# THE UPLINK Issue #40
# Additional Vitamin D Notes, Resources, and References

**Other Names for Forms of Vitamin D**

- 25-hydroxy-vitamin D or calcidiol, 25(OH)D
- 1,25-dihydroxy-vitamin D or calcitriol, 1,25(OH)2D

**Traditional Vitamin D metabolism**

- Cholesterol in skin → 7-dehydrocholesterol (pre-vitamin D)
- Sun (Ultraviolet-B) converts pre-vitamin D → Vitamin D-3 (cholecalciferol)
  - D-2 = ergocalciferol
  - Added to milk
  - Not very effective
- Liver converts D-3 → 25(OH) D
- Kidney concerts 25(OH) D → 1,25(OH) D
  - This conversion takes place in most other tissues also (See below)

**Most (probably all) cells in the body can synthesize 1,25(OH) D**

- Known for 15 organ tissues
- From circulating 25(OH) D
- Vitamin D is really a hormone – most cells have VDR (vitamin D receptors)
- The conversion of **25(OH) D → 1,25(OH) D** has a cell growth regulating effect

**Modern Vitamin D Indications**:

- (From Michael Holick, *The UV Advantage* (I Books - 2004) and Wolfgang Gerz, "Vitamin D – New Developments and AK" presented at ICAK International Meeting, Toronto, September, 2005)
  - Osteoporosis and other metabolic bone diseases
  - Cancer prevention: prostate, breast, colon, lung, others
  - Decreases autoimmune risk: MS, RA, Type 1 diabetes
  - Improves mental health: Seasonal Affective Disorder, PMS, depression, general mood
  - Improves hypertension and heart disease
  - Helps in obesity

**Old 25(OH) Vitamin D Laboratory Normals**

- Normal: 20-56 ng/ml

**New 25(OH) Vitamin D Laboratory Ranges (LabCorp)**

- Deficiency – 0-5 ng/ml
- Insufficiency – 5-20 ng/ml
- Hypovitaminosis – 20-40 ng/ml
- Sufficiency – 40-100 ng/ml
- Toxicity - > 100 ng/ml

**Hypovitaminosis D Incidence**

- 20% to 80% of Americans may be vitamin D deficient -- at least during winter months.
- In Calgary, Alberta, virtually 100 percent of the population is vitamin D deficient at least part of the year (200 people in study)
  - Reported by David A. Hanley, Experimental Biology meeting in Washington, D.C., April, 2004

**Vitamin D and Bone Activity**

- 1,25(OH) D should be produced in most if not all cells in body. When it is not, the kidney increases 1,25(OH) D production as a compensatory mechanism to increase calcium by mobilizing from bone.
- If decreased $Ca^{++}$ – body increases 1,25(OH) D which increases PTH to cause release of $Ca^{++}$ from bone.
    - Must increase 25(OH) D to level out the 1,25(OH) D to keep serum $Ca^{++}$ normal.
    - 1,25 from kidney does not help prevent cancer – <u>it is the production of 1,25 inside other tissues that has the cell regulating effect.</u>
- Must keep 25(OH) D high enough to keep 1,25(OH) D and PTH in low normal ranges to avoid osteoporosis.
- Vitamin D deficient patients can absorb only 1/3$^{rd}$ as much calcium as normal vitamin D intake people

**Vitamin D and Cancer**

- When the body is deficient in 25(OH) D - cells can go "haywire," become overly active or multiply too quickly.
- Adequate Vit D prevents cancer (prostate, colon, breast) by: the process of conversion of 25(0H) D to 1,25(OH) D. This conversion is a growth regulating process in cells.
    - Intracellular 1,25(OH) D is NOT reflective of circulating 25(OH) D…
    - The conversion of 25(0H) D to 1,25(OH) D is the intracellular cancer fighting mechanism
        - in vitro prostate cancer cells convert back when 25(OH) D is added
- In US - Increased Sun exposure would decrease in 185,000 internal cancers per year and decrease of 30,000 deaths from internal cancers.
    - Grant WB. An estimate of premature cancer mortality in the United States due to inadequate doses of solar ultraviolet-B radiation. Cancer. 2002;94:1867-75.)
    - The findings of the current study confirm previous results that solar UV-B radiation is associated with reduced risk of cancer of the breast, colon, ovary, and prostate as well as non-Hodgkin lymphoma. Eight additional malignancies were found to exhibit an inverse correlation between mortality rates and UV-B radiation: bladder, esophageal, kidney, lung, pancreatic, rectal, stomach, and corpus uteri.
- "We need adequate amounts of vitamin D to keep cell growth and activity in check,"
    - Michael Holick, MD, PhD, director of the Vitamin D Research Lab at Boston University Medical Center

**Vitamin D and Other Disease Processes**

- Vitamin D helps prevent certain autoimmune diseases: multiple sclerosis, type 1 diabetes and rheumatoid arthritis.
- Also linked to heart disease, unexplained muscle and joint pain.
- Plays an anti-inflammatory role in the body
- Women - least 400 international units from supplements (not foods) - 40% less likely to develop multiple sclerosis compared with those not taking over-the-counter supplements.
    - K. L. Munger, et al Vitamin D intake and incidence of multiple sclerosis. Neurology 2004;62:60-65.

**Sun blockers Effects on Vitamin D Synthesis**

- SPF 8 blocks body vitamin D production by 97.5%
- SPF 15 blocks body vitamin D production by 99.5%

**Good food sources of vitamin D include**:

- Fortified milk, 8 ounces contain approximately 100 IU of vitamin D. However, it is often in the form of D-2 (ergocalciferol) – an inferior Vitamin D source.
- Cod liver oil, 1 tablespoon contains approximately 1300 IU of vitamin D
- Cold-water fish. e.g., salmon and herring - 3 ounces contain approximately 400 to 750 IU of vitamin D, respectively.

**What is a good dose of Vitamin D?**

- Experts vary from 1000 IU / day to 4000 IU / day
- Wolfgang Gerz points out that Vitamin D must be matched by adequate amounts of other bone growth nutrients. He tests for Vitamin D in conjunction with different forms of:
    - Calcium
    - Magnesium
    - Zinc
    - Copper
    - Vitamin C
    - Potassium
    - Selenium
- Vitamin D weakening response may represent a deficiency of one or more of these other nutrients rather than a Vitamin D toxicity (Gerz)

## OTHER VITAMIN D RESOURCES THAT MAY BE OF INTEREST

**RELATED DISEASES** - "The role of vitamin D deficiency increases the risk of many common and serious disease processes including some common cancers, type 1 diabetes, cardiovascular disease and osteoporosis… Vitamin D deficiency is often mistaken or misdiagnosed as fibromyalgia… It is reasonable to perform annual Vitamin D testing to monitor for deficiency.
*Holick, MF, Vitamin D: importance in prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr. 2004 Mar;79(3):362-71.*

**MAYO CLINIC STUDY** – 150 Patients with persistent, nonspecific musculoskeletal pain for 4 consecutive months were virtually all found to be vitamin D deficient (< or = 20 ng/ml) level and many were severely deficient. They concluded that: All patients with persistent, nonspecific musculoskeletal pain are at high risk for the consequences of unrecognized vitamin D deficiency, including those considered at low risk for such deficiency. Vitamin D testing for such individuals should be standard practice.
*Plotnikoff GA, Quigley LM, Mayo Clinic Proc. 2003 Dec; 78(12):1463-70 Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain.*

**LOW BACK PAIN** – A study of 360 patients (where 90% were Saudi Arabian women where most women are veiled) experiencing low back pain with no obvious cause for 6 months found 83% of the patients had abnormally low vitamin D levels.
*Spine. 2003 Jan 15;28(2):177-9. Vitamin D deficiency and chronic low back pain in Saudi Arabia*

**DOSE** - For adults, the 5 mcg (200 IU) vitamin D recommended dietary allowance may prevent osteomalacia in the absence of sunlight, However, a higher dose is needed to help prevent osteoporosis and secondary hyperparathyroidism. Other vitamin D supplementation benefits are implicated epidemiologically: prevention of some cancers, osteoarthritis progression, multiple sclerosis, and hypertension. Published cases of vitamin D toxicity with hypercalcemia, for which the 25(OH)D concentration and vitamin D dose are known, all involve intake of greater than or equal to 1000 mcg (40,000 IU)/d. Because vitamin D is potentially toxic, intake of greater than 25 mcg (1000 IU)/d has been avoided even though the most evidence shows that the currently accepted, no observed adverse effect limit of 50 microg (2000 IU)/d is too low by at least 5-fold.
*Vieth R, Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. Am J Clin Nutr. 1999 May;69(5):842-56.*

## A POTPOURRI OF OTHER VITAMIN D RESOURCES & REFERENCES

**From: http://www.sunlightd.org/**
**Every body needs sunlight and vitamin D. Deficiency or insufficiency has been associated with:**

- **adrenal insufficiency**
- **Alzheimer's**
- **allergy**
- **autoimmune disorders**
- **cancers of the colon, breast, skin and prostate**
- **depression**
- **diabetes, Type 1 and 2**
- **gluten intolerance**
- **heart disease**
- **heavy metal toxicity**
- **hypertension**
- **infertility**
- **learning disorders**
- **lectin intolerance**
- **misaligned teeth and cavities**
- **myopia**
- **obesity**
- **osteomalacia**
- **osteoporosis**
- **Parkinson's**
- **PMS**
- **psoriasis**
- **rickets**
- **seasonal affective disorder**
- **Syndrome X**
- **use of corticosteroids and more...**

**TEST YOUR VITAMIN D KNOWLEDGE:**

http://www.mercola.com/2005/oct/4/test_your_knowledge_of_vitamin_d.htm
"Test Your Knowledge of Vitamin D" is a fun to read and enlightening (so to speak) Q & A format overview of a number of important and interesting facts about vitamin D from Dr. Mercola's web site.

**VITAMIN C AND VITAMIN D METABOLISM:**

Sergeev IN, Arkhapchev YP, Spirichev VB., *Ascorbic acid effects on vitamin D hormone metabolism and binding in guinea pigs.* J Nutr. 1990 Oct;120(10):1185-90.
(Institute of Nutrition, Academy of Medical Sciences of the USSR, Moscow.)

Abstract: Ascorbic acid deficiency in guinea pigs fed a vitamin D-replete diet caused a moderate reduction of Ca level in serum and bone; 25-hydroxy-cholecalciferol or 25-hydroxyergocalciferol (25-OHD) serum concentration tended to decline; renal 25-hydroxycholecalciferol-1-hydroxylase (1-OHase) activity decreased 50%; and 25-hydroxycholecalciferol-24-hydroxylase activity increased 1.6-fold. Chromatin 1,25-dihydroxycholecalciferol [1,25-(OH)2D3] receptor concentration in the intestinal mucosa decreased 20-30%, and the percentage of occupied receptors decreased from 12-15% to 6-8%. Receptor affinity for 1,25-(OH)2D3 did not change (Kd = 0.24-0.26 nmol/L, Kd2 = 0.06-0.10 nmol/L), but the cooperativity coefficient decreased from 1.7 to 1.4. Vitamin C deficiency potentiated effects of vitamin D deprivation and impaired a restorative action of vitamin D. It was accompanied by a marked delay in the elevation of 25-OHD concentration in serum as well as decreased 1-OHase activity in kidneys and a lower concentration of occupied 1,25-(OH)2D3 receptors in the intestinal mucosa. The data demonstrate a critical role for ascorbic acid in vitamin D metabolism and binding.

**SEASONAL AFFECTIVE DISORDER:**

Gloth FM 3rd, Alam W, Hollis B., *Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder.* J Nutr Health Aging. 1999;3(1):5-7.
(The Department of Medicine, The Union Memorial Hospital, Baltimore, Maryland 21218-2895, USA.)

Abstract: Seasonal Affective Disorder (SAD) is prevalent when vitamin D stores are typically low. Broad-spectrum light therapy includes wavelengths between 280-320 nm which allow the skin to produce vitamin D. This study was designed to test the hypothesis that vitamin D deficiency might play a role in SAD. A prospective, randomized controlled trial was conducted in a group of 15 subjects with SAD. Eight subjects received 100,000 I.U. of vitamin D and seven subjects received phototherapy. At the onset of treatment and after 1 month of therapy subjects were administered the Hamilton Depression scale, the SIGH-SAD, and the SAD-8 depression scale. All subjects also had serum levels of 25-hydroxyvitamin D (25-OH D) measured before and 1 week after intervention therapy. All subjects receiving vitamin D improved in all outcome measures. The phototherapy group showed no significant change in depression scale measures. Vitamin D status improved in both groups (74% vitamin D group, $p < 0.005$ and 36% phototherapy group, $p < 0.01$). Improvement in 25-OH D was significantly associated with improvement in depression scale scores ($r2=0.26$; $p=0.05$). Vitamin D may be an important treatment for SAD. Further studies will be necessary to confirm these findings.

**MOOD DURING WINTER:**

Lansdowne AT, Provost SC., *Vitamin D3 enhances mood in healthy subjects during winter.* Psychopharmacology (Berl). 1998 Feb;135(4):319-23.
(Department of Psychology, The University of Newcastle, Callaghan NSW, Australia.)

Abstract: Mood changes synchronised to the seasons exist on a continuum between individuals, with anxiety and depression increasing during the winter months. An extreme form of seasonality is manifested as the clinical syndrome of seasonal affective disorder (SAD) with carbohydrate craving, hypersomnia, lethargy, and changes in circadian rhythms also evident. It has been suggested that seasonality and the symptoms of SAD may be due to changing levels of vitamin D3, the hormone of sunlight, leading to changes in brain serotonin. Forty-four healthy subjects were given 400 IU, 800 IU, or no vitamin D3 for 5 days during late winter in a random double-blind study. Results on a self-report measure showed that vitamin D3 significantly enhanced positive affect and there was some evidence of a reduction in negative affect. Results are discussed in terms of their implications for seasonality, SAD, serotonin, food preference, sleep, and circadian rhythms.

**VITAMIN D & WELLBEING:**

Reinhold Vieth, Samantha Kimball, Amanda Hu and Paul G Walfish, *Randomized comparison of the effects of the vitamin D3 adequate intake versus 100 mcg (4000 IU) per day on biochemical responses and the wellbeing of patients.* Nutrition Journal 2004, 3:8
http://www.nutritionj.com/content/3/1/8 

**Abstract**

**Background**

For adults, vitamin D intake of 100 mcg (4000 IU)/day is physiologic and safe. The adequate intake (AI) for older adults is 15 mcg (600 IU)/day, but there has been no report focusing on use of this dose.

**Methods**

We compared effects of these doses on biochemical responses and sense of wellbeing in a blinded, randomized trial. In Study 1, 64 outpatients (recruited if summer 2001 25(OH)D <61 nmol/L) were given 15 or 100 mcg/day vitamin D in December 2001. Biochemical responses were followed at subsequent visits that were part of clinical care; 37 patients completed a wellbeing questionnaire in December 2001 and February 2002. Subjects for Study 2 were recruited if their 25(OH)D was <51 nmol/L in summer 2001. 66 outpatients were given vitamin D; 51 completed a wellbeing questionnaire in both December 2002 and February 2003.

**Results**

In Study 1, basal summer 25-hydroxyvitamin D [25(OH)D] averaged 48 ± 9 (SD) nmol/L. Supplementation for more than 6 months produced mean 25(OH)D levels of 79 ± 30 nmol/L for the 15 mcg/day group, and 112 ± 41 nmol/L for the 100 mcg/day group. Both doses lowered plasma parathyroid hormone with no effect on plasma calcium. Between December and February, wellbeing score improved more for the 100-mcg/day group than for the lower-dosed group (1-tail Mann-Whitney p = 0.036). In Study 2, 25(OH)D averaged 39 ± 9 nmol/L, and winter wellbeing scores improved with both doses of vitamin D (two-tail p < 0.001).

**Conclusion**

The highest AI for vitamin D brought summertime 25(OH)D to >40 nmol/L, lowered PTH, and its use was associated with improved wellbeing. The 100 mcg/day dose produced greater responses. Since it was ethically necessary to provide a meaningful dose of vitamin D to these insufficient patients, we cannot rule out a placebo wellbeing response, particularly for those on the lower dose. This work confirms the safety and efficacy of both 15 and 100 mcg/day vitamin $D_3$ in patients who needed additional vitamin D.

**CANCER:**

Holt PR, Arber N, Halmos B, Forde K, Kissileff H, McGlynn KA, Moss SF, Kurihara N, Fan K, Yang K, Lipkin M., *Colonic epithelial cell proliferation decreases with increasing levels of serum 25-hydroxy vitamin D.* Cancer Epidemiol Biomarkers Prev 2002 May;11(5):501. (Gastrointestinal Division, St. Luke's-Roosevelt Hospital Center, New York, NY 10025, USA.)

**CANCER:**

From: http://www3.interscience.wiley.com/cgi-bin/abstract/91016211/ABSTRACT
William B. Grant, Ph.D., *An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation.* Cancer 2002;94:1867-75. © 2002 American Cancer Society.
Background: There are large geographic gradients in mortality rates for a number of cancers in the U.S. (e.g., rates are approximately twice as high in the northeast compared with the southwest). Risk factors such as diet fail to explain this variation. Previous studies have demonstrated that the geographic distributions for five types of cancer are related inversely to solar radiation. The purpose of the current study was to determine how many types of cancer are affected by solar radiation and how many premature deaths from cancer occur due to insufficient ultraviolet (UV)-B radiation.
Methods: UV-B data for July 1992 and cancer mortality rates in the U.S. for between 1970-1994 were analyzed in an ecologic study.
Results: The findings of the current study confirm previous results that solar UV-B radiation is associated with reduced risk of cancer of the breast, colon, ovary, and prostate as well as non-Hodgkin lymphoma. Eight additional malignancies were found to exhibit an inverse correlation between mortality rates and UV-B radiation: bladder, esophageal, kidney, lung, pancreatic, rectal, stomach, and corpus uteri. The annual number of premature deaths from cancer due to lower UV-B exposures was 21,700 (95% confidence interval [95% CI], 20,400-23,400) for white Americans, 1400 (95% CI, 1100-1600) for black Americans, and 500 (95% CI, 400-600) for Asian Americans and other minorities.
Conclusions: The results of the current study demonstrate that much of the geographic variation in cancer mortality rates in the U.S. can be attributed to variations in solar UV-B radiation exposure. Thus, many lives could be extended through increased careful exposure to solar UV-B radiation and more safely, vitamin D3 supplementation, especially in nonsummer months.

**VITAMIN D AND SKIN:**

Chandra Shekhar, Vitamin D Protects the Skin? The Scientist.com, January 29, 2007
http://www.the-scientist.com/news/home/44290/
This article reviews research that vitamin D protects the skin even from sunlight itself.

**VITAMIN D LABORATORY INFORMATION:**

See: http://www.professionalco-op.com/research/index.html. From Professional Co-op laboratory services – an excellent overview of Vitamin D information but you need a password. Contact them at: info@professionalco-op.com

**LOW VITAMIN D LABORATORY RESULTS:**

From: http://www.sciencenews.org/articles/20041016/bob9.asp
Few people have the blood concentrations of 25-D that researchers recommend. For instance, Hanley described findings from 200 Calgary adults at the Experimental Biology meeting in Washington, D.C., last April. A third of the study's population showed less than 30 nmol/l during at least part of the year. "The average level of 25-D through the four seasons was in the low 60s [nmol/l]," Hanley told Science News. If 80 nmol/l is taken as the cutoff for adequate 25-D, "virtually 100 percent of the population is vitamin D–deficient at least part of the year," he says.

**VITAMIN D [25(OH)D AND 1,25-(OH)2D] LABORATORY TESTS:**

From: http://www.cmaj.ca/cgi/content/full/167/8/849-a
Hanely, David, Puzzling Vitamin D results. CMAJ • October 15, 2002; 167 (8)
(David A. Hanley Professor and Head Division of Endocrinology and Metabolism Department of Medicine University of Calgary Calgary, Alta.)

…Our 1,25-(OH)2D assay still provided results consistent with known vitamin D physiology. The 2 seasons with the highest mean levels of 1,25-(OH)2D were associated with the highest mean levels of parathyroid hormone and the lowest mean levels of serum inorganic phosphate, both known stimuli to conversion of 25(OH)D to 1,25-(OH)2D by renal 1α-hydroxylase.

Although 1,25-(OH)2D is the most biologically active form of vitamin D, it is generally accepted that, when assessing patients' vitamin D stores, measurement of 25(OH)D in blood is much more clinically useful than that of 1,25-(OH)2D.2,3 Serum 25(OH)D levels are consistently low in malabsorption syndromes and clinical osteomalacia, although 1,25-(OH)2D levels may be normal or high.4 In osteomalacia due to vitamin D deficiency, the serum 25(OH)D level, not the 1,25-(OH)2D level, correlates with the mineralization status of bone.5 Recent identification of 1α-hydroxylase activity in nonrenal tissue provides a plausible explanation of how 25(OH)D may mediate vitamin D action at a cellular level,6,7 and evidence also exists of direct effects of 25(OH)D on calcium absorption.8

**NOTE:** There are thousands and thousands of references and resources available regarding Vitamin D. This is by no means intended to be a complete representation, but rather a sampling of a variety of notes, references, and resources to give a bit of an overview and starting places for further looking based on your own interests.
-WHS