

VITAMIN D IN THE PREVENTION OF OSTEOPOROSIS AND CANCER

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Vitamin D acts in the body as both a vitamin and a hormone, exerting a powerful influence on maintaining bone density and preventing vital steps in the development of breast, prostate and colon cancers (and possibly other cancers). There is also evidence to suggest that more optimal vitamin D levels can reduce the risk of multiple sclerosis through its effects on immune system function.

Throughout younger adult life supplementation with vitamin D of 400 IU per day from a high potency multi-vitamin and mineral, combined with the vitamin D intake most people acquire from fortified dairy products and fish, is usually adequate to maintain blood levels of vitamin D in a range that is associated with healthy bone development, and the prevention of breast, prostate and colon cancers, and multiple sclerosis, according to available studies. However, by age 45-50 the enzyme in the kidney (alpha-hydroxylase) that converts vitamin D into its most active form (1,25 dihydroxy vitamin D, also known as calcitriol) becomes less active. This results in decreased synthesis of calcitriol and thus, tissues that rely on the health promoting influences of calcitriol are left to feel the effects of a calcitriol insufficiency state. Studies strongly suggest that the age-related decline in synthesis of calcitriol within the kidneys is a major contributing factor to the development of osteoporosis in women and men over 50 years of age, as well as the age-related increase in risk of breast, prostate and colon cancers that is common in North America and many industrialized countries. However, studies also indicate that individuals over the age 45 can compensate for the decline in calcitriol synthesis by raising their blood levels of the less potent form of vitamin, known as 25-hydroxy vitamin D.

Abundant evidence exists to show that adults who maintain blood levels of 25-hydroxy vitamin D in the range of 85-120 nmol/L (nanomoles per milliliter) have a significantly lower risk of developing osteoporosis, breast cancer, ovarian cancer, prostate cancer, colon cancer and multiple sclerosis. Studies also show that to ensure that blood levels of 25-hydroxy vitamin D are within this protective range, it is important to increase vitamin D supplementation to 800-1,000 IU per day, after the age of 45. Up until age 45 the 400 IU of vitamin D per day from a high potency multiple vitamin and mineral is adequate to meet vitamin D needs in most cases. However, after age 45, many experts strongly advise the addition of a daily supplement that contains 400-600 IU of vitamin D in a formulation that also provides an additional 500-700 mg of calcium (If the product also contains some additional magnesium, zinc and other bone support nutrients, that is perfectly acceptable).

Vitamin D and Bone Density

Vitamin D is required at all stages in life to optimize calcium absorption from the intestinal tract, which in turn, helps to increase bone mineral density during the developmental years and helps prevent the loss of calcium from bone after the age of 50. The increased deposition of calcium into our bones that occurs at an optimal rate up to age 24, and the prevention of calcium being leached from bones after age 50, are both essential aspects related to the prevention of osteoporosis.

Unfortunately, vitamin D insufficiency is wide spread in North America, especially in the more northern regions (above the 42 degree latitude), where sunlight intensity is very limited between October and May. Older individuals have also been shown to be at very high risk for vitamin D due to poor intake of vitamin D containing foods, reduced sunlight exposure and reduced conversion of 25-hydroxy vitamin D into calcitriol. Calcitriol is twice as potent as 25-hydroxy vitamin D in regards to its vitamin D effects on calcium metabolism, our bones and other tissues. Vitamin D deficiency is considered to correlate with a blood level of 25-hydroxyvitamin D below 20 ng/mL. Optimal levels of vitamin D are considered to be in the range of 85-120 ng/mL. It is this range of vitamin D status that is most strongly associated with a reduced risk of

osteoporosis, many cancers and multiple sclerosis. Unfortunately, a great number of adults fall into the range above the deficiency threshold and below the optimal range of vitamin D blood levels, which would be defined as a blood level of 21-79 nmol/L. This middle ground is often referred to as vitamin D insufficiency.

Your Bones Need More Vitamin D Support After 45

As I have mentioned, after the age of 45-50 the body is less able to convert 25-hydroxy vitamin D into calcitriol, due to a decline in the activity of the kidney enzyme known as alpha-hydroxylase. However if blood levels of 25-hydroxy vitamin D can be raised into the range of 85-120 nmol/L this amount of 25-hydroxy vitamin D has been shown to compensate for the drop off in calcitriol levels. Studies show that supplementation with 800-1,000 IU of vitamin D per day, after the age of 45, can elevate blood levels of 25-hydroxy vitamin D into the ideal range of 85-120 nmol/L and has been shown to reduce risk of osteoporotic fractures by more than 40%. Let's look at several studies that clearly illustrate this point.

In a large study of 3,720 elderly women living in nursing homes, those receiving 1,200 mg of calcium and 800 IU of vitamin D supplementation each day showed a 43% reduction in hip fractures over a 3-year period compared to those not taking these supplements (M. Chapuay, 1994). Another study showed that supplementation of postmenopausal women with 700 IU of vitamin D daily can reduce the annual rate of hip fractures from 1.3% to 0.5%, which is nearly a 60% reduction (B. Dawson-Hughes, 1995). Another study combining the supplementation of 500 mg of calcium and 700 IU of vitamin D revealed a significant reduced hip fracture rate in men and women taking this combination, compared to the placebo group, in a 3-year follow-up study (B. Dawson-Hughes, 1997).

There is now ample evidence to suggest that after the age of 45 it is extremely prudent to increase your vitamin D supplementation to reach a total daily value of 800-1,000 IU, in order to significantly reduce your risk of osteoporosis. This advice is meant for both men and women as osteoporosis now affects one in four women and one in eight men over the age of 50. However, the benefits of increased vitamin D supplementation doesn't end with the prevention of osteoporosis, but also has important implications for the prevention of breast, ovarian, prostate and colon cancer, as we shall explore next in part two of this article.

Vitamin D Prevents Cancer

Vitamin D receptors exist on intestinal cells and bone for regulating calcium absorption and bone metabolism as I have discussed. However, vitamin D receptors are also present in a wide variety of other tissues and organs, including the brain, pancreas, skin, gonads, prostate, stomach, colon, breast, kidney, connective tissue, parathyroid gland, mononuclear cells, and activated T and B-lymphocytes. Recent studies indicate that tissues expressing Vitamin D receptors are able to convert 25-hydroxyvitamin D, which they extract from the bloodstream, into calcitriol for their own internal use. As I have stated, the calcitriol form of Vitamin D is the most potent form of vitamin D, and this is not only true with respect to bone support, but studies also illustrate that calcitriol exerts a number of anti-cancer effects on local tissues that convert 25-hydroxy vitamin D into calcitriol for their own purposes, such as breast cells, prostate cells and colon cells. As such, circulating levels of 25 hydroxy vitamin D serves as the raw material from which many tissues synthesize calcitriol for their own internal use. Studies reveal that higher amounts of circulating 25-hydroxy vitamin D in the blood enables local tissues, such as breast, prostate and colon cells, to synthesize greater amounts of calcitriol for their own needs.

Epidemiological (observational) studies suggest that lower blood levels of 25-hydroxy vitamin D are associated with a higher risk of developing breast, colon, ovarian, and prostate cancer. This is an important finding as one in nine women are expected to develop breast cancer in their lifetime, one in eight men are expected to develop prostate cancer in their lifetime, and one in 16 women and one in 15 men, will develop colon or rectal cancer in their lifetime.

Interestingly, studies show that rates of breast, prostate and colon cancers increase as you travel further from the equator (either north or south) and that populations residing further from the equator also have

lower year round average blood levels of vitamin D. This is related to the fact that our bodies make vitamin D in response to direct exposure to sunlight (but not through a window). When sunlight hits our skin it triggers the conversion of 7-dehydrocholesterol into vitamin D (cholecalciferol) within our skin. From there, the vitamin D made in our skin (cholecalciferol) enters the blood stream and travels to the liver, where it is converted to 25-hydroxy vitamin D, which is five times more potent than cholecalciferol in terms of its vitamin D activity. Thus, populations living closer to the equator, who enjoy more year round sunlight intensity and exposure, manufacture more cholecalciferol in their skin and demonstrate higher year round average blood levels of 25-hydroxy vitamin D. As a general statement, populations in North America that live at or above the 42nd latitude have significantly higher rates of breast, colon and prostate cancer than populations living below the 42nd degree latitude. The 42nd degree latitude essentially divides the U.S. into two equal halves, north and south (running through the middle of California, and the tops of Arizona, New Mexico, Texas, Tennessee and the Carolinas). Some exceptions to this observation exist, in that people living in large cities in the South of the U.S. also have higher rates of these cancers per capita. C.F. Garland and F.C. Garland, who first published this data in the 1980's, explain this finding by indicating that the air pollution in large cities and tall buildings block much of the sunlight, and that city-dwellers tend not to wear short-sleeve shirts and shorts as often as country folk, and tend not to be outdoors during the sunniest hours of the day. As such, individuals in large cities in the South do not have blood levels of vitamin D that are high enough to protect them from breast, colon and prostate cancer as do individuals living in the more rural parts of the South, according to these researchers.

Overall, studies indicate that blood levels of 85-120 nmol/L are associated with a high degree of protection with respect to risk of breast, prostate and colon cancer, and may significantly reduce the risk of developing multiple sclerosis via its immune modifying influences.

How Does Calcitriol Reduce Cancer Risk In The Breast, Prostate, Colon and Possibly Other Tissues?

Experimental studies reveal that calcitriol exhibits a number of anti-cancer effects. Essentially prostate cells, breast cells, colon cells, and other cells that contain vitamin D receptors, extract 25-hydroxy vitamin D from the bloodstream and convert it into calcitriol once inside the cell. Calcitriol, in turn, slows down the rate of replication of these cells, an effect associated with decreased cancer development. The presence of calcitriol has also been shown to slow the rate of replication of human prostate, breast and colon cancer cells, under experimental conditions. Calcitriol also promotes newly formed cells to mature to their full adult potential, which also decreases the chance of these cells being transformed into a cancer cell by some external influence. Calcitriol also exerts a favorable effect on immune function, which is also thought to account for some of its anti-cancer influences. Calcitriol has also been shown to transform the appearance of human cancer cells (e.g. prostate cancer cells) back to healthy, non-malignant looking cells, and inhibit their replication, an effect that is lost once the calcitriol is no longer administered.

The Problem With Relying Upon Vitamin D From Sunlight and Food Sources

From an evolutionary standpoint, exposure to direct sunlight is the principle way in which we are set up to derive our Vitamin D stores. To maximize vitamin D synthesis within the skin all that is required is 15-20 minutes of direct sunlight exposure to your face, arms and legs, three times per week. However, experts warn that even this amount of cumulative sun exposure increases risk of skin cancer over our lifetime and that it is best to derive vitamin D from the consumption of fish, vitamin D-fortified dairy products and supplements. The point is that many people don't get 15-30 minutes of direct sunlight exposure each day, especially those of us living above the 42nd degree latitude within North America, where sunlight intensity between October and May is insufficient for our bodies to make vitamin D inside our skin.

Very few foods contain Vitamin D in their native form. It is best to eat fatty fish such as sardines, salmon and mackerel 3-4 times per week to help satisfy the body's Vitamin D requirement. Of course, there is suppose to be 100 IU of Vitamin D in every eight ounces of fortified milk, but studies undertaken by M. Holick and others showed that nearly two-thirds of the whole milk samples tested in one study had less than 80%, and several skim milk samples had 0%-50% of the amount of vitamin D appearing on the label. This

problem will continue as vitamin D levels in milk are affected by season, the breed of cow, the animal's diet, its exposure to sunlight, and procedures used in fortification. Although the 1997 recommendations by the Institute of Medicine suggest that middle-aged adults (50-70 yrs) should consume 400 IU of Vitamin D per day and older subjects should consume 600 IU of Vitamin D per day, evidence is strong to indicate that in the absence of exposure to sunlight, the adequate intake for Vitamin D should be at least 800–1,000 IU per day by age 45-50. M. Holick points out that Vitamin D intake is completely safe up to 2,000 IU per day for ages 1 year and above and that the risk of Vitamin D toxicity is greatly exaggerated by many health policy makers.

Low Fat Food Sources Of Vitamin D

Foods	Approximate I.U. of Vitamin D per 3.5 oz.
Sardines (canned)	1150-1570
Mackerel (raw)	1100
Salmon (fresh)	154-550
Salmon (canned)	220-440
Herring (fresh)	315
Herring (canned)	330
Shrimp	150
Halibut	44
Chicken (raw)	50-67
Oysters	5 I.U. per 3-4 medium sized oysters
Non fat and 1% Milk and Yogurt (Vitamin D fortified)	100 I.U. per 8 ounces
Low fat cheese (less than 4% milk fat)	12-15

Ensuring Optimal Vitamin D Status

The totality of evidence suggests that many North Americans are either Vitamin D deficient or more commonly insufficient, and would benefit from additional Vitamin D supplementation. Most multiple vitamins contain 400 IU of Vitamin D, an amount that is reported to raise Vitamin D blood levels (25-hydroxyvitamin D) by approximately 45 nmol/L. However, even higher amounts of total supplemental Vitamin D (800 – 1,000 IU per day) should be implemented after the age of 45 or 50, as the body's ability to convert 25-hydroxy vitamin D to calcitriol slows down to a significant degree. Studies prove that higher blood levels of the less potent 25-hydroxy vitamin D (in the range of 85-120nmol/L) can compensate for the reduced synthesis and availability of calcitriol in the bloodstream after ages 45-50, and can significantly reduce your risk of osteoporosis. Furthermore, this amount of 25-hydroxy vitamin D in your blood is also strongly associated with a reduction in risk of breast, colon, prostate and ovarian cancers, as well as multiple sclerosis. In a study released in 2004, K.L Munger and fellow researchers showed that participants in the Nurses' Health Study who ingested 400 IU of Vitamin D from supplements each day (most notable from a multivitamin product) showed a 40% reduction in risk of multiple sclerosis compared to women who did not use supplements containing vitamin D. This group of 95,253 female registered nurses, residing in the United States, have been followed by researches since 1980. Vitamin D has been shown to exert

favourable influences on immune cells that are consistent with preventing events related to multiple sclerosis, which have been confirmed in animal and human investigations. Over and above vitamin D supplementation, note that sardines, mackerel, herring and salmon are excellent food sources of vitamin D as well.

REFERENCES

- Brodie MJ, et al. Rifampicin and vitamin D metabolism. *Clin Pharmacol Ther* 1980;27(6):810-4
- Chapuy MC, et al. Effect of Calcium and chole-calciferol treatment for three years on hip fractures in elderly women. *Br Med J* 1994;308:1081-2
- Chen TC, Holick MF. Vitamin D and prostate cancer prevention and treatment. *TEM* 2003 Nov;14(9):423-30
- Chesney RW, et al. Decreased serum 24,25-dihydroxyvitamin D₃ in children receiving glucocorticoids. *Lancet* 1978;2(8100):1123-5
- Crowle AJ, et al. Inhibition by 1,25 dihydroxy vitamin D₃, of the multiplication of virulent tubercle bacilli in cultured human macrophages. *Infect Immun*, 1987;55:2945-50
- Dawson-Hughes B, et al. Effect of calcium and Vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 1997;337:670-6
- Dawson-Hughes B, et al. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of the Vitamin D. *Am J Clin Nutr* 1995;61:1140-5
- Dawson-Hughes B. Calcium and Vitamin D requirements of elderly women. *J Nutr* 1996;126(Suppl4):1165S-7S
- DeLuca HF. The Vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 1988;2:224-36
- Diarrhea and constipation. In: Berkow R, Fletcher AJ, Beers MH, et al, editors. *The Merck Manual of Diagnosis and Therapy*. 16th ed. Rahway, NJ: Merck Research Laboratories; 1992
- Feldman D, et al. Vitamin D and prostate cancer. *Adv Exp Med Biol* 1995; 375:53-63
- Fukazawa T, et al. Association of Vitamin D receptor gene polymorphism with multiple sclerosis in Japanese. *J Neurol Sci* 1999;166(1):47-52
- Gahn PH, et al. Circulating Vitamin D metabolites in relation to subsequent development of prostate cancer. *Epidemiol Biomarkers Prev* 1995;5(2):121-6
- Garland CF, et al. Can colon cancer incidence and death rates be reduced with Calcium and Vitamin D? *Am J Clin Nutr* 1991;54(Suppl 1):193S-201S
- Garland CF, Garland FC, Gorham ED. Calcium and vitamin D. Their potential roles in colon and breast cancer prevention. *Ann NY Acad Sci* 1999;889:107-19
- Garland FC, et al. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. *Prev Med* 1970;19:614-22.
- Hayes C, et al. Vitamin D and multiple sclerosis. *Proc Soc Exper Biol Med* 1997;216:21-7
- Healthnotes, 2000 Inc. Available from: URL: <http://www.healthnotes.com>.
- Holick M. Too little vitamin D in premenopausal women: why should we care? *Am J Clin Nutr*. 2002; 76: 3-4.
- In the news...Vitamin D and colon cancer. *Harvard Women's Health Watch* 2004 Feb;Vol.11(6)p7
- James WP, Avenell A, Broom J, et al. A one-year trial to assess the value of Orlistat in the management of obesity. *Int J Obes Relat Metab Disord* 1997;21(Suppl3):24S-30S
- Kállay E, Adlercreutz H, Farhan H, Lechner D, Bajna E, Gerdenitsch W, Campbell M, Cross HS. Phytoestrogens regulate vitamin D metabolism in the mouse colon: relevance for colon tumor prevention and therapy. *J Nutr* 1001 Nov;132(11):3490S-3493S
- Knodel LC, et al. Adverse effects of hypolipidaemic drugs. *Med Toxicol* 1987;2(1):10-32
- Lore F, et al. Vitamin D metabolites in postmenopausal osteoporosis. *Horm Metab Res* 1984;16:161-6

Martinez ME, et al. Calcium, Vitamin D and the occurrence of colorectal cancer among women. *J Natl Cancer Inst* 1996;88(19):1375-82

Mehta RG, et al. Prevention of preneoplastic mammary lesion development by a novel Vitamin D analogue, 1-alpha-hydroxyvitamin D5. *J Natl Cancer Inst* 1997; 89(3):212-8.

Munger KL et al. Vitamin D intake an incidence of multiple sclerosis. *Neurology* 2004: 62: 60-65.

Odes HS, et al. Effect of cimetidine on hepatic vitamin D metabolism in humans. *Digestion* 1990;46(2):61-4.

Optimal Calcium Intake: NIH consensus conference. *JAMA* 1994;272(24):1942-8.

Peehl DM. Vitamin D and prostate cancer risk. *Eur Urol* 1999;35(5-6):392-4

Rozen F, Yang XF, Huynh H, Pollak M. Antiproliferative action of Vitamin D – related compounds and insulin-like growth factor – binding protein 5 accumulation. *J Natl Cancer Inst* 1997;89(3):652-6

Schmidt J, Wittenhagen P, Hørder M. Molecular effects of vitamin D on cell cycle and oncogenesis. *Ugeskrift for laeger* 1998 Jul 20;160(30):4411-4

Shabahang M, et al. Growth inhibition of HT-29 human colon cancer cells by analogues of 1,25 dihydroxy vitamin D3. *Cancer Res* 1994;54:407-64

Toppet M, et al. Sequential development of vitamin D metabolites under isoniazid and rifampicin therapy. *Arch Fr Pediatr* 1998;45(2):145-8

Veith R. Vitamin D supplementation, 25-hydroxy Vitamin D concentrations and safety. *Am J Clin Nutr* 1999; 69(5):842-56

Zerwekh JE, et al. Decreased serum 24,25-Dihydroxyvitamin D concentration during long-term anticonvulsant therapy in adult epileptics. *Ann Nerol* 1982;12(2):184-6

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