor deficits. Malnutrition (e.g. of vitamin D) may coexist with overnutrition (excessive calory intake) particularly among those with abnormal cognition or autistic spectrum.<sup>1,2</sup>

## AUTOIMMUNE ILLNESS

Links exist between the immune, nervous, and endocrine systems. Hormones of the endocrine system, such as vitamin D, help the immune and nervous systems defend the body, with defects leading to autoimmune disorders.

Vitamin D in immunity is involved in feedback reactions to eliminate inflammation or to influence CD4 T-cell differentiation, or to increase the function of T suppressor cells. The active form of vitamin D produces and maintains self-immunologic tolerance: some studies show that 1,25(OH)2D inhibits induction of disease in autoimmune encephalomyelitis, thyroiditis, type-1 diabetes mellitus, inflammatory bowel disease (IBD), systemic lupus erythematosus, and collagen-induced arthritis and Lyme arthritis.<sup>3</sup>

Autoimmune diseases like multiple sclerosis (MS) and inflammatory bowel disease (IBD) occur because of an inappropriate immune-mediated attack against self-tissue. Analyses of genetically identical twins shows that besides genetics there are important environmental factors that contribute to MS and IBD development. Reduced vitamin D availability due to limited sunshine exposure or diet may play a role in the development of MS and IBD.<sup>4</sup>

## CANCER

Vitamin D inhibits inappropriate cell division and metastasis, reduces blood vessel formation around tumors, and regulates proteins that affect tumor growth. It also enhances anti cancer actions of immune system chemicals and chemotherapy drugs.

Low levels of vitamin D are associated with increased risk of oesophageal cancer in men, but not in women.<sup>5</sup> In addition to sun exposure in adulthood, sun exposure in early life protects against the development of prostate cancer.<sup>6</sup> Improving calcium and vitamin D nutritional status substantially reduces all-cancer risk in postmenopausal women (Relative risk 0.402, p=0.01)<sup>7</sup>. Higher intakes of calcium and vitamin D are associated with a lower risk of developing premenopausal breast cancer.<sup>8</sup> The incidence of colorectal cancer could be halved with a vitamin D intake of 1000-2000 IU/day<sup>9</sup>.

A systematic review of the literature on the role of sunlight in preventing cancer (excluding skin cancer) showed a significant inverse correlation for prostate, breast and ovarian cancers<sup>10</sup>.

## CHRONIC PAIN

Vitamin D deficiency is a major contributor to chronic low back pain in areas where vitamin D deficiency is endemic. A recent large study has shown the association between severe hypovitaminosis D and persistent, non-specific musculoskeletal pain, further suggesting that patients with no apparent cause of pain should be assessed and possibly treated for vitamin D deficiency<sup>11</sup>.

## COGNITIVE FUNCTION

Recent research indicates vitamin D deficiency is associated with low mood and cognitive impairment in the elderly<sup>12</sup>.

## DIABETES

Vitamin D helps maintain adequate insulin levels. Preliminary evidence suggests supplementation can increase insulin levels in people with type 2 diabetes. Prolonged supplementation may help reduce blood sugar levels.

Decreased vitamin D concentrations are independently associated with prevalent CVD in type-II diabetic patients with mild kidney dysfunction<sup>13</sup>. Genetic variations in vitamin D metabolism affects susceptibility to type-I diabetes<sup>14</sup>. There is a positive correlation between low 25(OH) vitamin D concentrations and insulin resistance<sup>15</sup>. Vitamin D and calcium insufficiency may negatively influence glycaemia, whereas combined supplementation with both nutrients may be beneficial in optimising glucose metabolism<sup>16</sup>. Further, in otherwise healthy older adults with impaired fasting glucose (in range 5.6 – 6.9 mmol/L) supplementation with calcium and vitamin D slowed the increase in glycaemia and insulin resistance that would have been expected over time<sup>17</sup>.

## HEART DISEASE

Studies have indicated reduced ultraviolet B exposure in CHF patients during childhood, adolescence, and early adulthood. Activated vitamin D has been shown to increase survival in patients with cardiovascular disease<sup>18</sup>. Vitamin D levels are associated with important cardiovascular risk factors that supplementation may reduce<sup>19</sup>.

## HYPERTENSION

Clinical and experimental data support the view that vitamin D metabolism is involved in blood pressure regulation and other metabolic processes. Epidemiological studies suggest that vitamin D insufficiency is related to several disorders observed among the elderly such as breast, prostate and colon cancers, type-2 diabetes and cardiovascular disorders including hypertension. It seems that 800IU of vitamin D daily in combination with calcium, reduces systolic blood pressure in elderly women<sup>20</sup>.

## MELANOMA

An inability to tan is the number one risk factor for melanoma. Those who tan easily or who have darker skin are far less likely to develop the disease. A new theory is that melanoma is actually caused by sunlight (vitamin D) deficiency and that safe sun exposure actually helps prevent the disease<sup>21, 22, 23, 24</sup>.

## MENTAL ILLNESS

Vitamin D deficiency has been implicated in various psychiatric and neurologic disorders, including mood and cognitive performance in the elderly<sup>25</sup>. Vitamin D supplementation to maintain bone health may also retard some consequences of brain aging<sup>26</sup>.

## MULTIPLE SCLEROSIS

Vitamin D supplementation may help prevent the development of MS as well as provide additional treatment benefits.<sup>27, 28</sup> High circulating levels of vitamin D are associated with a lower risk of multiple sclerosis<sup>29</sup>.

## MUSCULAR WEAKNESS AND FALLS

Specific receptors for vitamin D have been identified in human muscle tissue. Cross sectional studies show that elderly persons with higher vitamin D serum levels have increased muscle strength and a lower number of falls<sup>30,31</sup>.

## OBESITY

Serum vitamin D is significantly lower in obese individuals- deficiency is associated with the metabolic syndrome in morbidly obese patients<sup>32</sup>. Consumption of a calcium plus vitamin D supplement during a weight-loss intervention enhanced the beneficial effect of body weight loss on the lipid and lipoprotein profile in overweight and obese women, whose usual daily calcium intake was low<sup>33</sup>.

## OSTEOARTHRITIS

Low intake and low serum levels of vitamin D appear to be associated with an increased risk for progression of osteoarthritis. The increase in bone mineral density associated with supplementation by vitamin D improves outcomes for osteoarthritis sufferers<sup>34</sup>, a recommended strategy as opposed to chronic pharmacological interventions<sup>35</sup>.

## OSTEOPOROSIS

Vitamin D deficiency is extremely prevalent in the elderly. Most often the first symptoms are myopathy with muscle pain, fatigue, muscular weakness, and gait disturbances. More severe deficiency causes osteomalacia with deep bone pain, reduced mineralization of bone matrix, and low energy fractures<sup>31,36,37</sup>.

## PREGNANCY AND LACTATION

Studies indicate human milk contains inadequate levels of vitamin D (usually because the mother is vitamin D deficient) and that routine vitamin D supplementation is advisable for breast fed infants who are deprived of sunlight exposure<sup>38,39</sup>.

## MISCELLANEOUS

Vitamin D has been implicated in the pathology of various other health disorders including influenza, psoriasis, gout, otosclerosis, interstitial cystitis, decreased pulmonary function, thrombosis, chronic kidney disease, pancreatitis, rheumatology, hepatitis B infections, haemochromatosis, and gastrointestinal diseases<sup>40,41,42</sup>.

## CONCLUSIONS

These and many other studies emphasise that vitamin D is not just for bones. Maintaining adequate levels is important for many tissues and hence health outcomes.

## ACKNOWLEDGEMENTS

This paper highlights a few, of hundreds of articles on vitamin D collated by the Vitamin D Council, and available on their Web site at: <http://www.vitaminCouncil.org/research.shtml>

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