



Prevention of Chronic Diseases by Maintaining Physiological Concentrations of Vitamin D

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Vitamin D deficiency is prevalent worldwide and common in all age groups. The seriousness of this nutrient deficiency is grossly underestimated. It affects most ethnic groups and is a major global public health problem. In fact, vitamin D deficiency is now the commonest nutrient deficiency and a pandemic, that threatens approximately half the world's population.

Common Causes of Vitamin D Deficiency

Except for vitamin-D-fortified foods, sun-exposed mushrooms, and oily fish (including sardines, mackerel, and salmon), foods contain minimal amounts of vitamin D. Thus, diet does not provide an adequate amount of the vitamin to meet daily needs in most people. Consequently, more than 50% of the world's population is vitamin D insufficient or deficient [1,2].

The most common causes of vitamin D deficiency are (a) insufficient exposure to sunlight, (b) inefficient conversion of ergosterol to vitamin D in the skin, (c) insufficient intake of dietary vitamin D, (d) gastrointestinal abnormalities that hinder vitamin D absorption, (e) increased catabolism of vitamin D (e.g., taking certain medication), (f) failure of activation of vitamin D because of liver or renal disease, and (g) rare genetic diseases that affect absorption, transportation, or activation of vitamin D.

In vivo Generation of Vitamin D

Dietary vitamin D is an essential micronutrient, but food contains little of this. Thus, the vast majority of the need is supposed to generate in the skin after exposure to ultraviolet B (UVB) rays; however, many do not have the opportunity to receive adequate exposure to the light and other choose not get exposed due to various reasons, especially in fear of causing skin cancers [3]. Following UV exposure, 7-dehydrocholesterol present in the skin is photo-converted to form previtamin D. Subsequently, previtamin D isomerizes to form vitamin D, binds to vitamin D binding protein and transported to the liver via the bloodstream [4].

In the liver, vitamin D undergoes hydroxylation to form 25-hydroxyvitamin D [25(OH)D] by CYP27A1, one of many cytochrome P450 enzymes. 25(OH)D is the storage form of vitamin D and the precursor of the active vitamin D hormone, 1,25-dihydroxyvitamin D [1,25(OH)₂D] [25(OH)D] [5]. This binds to vitamin D binding protein and transported to the renal tubular cells where it gets further hydroxylated to form 1,25(OH)₂D, the active steroid hormone calcitriol, by the enzyme CYP27B1 [6].

Calcitriol is an obligatory, secosteroidal hormone, of which adequate concentration is essential for optimal physiological activities and maintenance of health [7]. In addition to renal tubular cells, many extra-renal target tissue cells also have the enzyme CYP27B1 intracellularly, capable of converting 25(OH)D into highly biologically active, calcitriol. The biological and clinical importance of the non-hormonal form of calcitriol has been neglected till recently. The latter is important for many intracellular activities of target cells, outside the renal and musculoskeletal tissues such as subduing inflammation and oxidative stress [8], and likely to be a key defense against invading pathogens, autoimmune disorders and cancer.

Exposure to UVB Rays from the Sun

Despite the availability of adequate sunlight throughout the year, in many parts of the world, many continue to be vitamin D deficient. The reasons for such deficiency include geographic locations of people—such as living far from the equator—higher and lower latitudes; sun-avoidance behavior; the overuse of sunscreens that block UVB rays that cut off the 290–315-nm spectra; the health of an individual's skin; the use of medications that enhance the breakdown of vitamin D (e.g., anti-epileptic drugs, anti-retroviral agents, glucocorticoids, etc.); and gastrointestinal absorption issues (celiac disease, Chron's disease, gastric bypass surgery, and so forth). Whilst, shorter wavelengths, below 295 nm, are the most effective in generating vitamin D, the atmospheric ozone layer filter out a significant portion of UVB and UVA rays.

The Use of Sunscreens and Generation of Vitamin D in the Skin

Most individuals who avoid sun exposure become vitamin D deficient. Commercially available sunscreens with a sun protection factor (SPF) greater than 15 block UV rays from reaching the skin. These sunscreens primarily block UVA rays, which account for more than 90% of solar radiation; UVB rays are blocked to a lesser extent, especially by sunscreens with a high UVA-protection factor. Thus, the use of sunscreens may still allow some UVB rays to reach the skin (dermis) to generate some amount of vitamin D. However, the best option is the exposure to the skin for 15 to 30 minutes based on the skin color, and then apply sunscreen of SPF greater than 20 to protect sunburns/erythema formation, photo aging of the skin, and skin cancer in later life.

In fact, a recent review concluded that daily and recreational use of sunscreen photoprotection does not compromise vitamin D synthesis,

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even when the sunscreen is applied under optimal conditions [9]. Another study concluded that sunscreens may be used to prevent sunburn while allowing vitamin D synthesis in the skin. The use of high UVA-SPF sunscreen enables significantly higher vitamin D synthesis than does a low UVA-PF sunscreen because the former, by default, transmits more UVB than does the latter [10]. Those who are unable to adhere to such recommendations because of lack of sunlight or cultural or medical reasons should consider vitamin D supplementation in recommended dosages.

Requirements of Vitamin D

During the first year of life, infants need at least 400 IU of vitamin D per day, and the requirement gradually increases to 1,000 IU/day. Most healthy adults require an intake of 1,000 to 2,000 IU/day, but elderly individuals require additional 2,000 IU/day, as the ability of the skin to generate vitamin D gradually reduced with age. Similar effects seen those with damage or scared skin, such as following burns and skin fibrosis.

Those with inherent disorders that affect the synthesis of vitamin D such as abnormalities of CYP-enzymes or who have enhanced catabolism of vitamin D for any reason will require much higher doses of vitamin D to maintain physiological 25(OH)D concentration and optimal health. Vitamin D₃ is the right choice as supplement, except for vegans who might prefer vitamin D₂.

Mode of Supplementing Vitamin D

From the time of ingestion of vitamin D or a reasonable exposure to sun, it takes approximately 3 days to see an increase in 25(OH)D concentration in the blood. Following oral intake, it takes several weeks to achieve the plateau of serum 25(OH)D concentration. Taking the usual supplemental doses of about 1,000 IU of vitamin D, person with serum 25(OH)D concentration of approximately 15 ng/mL, requiring 0.5 million IU of vitamin D will take more than one and half years to reach the minimum required serum concentration.

Similarly, a person who is deficient (i.e., serum 25(OH)D concentration under 10 ng/L) thus requiring approximately one million of IU of vitamin D will take more than three years to bring their serum 25(OH)D. In these examples, in the absence of upfront loading doses of oral vitamin D patients will continue to suffer and are at higher risks to contract other diseases for years. Thus, the importance of prescribing high doses of oral vitamin D, over a short period to bring the serum 25(OH)D concentration above 30 ng/mL and to start replenishing the body stores of vitamin D.

It is also important that, following completion of a course of high-dose (loading dose) of oral vitamin D supplementation, one should wait for at least three to four months before repeating serum 25(OH)D levels. This is in part because of the longer half-life, large storage capability, and the time taken to establish equilibrium of serum 25(OH)D concentration. If the blood level is still deficient, a second 6- to 10-week course of higher-dose (e.g., 50,000 IU/week) cholecalciferol (D₃) can be prescribed.

Maintenance of Serum 25(OH)D Levels

The amount of vitamin D a person needs daily to maintain a normal serum 25(OH)D concentration depends on several factors, including the darkness of the skin, age, sun exposure (time of the day and the month of the year—season), body storage, dietetic ingredients, and underlying medical conditions, and the ability of the liver and kidneys to hydroxylate precursors. As discussed, the latter two organs are essential for activation of vitamin D.

Infants, especially those who are exclusively breastfed, should be given nonprescription vitamin D drops containing 400 IU starting within the first few days after birth; the dosage should later be increased to 1,000 IU/day. Most elderly would be benefitted by consuming at least 2,000 IU/day. The use of tanning beds (which provide high doses of both UVB and UVA) is not recommended as a source for vitamin D because of the higher risk of skin damage and cancer.

What is an adequate level of vitamin D in the blood?

Vitamin D status is determined by measuring the serum 25(OH)D concentration, not by measuring 1,25(OH)₂D. 25(OH)D is a sensitive biomarker and the only means of determining vitamin D sufficiency or deficiency. The minimum blood 25(OH)D concentration requires for physiological activities is 30 ng/mL (75 pmol/L)—vitamin D sufficiency. However, a handful of recommendations, such as those of the U.S., Institute of Medicine suggest that 20 ng/mL (50 nmol/L), which is only sufficient to prevent osteomalacia and rickets. Since, such a low level has no beneficial effects on extra musculoskeletal system, most clinicians and scientists do not accept this.

As mentioned, 25(OH)D concentrations of less than 20 ng/mL are adequate only for preventing osteomalacia (and bone mineralization) but not for controlling infections, metabolic disorders, autoimmune diseases or cancer. The levels below 20 ng/mL have no protective effect on extraskeletal disorders mentioned above and in fact, make conditions such as diabetes and obesity worse. Consequently, 20 ng/mL is not considered as the minimum serum 25(OH)D concentration required to maintain good health.

The goal should be to reach and sustain serum level of 25(OH)D above the minimum concentration of 30 ng/mL; the optimal range is between 30 and 60 ng/mL. To achieve such via the sun exposure, depending on the skin color, one need to expose a third of the body surface to summer like sunlight for between 15 to 40 mins. However, for practical reasons, regular exposure to sunlight between the hours of late morning to midafternoon is not feasible for many people. They will be benefitted by a daily maintenance dose of an oral vitamin D₃ supplements, so as the elderly.

Summary

Except for vitamin-D-fortified foods, sun-exposed mushrooms, and oily fish (including sardines, mackerel, and salmon), food items contain minimal amounts of vitamin D. Thus, diet does not provide an adequate amount of the vitamin to meet daily needs in most people and many people are not getting adequate exposure to sunlight. Consequently, more than 50% of the world's population is vitamin D insufficient or deficient. In the absence of adequate exposure to sunlight, supplements are necessary for a healthier life.

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