Vitamin D3

Stock #1155-1 (60 tablets)

Once thought to have been conquered, vitamin D deficiency is now recognized as an epidemic in the United States. Meanwhile, epidemiologic (population) studies suggest that vitamin D deficiency is also a problem world-wide, with greater than 50% of the global population at risk for vitamin D deficiency. In fact, it is estimated that 50,000-70,000 people in the U.S. and 30,000-35,000 people in the U.K. die prematurely from cancer each year due to insufficient vitamin D.[1-6]

The primary source of vitamin D for both children and adults is from sun exposure, not from diet. Vitamin D is naturally produced in the skin following exposure to sunlight. In contrast, very few foods naturally contain vitamin D (namely fatty fish, egg yolks and liver) or are fortified with vitamin D. As a result, a varying percentage of people are vitamin D deficient at any time, with this percentagebeing higher in the winter, among the elderly or obese, in sun-deprived individuals, in dark-skinned people (heavy melanin effectively blocks skin synthesis of vitamin D), and in populations living in more poleward regions with lower sunlight exposure. Research also indicates that sunscreen inhibits the formation of vitamin D in the skin, even with extensive sun exposure. A sunscreen with a sun protection factor (SPF) of only 8 reduces the skin's production of vitamin D by 95%. Furthermore, certain medications such as bile acid sequestrants (i.e. cholestyramine and colestipol) and anticonvulsants (i.e. phenobarbital) can cause vitamin D deficiency.[2,7-18]

Over the past several decades, the physiological role and importance of vitamin D has dramatically expanded, with recent findings indicating an increasing range of health benefits and therapeutic applications. Today, vitamin D is not only recognized for its crucial role in promoting bone health, but also for its emerging significance in regulating immune system function, reducing the risk of infectious and chronic diseases such as cancer, and facilitating normal brain function, central and peripheral nervous system function, blood clotting and blood cell formation, cardiac activity, and optimal muscle strength. Vitamin D also appears to play an important role in glucose metabolism—the conversion of blood sugar into energy.[1,6,8,9,19-31]

Perhaps the most well-known function of vitamin D is to regulate calcium absorption and metabolism for bone health. To this end, vitamin D promotes intestinal absorption of calcium and phosphorous, facilitates calcium transport, and reduces urinary calcium loss in order to keep calcium in the body and spare calcium stores in the bones. Vitamin D also promotes calcium deposition in bones and is required for the proper utilization of magnesium.[6,9,12,25-29,31]

However, vitamin D also exerts profound effects on human immune function. Vitamin D acts as an immune system modulator, increasing the activity of macrophages (white blood cells that destroy bacteria, protozoa and tumor cells) and providing anti-inflammatory effects. For example, recent research on the immunomodulating potential of vitamin D has shown that greater vitamin D intake is associated with both a lower risk of rheumatoid arthritis, as well as significant clinical improvement in patients treated with vitamin D. In addition, vitamin D dramatically stimulates the production of anti-microbial compounds that play a crucial role in protecting the respiratory tract against infection. Evidence from a 3-year randomized, controlled trial found that 104 women given a low dose of vitamin D (800 IU per day) were 3 times less likely to report cold and flu symptoms than an equal number of those given placebo. During the last year of the trial, a higher dose of vitamin D (2000 IU per day) was found to virtually eliminate all reports of colds and flu. Furthermore, experimental studies suggest that vitamin D may lower the risk of cancer by regulating cellular proliferation and differentiation and inhibiting angiogenesis—the formation of new blood vessels that contribute to tumor growth. In a recent randomized, controlled trial, daily intake of 1100 IU of vitamin D_3 during a 4-year period was shown to dramatically reduce the occurrence of non-skin cancers. Such results corroborate other evidence indicating that higher vitamin D levels are associated with lower incidences of cancer.[9,25,32-38]

Vitamin D_3, also known as cholecalciferol, is one of two forms of vitamin D used for nutritional supplementation. Vitamin D_3 is manufactured from lanolin derived from the wool fat of sheep. The other form, known as vitamin D_2 or ergocalciferol, is a vegetarian form of vitamin D manufactured by the ultraviolet radiation of yeast. Vitamin D_3 has been proven to be the more potent form of vitamin D in both animal and human studies. Vitamin D_3 has been shown to be at least 3 times more effective than vitamin D_2 at raising serum vitamin D levels in.[8,39-42]

Current consensus among experts is that intakes of vitamin D between 1000 and 4000 IU will lead to more healthy serum levels of vitamin D. In fact, the physiologic requirement for vitamin D may be as high as 5000 IU per day for many individuals. For example, 4000 IU of vitamin D_3 daily has been shown to safely and effectively increase serum vitamin D levels to high-normal concentrations in healthy adults. Likewise, daily oral intake of 2000 to 4000 IU of vitamin D appears to be the most effective way to improve vitamin D status in patients with congestive heart failure. Current research has also shown that the actual dietary need for vitamin D during pregnancy and lactation may be as

high as 6000 IU per day and that the present recommended dietary requirement of 200 IU per day is based on little, if any, scientific or clinical evidence. In truth, high doses of vitamin D_3 (6400 IU per day) have been shown to safely increase circulating serum vitamin D levels in both mothers and nursing infants, thus confirming that vitamin D intake above the currently recognized upper limit is safe by a large margin. It is important to point out that the Institute of Medicine's present Dietary Reference Intakes for vitamin D were not designed and are not effective for preventing or treating vitamin D deficiency. Instead, government agencies designed current vitamin D intake recommendations only as guidelines to prevent particular metabolic bone diseases. Recent human clinical trials have confirmed that even prolonged daily intake of 10,000 IU of vitamin D_3 is a safe tolerable upper intake level that has shown no evidence of adverse effects and is likely to pose no risk of toxicity, except in those with specific health conditions causing known hypersensitivity.[9,37,43-55]

Vitamin D deficiency can have serious consequences on overall health and well-being, especially considering that vitamin D status has been linked to greater disease susceptibility and/or mortality (death). In fact, vitamin D deficiency has been implicated in a host of diseases. For example, research indicates that vitamin D deficiency predisposes children to respiratory infections and is also associated with a higher risk of active tuberculosis. Growing scientific evidence has also demonstrated an association between low levels of vitamin D and a greater risk of hypertension, cardiovascular disease, depression, obesity, Type 1 diabetes, osteoporosis, cancer, and autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus. In addition, vitamin D deficiency is increasingly being diagnosed and treated in patients with cystic fibrosis.[2,4,9,10,19,21,32,34,37,56-64]

Results of several clinical and epidemiologic studies indicate an excess risk of both hypertension and diabetes mellitus in individuals with low vitamin D intake. Available data also indicate that the majority of patients with congestive heart failure have insufficient serum levels of vitamin D. In addition, vitamin D deficiency in pregnant women may be an independent risk factor for preeclampsia.[48,58,65,66]

Vitamin D deficiency in adults can also result in secondary hyperparathyroidism, which causes a loss of bone matrix and minerals that, in turn, increases the risk of osteoporosis and fractures. A high prevalence of low vitamin D levels has been reported in a number of populations worldwide, including women being treated for osteoporosis and those with fragility fractures—a bone fracture that occurs from a fall from standing height or less. Plus, poor mineralization of newly-formed bone matrix in adult bones causes osteomalacia—a painful bone disease that is often misdiagnosed as fibromyalgia or chronic pain syndrome or simply dismissed as depression. Vitamin D deficiency also causes muscle weakness, which increases the risk of falling and fractures.[2,12,67-69]

In addition, vitamin D deficiency has been found to cause dull, achy non-specific musculoskeletal pain that often persists despite pharmaceutical interventions and manual treatments. Several clinical investigations have confirmed that vitamin D deficiency is especially common among individuals with musculoskeletal pain, with some patients exhibiting severely deficient serum levels or even serum levels below the level of detection. Pain can be widespread or isolated to a particular area and is most commonly reported in the low-back and lumbar spine. In one study, 81% of female patients with chronic low back pain longer than 3 months exhibited vitamin D deficiency and significantly lower serum vitamin D levels than controls. In another study involving 267 adults undergoing outpatient treatment for chronic pain, 1 in 4 patients lacked sufficient serum levels of vitamin D. Patients with vitamin D deficiency were found to need higher doses of morphine for a longer duration, with 26% requiring nearly twice the morphine dose of those with adequate vitamin D levels. Patients with vitamin D deficiency also demonstrated overall poorer health, lower levels of physical functioning, and reported using morphine nearly twice as long as those with adequate vitamin D levels. Such results are not surprising considering that vitamin D deficiency has long been associated with pain and muscle weakness, with prior studies suggesting that pain-related symptoms associated with vitamin D deficiency respond poorly to pain medications. It is important to note that vitamin D deficiency is often misdiagnosed as fibromyalgia or chronic pain syndrome. Fortunately, high-dose vitamin D supplementation has been shown to eliminate musculoskeletal pain in a high percentage of patients with vitamin D deficiency.[9,12,21,25,70-74]

Mounting scientific evidence has implicated vitamin D deficiency with an increased risk of several deadly cancers. For example, epidemiologic evidence has demonstrated an inverse relationship between prostate cancer and serum vitamin D levels, suggesting that vitamin D deficiency increases the risk of prostate cancer. Likewise, observational studies indicate that inadequate vitamin D is associated with high incidence and mortality rates of breast cancer. According to the pooled analysis of two studies involving 1760 individuals, those with sufficient serum vitamin D levels (corresponding to a daily intake of 4000 IU) demonstrated a 50% lower risk of breast cancer than those with serum vitamin D deficiency. In addition, inadequate vitamin D is also associated with high incidence rates of colorectal cancer. Individuals with sufficient serum vitamin D levels or with a daily oral intake of 1000-2000 IU vitamin D_3 exhibited a 50% lower incidence of colorectal cancer. Death from colorectal cancer has also been shown to be inversely related to serum vitamin D levels, with high serum levels associated with a 72% less risk of death compared with lower serum levels. Furthermore, higher vitamin D indices in men with early stage non-small cell lung cancer have been correlated with higher survival rates than those with lower vitamin D indices. Higher intakes of vitamin D

have also been associated with lower risks for pancreatic cancer in both men and women.[1,2,6,9,19,25,75-84]

Vitamin D deficiency is also a common finding among patients with inflammatory and autoimmune diseases, such as ankylosing spondylitis, multiple sclerosis, systemic lupus erythematosus (SLE), and rheumatoid arthritis. For example, research has shown that multiple sclerosis is more prevalent where environmental supplies of vitamin D are lowest (i.e. more poleward regions). Another study confirmed that patients with multiple sclerosis had significantly lower serum vitamin D levels compared to healthy controls. Likewise, patients with SLE demonstrate multiple risk factors for vitamin D deficiency, with the severity of disease correlated with lower serum vitamin D levels.[33,35,85-87]

Furthermore, epidemiologic studies show that higher vitamin D intake by pregnant mothers reduces asthma risk by as much as 40% in children 3 to 5 years old. However, according to a recent study in *The Journal of Nutrition*, pregnant women and newborns living in the northern U.S. are at high risk of having insufficient vitamin D levels, including mothers taking prenatal vitamins. In fact, another study found that the amount of vitamin D commonly provided in prenatal vitamins failed to maintain adequate maternal serum vitamin D levels, and thus supplied only extremely limited amounts of vitamin D to nursing infants via breast milk. The results of these studies indicate that higher-dose supplementation is needed to improve maternal and newborn vitamin D nutritional status. Maintaining sufficient vitamin D levels is especially important for pregnant women, since vitamin D deficiency in utero and during the first year of life is associated with a higher incidence of Type 1 diabetes. Fortunately, a study of over 10,000 infants (less than 12 months of age) who received 2,000 IU of dietary vitamin D daily showed an 80% reduction in the incidence of Type 1 diabetes, with no evidence of adverse effects.[50,62,88-90]

References:

[1]Holick, MF. "Sunlight, UV-radiation, vitamin D and skin cancer: how much sunlight do we need?" *Advances in Experimental Medicine and Biology*; 2008, 624:1-15.

[2]—. "The vitamin D epidemic and its health consequences." *The Journal of Nutrition*; 2005, 135(11):2739S-2748S.

[3]Park, S., Johnson, M.A. "Living in low-latitude regions in the United States does not prevent poor vitamin D status." *Nutrition Reviews*; 2005, 63(6 Pt 1):203-209.

[4]Adams, J.S., Hewison, M. "Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity." *Nature Clinical Practice. Endocrinology & Metabolism*; 2008, 4(2):80-90.

[5]Binkley, N., et. al. "Low vitamin D status despite abundant sun exposure." *The Journal of Clinical Endocrinology & Metabolism*; 2007, 92(6):2130-2135.

[6]Grant, W.B., Holick, M.F. "Benefits and requirements of vitamin D for optimal health: a review." *Alternative Medicine Review*; 2005, 10(2):94-111.

[7]Cannell, J.J., et. al. "On the epidemiology of influenza." *Virology Journal*; 2008, 25;5(1):29.

[8]Armas, L.A., et. al. "Vitamin D2 is much less effective than vitamin D3 in humans." *The Journal of Clinical Endocrinology and Metabolism*; 2004, 89(11):5387-5391.

[9]Vasquez, A. "Integrative orthopedics and vitamin D: testing, administration, and new relevance in the treatment of musculoskeletal pain." *Townsend Letter for Doctors and Patients*; October 2004. <http://findarticles.com/p/articles/mi_m0ISW/is_255/ai_n6211963>. Accessed March 2008.

[10]Zittermann, A. "Vitamin D and disease prevention with special reference to cardiovascular disease." *Progress in Biophysics and Molecular Biology*; 2006, 92(1):39-48.

[11]Lamberg-Allardt, C. "Vitamin D in foods and as supplements." *Progress in Biophysics and Molecular Biology*; 2006, 92(1):33-38.

[12]Holick, M.F. "Optimal vitamin d status for the prevention and treatment of osteoporosis." *Drugs & Aging*; 2007, 24(12):1017-1029.

[13]Epstein, S. "The problem of low levels of vitamin D and osteoporosis: use of combination therapy with alendronic acid and colecalciferol (vitamin D3)." *Drugs & Aging*; 2006, 23(8):617-625.

[14]Hollis, B.W. "Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D." *The Journal of Nutrition*; 2005, 135(2):317-322.

[15]Sayre, R.M., Dowdy, J.C. "Darkness at noon: sunscreens and vitamin D3." *Photochemistry and Photobiology*; 2007, 83(2):459-463.

[16]Reichrath, J., Nürnberg, B. "Solar UV-radiation, vitamin D and skin cancer surveillance in organ transplant recipients (OTRs)." *Advances in Experimental Medicine and Biology*; 2008, 624:203-214.

[17]Hathcock, J.N. "Metabolic mechanisms of drug-nutrient interactions." *Federation Proceedings*; 1985, 44(1 Pt 1):124-129.

[18]Torkos Phm, S. "Drug-Nutrient Interactions: A Focus On Cholesterol-Lowering Agents." *International Journal of Integrative Medicine*; 2000, 2(3):9-13.

[19]Holick, M.F. "Vitamin D Status: Measurement, Interpretation, and Clinical Application." *Annals of Epidemiology*; 2008, March 8. [Epub ahead of print]

[20]Roth, D.E. "Bones and beyond: an update on the role of vitamin D in child and adolescent health in Canada." *Applied Physiology, Nutrition and Metabolism*; 2007, 32(4):770-777.

[21]21Holick, M.F. "Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis." *American Journal of Clinical Nutrition*; 2004, 79(3):362-371.

[22]Mullin, G.E., Dobs, A." Vitamin d and its role in cancer and immunity: a prescription for sunlight." *Nutrition in Clinical Practice*; 2007, 22(3):305-322.

[23]Grant, W.B. "Epidemiology of disease risks in relation to vitamin D insufficiency." *Progress in Biophysics and Molecular Biology*; 2006, 92(1):65-79.

[24]Kalueff, A.V., Tuohimaa, P. "Neurosteroid hormone vitamin D and its utility in clinical nutrition." *Current Opinion in Clinical Nutrition*

and Metabolic Care; 2007, 10(1):12-19.
[25]Mascarenhas, R., Mobarhan, S. "Hypovitaminosis D-induced pain." *Nutrition Reviews*; 2004, 62(9):354-359.
[26]Lininger DC, S., et al. *The Natural Pharmacy, 2nd ed*. Rocklin, CA: Prima Health, 1999.
[27]Dunne, L. *Nutrition Almanac, Third Edition*. McGraw-Hill Publishing, 1990.
[28]Bergner, P. *The Healing Power of Minerals, Special Nutrients and Trace Elements*. Rocklin, CA: Prima Publishing, 1997.
[29]Spiller PhD, G. & Bruce DPH, B. *Calcium: Nature's Versatile Mineral*. NY, NY: Avery, 2000.
[30]Tai, K., et. al. "Vitamin D, glucose, insulin, and insulin sensitivity." *Nutrition*; 2008, 24(3):279-285.
[31]Holick, M.F. "Vitamin D: its role in cancer prevention and treatment." *Progress in Biophysics and Molecular Biology*; 2006, 92(1):49-59.
[32]Raloff, J. "The Antibiotic Vitamin." *Science News*; 2006, 170:312-317. <http://www.sciencenews.org/articles/20061111/ bob9.asp>. Accessed March 2008.
[33]VanAmerongen, B.M., et. al. "Multiple sclerosis and vitamin D: an update." *European Journal of Clinical Nutrition*; 2004, 58(8):1095-1109.
[34]Cannell, J.J., et. al. "Epidemic influenza and vitamin D." *Epidemiology and Infection*; 2006, 134(6):1129-1140.
[35]Cutolo, M., Otsa, K. "Review: Vitamin D, immunity and lupus." *Lupus*; 2008;17(1):6-10.
[36]Cutolo, M., et. al. "Vitamin D in rheumatoid arthritis." *Autoimmunity Reviews*; 2007, 7(1):59-64.
[37]Cannell, J.J., et. al. "Diagnosis and treatment of vitamin D deficiency." *Expert Opinion on Pharmacotherapy*; 2008, 9(1):107-118.
[38]Ali, M.M., Vaidya, V. "Vitamin D and cancer." *Journal of Cancer Research and Therapeutics*; 2007, 3(4):225-230.
[39]Houghton, L.A., Vieth, R. "The case against ergocalciferol (vitamin D2) as a vitamin supplement." *American Journal of Clinical Nutrition*; 2006, 84(4):694-697.
[40]"Cholecalciferol." *Wikimedia Foundation, Inc.*<http://en.wikipedia.org/wiki/Cholecalciferol>. Accessed March 2008.
[41]Trang, H.M., et. al. "Evidence that vitamin D3 increases serum 25-hydroxyvitamin D more efficiently than does vitamin D2." *American Journal of Clinical Nutrition*; 1998, 68(4):854-858.
[42]Hart, G.R., et. al. "Measurement of vitamin D status: background, clinical use, and methodologies." *Clinical Laboratory*; 2006;52(7-8):335-343.
[43]Ingraham, B.A., et. al. "Molecular basis of the potential of vitamin D to prevent cancer." *Current Medical Research and Opinion*; 2008, 24(1):139-149.
[44]Bischoff-Ferrari, H.A. "Optimal serum 25-hydroxyvitamin D levels for multiple health outcomes." *Advances in Experimental Medicine and Biology*; 2008, 624:55-71.
[45]Heaney, R.P. "Barriers to optimizing vitamin D3 intake for the elderly." *The Journal of Nutrition*; 2006, 136(4):1123-1125.
[46]"Vitamin D and adult bone health in Australia and New Zealand: a position statement." *The Medical Journal of Australia*; 2005, 182(6):281-285.
[47]Vieth, R., et. al. "Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level." *American Journal of Clinical Nutrition*; 2001, 73(2):288-294.
[48]Zittermann, A., et. a. "Vitamin D insufficiency in congestive heart failure: why and what to do about it?" *Heart Failure Reviews*; 2006, 11(1):25-33.
[49]Hollis, B.W. "Vitamin D requirement during pregnancy and lactation." *Journal of Bone and Mineral Research*; 2007, 22 Suppl 2:V39-44.
[50]Wagner, C.L., et. al. "High-dose vitamin D3 supplementation in a cohort of breastfeeding mothers and their infants: a 6-month follow-up pilot study." *Breastfeeding Medicine*; 2006, 1(2):59-70.
[51]Kimball, S.M., et. al. "Safety of vitamin D3 in adults with multiple sclerosis." *American Journal of Clinical Nutrition*; 2007, 86(3):645-651.
[52]"Dietary Supplement Fact Sheet: Vitamin D." *National Institutes of Health*. <http://dietary-supplements.info.nih.gov/factsheets/ vitamind.asp>. Accessed March 2008.
[53]Vieth, R. "Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety." *American Journal of Clinical Nutrition*; 1999, 69(5):842-856.
[54]—. "Vitamin D toxicity, policy, and science." *Journal of Bone and Mineral Research*; 2007, 22 Suppl 2:V64-68.
[55]Hathcock, J.N., et. al. "Risk assessment for vitamin D." *American Journal of Clinical Nutrition*; 2007, 85(1):6-18.
[56]Nnoaham, K.E., Clarke, A. "Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis." *International Journal of Epidemiology*; 2008, 37(1):113-119.
[57]Michos, E.D., Melamed, M.L. "Vitamin D and cardiovascular disease risk." *Current Opinion in Clinical Nutrition and Metabolic Care*; 2008, 11(1):7-12.
[58]Martins, D., et. al. "Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey." *Archives of Internal Medicine*; 2007, 167(11):1159-1165.
[59]Wang, T.J., et. al. "Vitamin D deficiency and risk of cardiovascular disease." *Circulation*; 2008, 117(4):503-511.
[60]Berk, M., et. al. "Vitamin D deficiency may play a role in depression." *Medical Hypotheses*; 2007, 69(6):1316-1319.
[61]McGill, A.T., et. al. "Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity." *Nutrition Journal*; 2008, 28(7):4.
[62]Litonjua, A.A., Weiss, S.T. "Is vitamin D deficiency to blame for the asthma epidemic?" *The Journal of Allergy and Clinical Immunology*; 2007, 120(5):1031-1035.
[63]Lansdowne, A.T., Provost, SC. "Vitamin D3 enhances mood in healthy subjects during winter." *Psychopharmacology (Berlin)*; 1998, 135(4):319-323.
[64]Stephenson, A., et. al. "Cholecalciferol significantly increases 25-hydroxyvitamin D concentrations in adults with cystic fibrosis." *American Journal of Clinical Nutrition*; 2007, 85(5):1307-1311.
[65]Scragg, R., et. al. "Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey." *American Journal of Hypertension*; 2007, 20(7):713-719.

[66]Bodnar, L.M., et. al. "Maternal vitamin D deficiency increases the risk of preeclampsia." *The Journal of Clinical Endocrinology and Metabolism*; 2007, 92(9):3517-3522.
[67]Holick, M.F. "The role of vitamin D for bone health and fracture prevention." *Current Osteoporosis Reports*; 2006, 4(3):96-102.
[68]Jackson, C., et. al. "The effect of cholecalciferol (vitamin D3) on the risk of fall and fracture: a meta-analysis." *QJM: Monthly Journal of the Association of Physicians*; 2007, 100(4):185-192.
[69]Epstein S. "The problem of low levels of vitamin D and osteoporosis: use of combination therapy with alendronic acid and colecalciferol (vitamin D3)." *Drugs & Aging*; 2006, 23(8):617-625.
[70]Plotnikoff, G.A., Quigley, JM. "Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain." *Mayo Clinic Proceedings*; 2003, 78(12):1463-1470.
[71]Gerwin, R.D. "A review of myofascial pain and fibromyalgia--factors that promote their persistence." *Acupuncture in Medicine*; 2005, 23(3):121-134.
[72]Lotfi, A., et. al. "Hypovitaminosis D in female patients with chronic low back pain." *Clinical Rheumatology*; 2007, 26(11):1895-1901.
[73]Douaud, C. "Vitamin D deficiency linked to greater pain." *Decision News Media SAS*; 2008. <http://www.nutraingredients-usa.com/news/ng.asp?id=80574>. Accessed March 2008.
[74]Hooten, W.M., et. al. " Prevalence and Clinical Correlates of Vitamin D Inadequacy Among Patients with Chronic Pain" from American Society of Anesthesiologists Meeting 2007. *ProHealth, Inc.*; 2008. <http://www.immunesupport.com/library/showarticle.cfm?id=8540>. Accessed March 2008.
[75]Tokar, E.J., Webber, MM. "Cholecalciferol (vitamin D3) inhibits growth and invasion by up-regulating nuclear receptors and 25-hydroxylase (CYP27A1) in human prostate cancer cells." *Clinical & Experimental Metastasis*; 2005, 22(3):275-284.
[76]Lou, Y.R., et. al. "The role of Vitamin D3 metabolism in prostate cancer." *The Journal of Steroid Biochemistry and Molecular Biology*; 2004, 92(4):317-325.
[77]Garland, C.F., et. al. "Vitamin D and prevention of breast cancer: pooled analysis." *The Journal of Steroid Biochemistry and Molecular Biology*; 2007, 103(3-5):708-711.
[78]Gorham, E.D., et. al. "Vitamin D and prevention of colorectal cancer." *The Journal of Steroid Biochemistry and Molecular Biology*; 2005, 97(1-2):179-194.
[79]—. "Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis." *American Journal of Preventative Medicine*; 2007, 32(3):210-216.
[80]Grant, W.B., et. al. "An estimate of cancer mortality rate reductions in Europe and the US with 1,000 IU of oral vitamin D per day." *Recent Results in Cancer Research*; 2007, 174:225-234.
[81]Jiménez-Lara, A.M. "Colorectal cancer: potential therapeutic benefits of Vitamin D." *The International Journal of Biochemistry & Cell Biology*; 2007, 39(4):672-677.
[82]Freedman, D.M., et. al. "Prospective study of serum vitamin D and cancer mortality in the United States." *Journal of the National Cancer Institute*; 2007, 99(21):1594-1602.
[83]Skinner, H.G., et. al. "Vitamin D intake and the risk for pancreatic cancer in two cohort studies." *Cancer Epidemiology, Biomarkers & Prevention*; 2006, 15(9):1688-1695.
[84]Giovannucci, E. "Vitamin D and Cancer Incidence in the Harvard Cohorts." *Annals of Epidemiology*; 2008, February 19. [Epub ahead of print]
[85]Ozgocmen, S., et. al. "Vitamin D deficiency and reduced bone mineral density in multiple sclerosis: effect of ambulatory status and functional capacity." *Journal of Bone and Mineral Metabolism*; 2005, 23(4):309-313.
[86]Smolders, J., et. al. "Vitamin D as an immune modulator in multiple sclerosis, a review." *Journal of Neuroimmunology*; 2008, 194(1-2):7-17.
[87]Niino, M., et. al. "Therapeutic potential of vitamin d for multiple sclerosis." *Current Medicinal Chemistry*; 2008, 15(5):499-505.
[88]Bodnar, L.M., et. al. "High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates." *The Journal of Nutrition*; 2007, 137(2):447-452.
[89]Zipitis, C.S., Akobeng, AK. "Vitamin D Supplementation in Early Childhood and Risk of Type 1 Diabetes: a Systematic Review and Meta-analysis." *Archives of Disease in Childhood*; 2008, March 13. [Epub ahead of print]
[90]Hyppönen, E., et. al. "Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study." *Lancet*; 2001, 358(9292):1500-1503.

