

## **Understanding 1,25 dihydroxy Vitamin D and 25-hydroxy Vitamin D** (Compiled by Charles (Chuck) Maack – Prostate Cancer Advocate)

**1,25 dihydroxy Vitamin D (range 15.9-55.6pg/mL) is increased in sarcoidosis and hyperparathyroidism. It may be elevated in cases of hypercalcemia associated with malignant lymphoma. It is decreased in rickets, type I vitamin D-resistant rickets, hypoparathyroidism, pseudohypoparathyroidism, and renal osteodystrophy and psoriasis. Because of the complex, multifactorial control of calcium balance, it is often useful to measure parathyroid hormone in conjunction with vitamin D. This is NOT the assay to determine vitamin D deficiency. The 1,25-dihydroxy Vitamin D assay should never be used for detecting Vitamin D deficiency because levels will be normal or even elevated as a result of secondary hyperparathyroidism. Rather, 25-hydroxy Vitamin D is the appropriate assay.**

**25-hydroxy Vitamin D (range 32-100ng/ml) deficiency leads to the mobilization of calcium from bone. Individuals with more severe vitamin D deficiency can develop osteomalacia and/or osteoporosis. Osteomalacia in children, also referred to as rickets, results in well described skeletal malformations since their bones are actively growing. Recent clinical and epidemiological studies suggest that vitamin D deficiency may play a role in several conditions related to bone including prostate cancer, breast cancer, colon cancer, heart disease, hypertension, multiple sclerosis, and type 1 diabetes. A number of studies have shown that vitamin D deficiency is very common, especially in certain high-risk populations. This situation has occurred, in part, because the foods in the typical American diet are very low in vitamin D. Fatty fish, such as mackerel and salmon and fish liver oils, are some of the few natural dietary sources of vitamin D. Most people do not eat enough of these foods to maintain adequate vitamin D levels as well as many do not experience sufficient, safe, sun exposure. In the United States, vitamin D is added to milk in order to prevent the occurrence of rickets in the pediatric population. Unfortunately, too many children do not drink enough milk to raise their vitamin D levels to the optimum range. Also, recent studies have shown that the level of vitamin D in fortified milk is frequently much lower than that recommended by the FDA. Human milk contains very little vitamin D because many mothers are deficient, so children of mothers who choose to breast-feed are at risk of developing rickets if they are not given supplemental vitamin D. The American Academy of Pediatrics recommends that infants who are exclusively breast-feeding should be given a supplement of vitamin D. Several factors are associated with an increased risk of developing vitamin D deficiency. At risk populations include:**

- Individuals with low dietary vitamin D levels: Infants fed only mother's milk and children who do not drink fortified milk are at risk.**
- Individuals with malabsorption syndromes: Patients with pancreatic enzyme deficiency, Crohn disease, cystic fibrosis, celiac disease, and surgical resection of stomach or intestines are at risk.**
- Individuals with severe liver disease: Hepatic disease can reduce the conversion of vitamin D to 25-D and can lead to malabsorption of vitamin D.**
- Individuals with kidney disease: Nephrotic syndrome can increase the urinary loss of vitamin D.**

- **Individuals taking certain drugs:** Several medications, including phenytoin, phenobarbital, and rifampin accelerate the breakdown of vitamin D by the liver.
- **Individuals who live at higher latitudes:** Individuals who live in northern climates are at increased risk of deficiency, especially in winter months due to diminished exposure to UVB radiation.
- **Individuals who spend little time outside:** Individuals who are home-bound or simply choose to remain inside are at increased risk.
- **Older adults:** The skin becomes less efficient at producing vitamin D as one ages because of diminished levels of vitamin D precursors in the skin.
- **Individuals with decreased sun exposure for cultural reasons.** Women in some societies are required to cover themselves with heavy clothing, reducing exposure to the sun's rays.
- **Races with high melanin levels:** Increased skin pigmentation can reduce the efficiency of vitamin D conversion in the skin as much as 50-fold. Individuals with dark complexions living at higher latitudes are at increased risk.

Serum concentrations of 25-D are known to vary with age, sex, race, season, and geographic location. This has led to establish seasonal expected ranges for the geographic location and local population. This approach provides a "reference interval," but does not adequately determine health status with regard to vitamin D levels if a significant portion of the reference population is, in fact, deficient. A more useful parameter in clinical practice would be a nutritional threshold, below which an individual could be characterized as vitamin D deficient. Several investigators have approached this problem by assessing the correlation of plasma 25-D concentration with various biological markers. For example, plasma 25-D levels have been shown to have an inverse relationship to serum parathyroid hormone levels. Secondary hyperparathyroidism can be corrected with 25-D levels increased to >32ng/mL (80nmol/L). Serum concentrations <32ng/mL are associated with impaired insulin resistance and beta-cell function. Together these data suggest that 32ng/mL represents the appropriate threshold for identifying individuals with clinical vitamin D deficiency.

Interesting to note these remarks by John Cannell, M.D., of The Vitamin D Council:

"You see, the question is not "Should men with prostate cancer be treated with vitamin D?" The question is, "Should men with prostate cancer be allowed to die vitamin D deficient?" The evidence based medicine folks say they should. We say they shouldn't. All patients with prostate cancer should have their vitamin D deficiency aggressively and immediately corrected and that requires up to 4,000 units of cholecalciferol every day. Physicians, researchers, or scientists who say 4,000 units may be toxic are simply admitting their ignorance of current scientific literature.

Physicians who have read the recent scientific literature and who understand the physiology and pharmacology of cholecalciferol would be comfortable using up to 10,000 units of cholecalciferol a day while following the patient's PSA, urine and serum calcium, and 25(OH)D. Thanks to the Toronto group, scientific evidence now exists that suggests such an approach may help prostate cancer

patients;                      only                      time                      will                      tell.

Many patients with prostate cancer are on the long hopeless road towards death. Not only may plain old vitamin D help men with prostate cancer, it is likely to give them back their hope. Physicians have many rights, but the right to take away hope is not among them."

Medical Oncologist Charles "Snuffy" Myers provides this information regarding appropriate Vitamin D3 level:

"We use a broad goal of 50-100ng/ml. Most of what has been reported as Vitamin D toxicity is really toxicity from excessive calcium intake. From what I have seen, 25-hydroxyvitamin D appears to be very safe by itself. Clearly the literature is evolving rapidly and the direction is toward higher levels being also safe. In certain settings, hypercalcemia is quite unlikely. For example, in men on Zometa, it is hard to keep the calcium in the normal range - it all too easily slips into an abnormally low range, triggering hyperparathyroidism."

Note that Dr. Myers specifically remarks that the Vitamin D3 level should be within a "broad range" of 50-100ng/ml. That's his "broad range" spread. He assigns his patients specific goals, and for most that goal is in the 65ng/ml-75ng/ml range with total Vitamin D3 intake of up to 10,000 IU daily to reach that range. INCREASED VITAMIN D3 INTAKE SHOULD BE ACCOMPANIED BY REGULAR MONITORING OF BLOOD SERUM 25-HYDROXY VITAMIN D, BLOOD SERUM AND URINE CALCIUM LEVELS, AND PARATHYROID HORMONE LEVEL.

Of key importance is to have your Vitamin D level tested with a 25-hydroxy Vitamin D blood serum test and if deficient take action with increased but safe sun exposure as well as supplement consideration – in any event, include discussion with your physician).

Disclaimer: Please recognize that I am not a Medical Doctor. I have been an avid student researching and studying prostate cancer as a survivor and continuing patient since 1992. **The comments or recommendations I make are not intended to be the procedure for you to now follow; rather, they are to be reviewed along with the comments or recommendations of others for your own further research, study, and discussion with the physician providing your prostate cancer care to come to your own, personal conclusion.**