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Optimize Vitamin D

What We Have Learned About Vitamin D Dosing?

Integrative Medicine
Vol. 9, No. 1, Feb/Mar 2010

Joseph Pizzorno, ND, Editor in Chief

BACKGROUND FROM DAN MURPHY

The world standard uses nmol/l, while US standard uses mg/dl.

For vitamin D, to convert mg/dl to nmol/l, divide the mg/dl by 2.5.

For vitamin D, to convert nmol/l to mg/dl, just multiply by 2.5.

KEY POINTS FROM THIS ARTICLE:

1) "Over the past several years, the surprising prevalence of vitamin D deficiency has become broadly recognized."

2) Vitamin D deficiency is linked to:
Osteoporosis
Cardiovascular disease
Cancer
Autoimmune diseases
Multiple sclerosis
Pain
Loss of Cognitive function
Decreased strength
Increased rate of all-cause mortality

3) "Deficiency of vitamin D is now recognized as a pandemic, with more than half of the world's population at risk."

4) Approximately 50% of the healthy North American population and more than 80% of those with chronic diseases are vitamin D deficient.

5) 80% of healthy Caucasian infants are vitamin D deficient. [And the rate of vitamin D deficiency tends to be greater in African American and Hispanic children].

6) Those with vitamin D deficiency experience 39% higher annual healthcare costs than those with normal levels of vitamin D.

7) Suggested levels of vitamin D as measured by 25(OH)D3 is:

Caucasians	125 – 175 nmol/l	=	50 - 70 mg/dl
Hispanics	100 – 150 nmol/l	=	40 - 60 mg/dl
African Americans	80 – 120 nmol/l	=	32- 48 mg/dl

8) The minimum blood levels of vitamin D [25(OH)D3] is 80 nmol/l (32 mg/dl).

9) Prolonged intake of 10,000 IU of supplemental vitamin D3 "is likely to pose no risk of adverse effects in almost all individuals."

10) The maximum safe levels for vitamin 25(OH)D3 in the blood is 275 nmol/l (100 mg/dl).

11) Sarcoidosis patients (and other granulomatous diseases) should not supplement with vitamin D because it increases granuloma production increasing the risk of hypercalcemia.

12) A loading dose of supplemental vitamin D3 of 10,000 IU/day for 3 months and maintenance dose of 5,000 IU/day "is not enough for most people in northern climes."

13) The loading dose of supplemental vitamin D3 should be about 20,000 IU/day for 3 – 6 months with a maintenance dose of 5,000 IU/day. Those taking this amount of supplemental vitamin D3 should periodically have their serum 25(OH)D3 levels measured.

COMMENTS FROM DAN MURPHY

The lab we use to test blood vitamin D3 [25(OH)D3] uses a finger prick analysis:
ZRT Laboratory
8605 SW Creekside Pl
Beaverton, OR 97008
866-600-1636
www.zrtlab.com
Vitamin D Testing Finger prick

The vitamin D3 my family takes is ***Complete Hi D3***, from Nutri-West (5,000 IU):
800-443-3333
The primary researcher on this product was Don Bellgrau, PhD. Dr. Bellgrau is a tenured Professor of Immunology and Medicine at the University of Colorado, Denver, where he is a Program Leader in Immunology and Immunotherapy at the Cancer Center on vitamin D3 supplementation. Dr. Bellgrau has conducted experiments with nutrients/vitamin D and immune cells. He has published in over 100 peer-reviewed articles, including the Journal of Neurooncology, Nature, Clinical Immunology, Cancer Research, Cancer Immunology and Immunotherapy, and Cell Transplantation.

Fighting infections with vitamin D

Nature Medicine
April 2006, 12(4): 388 - 390

Michael Zasloff
The author is in the Departments of Surgery and Pediatrics, Georgetown University School of Medicine, Washington, DC

KEY POINTS FROM DAN MURPHY

1) It has been known for more than a century that sunlight can treat tuberculosis.

2) In 1895, Niels Finsen of Denmark effectively treated tuberculosis with exposure to high-intensity light produced from an electric arc lamp. This phototherapy "cured or substantially improved the disease in about 95% of affected people, and by the 1920s sun exposure for the treatment of pulmonary tuberculosis had become routine."

3) Sunlight effectively treats tuberculosis because it produces vitamin D, which in turn produces a microbe-fighting peptide.

4) Treating tuberculosis with sunshine was so effective that its discoverer was awarded the Nobel Prize in 1903.

5) Sunlight helps us battle tuberculosis and other microbes "by stimulating the synthesis of vitamin D, [which] upregulates the expression of a microbe-fighting peptide."

6) Vitamin D stimulates the synthesis of the potent antimicrobial peptide called LL-37 in skin and in circulating phagocytic cells that make up the innate immune response. This improves the immune response.

7) Macrophages [innate immune response] more effectively kill tuberculosis after they are exposed to vitamin D3.

8) American blacks are particularly susceptible to infection by tuberculosis because they have substantially lower serum vitamin D levels than whites, as a result of the greater UV shielding afforded by their skin's higher melanin content. Treatment with vitamin D3 should augment the microbicidal capacity of monocytes in blacks.

9) "We currently base vitamin D requirements on amounts required to sustain optimal health of our skeleton. The studies reported here suggest that optimal functioning of our innate immune system might require more vitamin D."

10) "Perhaps in the future we might be able to treat or prevent certain infectious diseases with safe and inexpensive substances that induce expression of endogenous antimicrobial peptides."

RE: Epidemic Influenza and Vitamin D

Epidemiology and Infection
October 2007, Vol. 135, No. 7, pp. 1095-1098

JOHN F. ALOIA and MELISSA LI-NG

KEY POINTS FROM DAN MURPHY

1) "There is an epidemic of vitamin D insufficiency in the United States, the public health impact of this observation could be great."

2) "The occurrence of the common cold and influenza shows clear seasonality. The cold and influenza season corresponds to the season of vitamin D insufficiency."

3) "The lack of vitamin D during the winter may be a 'seasonal stimulus' to the infectivity of the influenza virus."

4) "Vitamin D is produced in the skin when sunlight is absorbed. Thus, vitamin D levels, or serum 25-hydroxyvitamin D (25-OHD), fluctuate seasonally."

5) Vitamin D has important functions in the immune system, specifically the innate immune system.

6) Over a 3-year period, taking 800 IU of vitamin D3 reduced the incidence of colds and flus by 70%. Taking 2,000 IU of vitamin D3 reduced the incidence of colds and flus to nearly zero (only one case out of 104 users).

7) "Vitamin D supplementation, particularly at higher doses, may protect against the 'typical' winter cold and influenza."

8) "The physiological basis of the protective effect of vitamin D lies in its ability to stimulate innate immunity and to moderate inflammation."

9) "These reports provide a rationale for vitamin D supplementation in the prevention of colds and influenza."

10) Only vitamin D3 is bioactive; vitamin D2 (ergocalciferol) "is not vitamin D but a less potent vitamin D analogue that plays no role in normal human physiology."

11) "Physiological doses [800 – 2,000 IU / day] of vitamin D prevent many viral respiratory infections."

12) "It is also reasonable to postulate that pharmacological doses of vitamin D may be effective adjuvants in a breathtakingly large number of life-threatening infections."

On the Epidemiology of Influenza

Virology Journal
February 25, 2008, Volume 5

John J Cannell, Michael Zasloff, Cedric F Garland, Robert Scragg and Edward Giovannucci

KEY POINTS FROM DAN MURPHY

1) Vitamin D upregulates the endogenous antibiotics of innate immunity and suggest that the incongruities in flu behaviour may be secondary to the epidemiology of vitamin D deficiency.

2) Recently epidemiological studies question vaccine effectiveness because "influenza mortality and hospitalization rates for older Americans significantly increased in the 80's and 90's, during the same time that influenza vaccination rates for elderly Americans dramatically increased."

3) A 2006 study stated "We found no evidence of reduction in influenza-related mortality in the last 15 years, despite the concomitant increase of influenza vaccination coverage from ~10% to ~60%."

4) The seasonality of influenza indicates that it is controlled by a "seasonal stimulus." This "seasonal stimulus" may be seasonal impairments of the antimicrobial peptide systems crucial to innate immunity caused by dramatic seasonal fluctuations in vitamin D3.

5) Innate immunity is that branch of host defense that is "hard-wired" to respond rapidly to microorganisms.

6) "The evidence that vitamin D has profound effects on innate immunity is rapidly growing." "Vitamin D is the 'antibiotic vitamin' due primarily to its robust effects on innate immunity."

7) In a 2007 study, 104 women given vitamin D were three times less likely to report cold and flu symptoms than placebo controls. "A low dose (800 IU/day) not only reduced reported incidence, it abolished the seasonality of reported colds and flu. A higher dose (2000 IU/day), given during the last year of their trial, virtually eradicated all reports of colds or flu."

8) "Relative – but easily correctable – deficiencies in innate immunity probably exist in many dark-skinned and aged individuals, especially during the winter," because of reduced ability to produce vitamin D.

9) During the 1918 flu pandemic, there were five attempts to transmit the flu to a well person from a sick person, and these attempts exceeded a combined total of

150 well patients. Methods of transmission included cough, spit, and breathe. None of these attempts succeeded. **[Very Interesting]**

10) In previous ages, flu epidemics spread rapidly despite the lack of modern transport because influenza was already embedded in the population and erupted when impairments in innate immunity occurred as a consequence of seasonal reduced vitamin D.

11) These authors propose individual variations in vitamin D3 levels explain the variations in the innate immunity of the volunteers who purposefully exposed themselves to the flu but did not become ill.

12) Influenza mortality has not declined with increasing vaccination rates because influenza vaccines improve adaptive immunity, and the key is innate immunity. **[The innate immune response rules the adaptive immune response: if the innate immune response ignores an invader, one will not make antibodies {adaptaive immune response} to that invader. How the Immune System Works, by Loren Sompayrac, Blackwell Science, 2008]**

"The innate immunity of the aged declined over the last 20 years due to medical and governmental warnings to avoid the sun. While the young usually ignore such advice, the elderly often follow it. We suggest that improvements in adaptive immunity from increased vaccination of the aged are inadequate to compensate for declines in innate immunity the aged suffered over that same time."

13) "Compelling epidemiological evidence indicates vitamin D deficiency is the 'seasonal stimulus' [responsible for flu outbreaks]."

14) Lower respiratory tract infections are more frequent in those with low vitamin D3 levels.

15) Vitamin D3 regulates 1,000 human genes.

16) A 2007 study found 2,000 IU of vitamin D per day "abolished the seasonality of influenza."

Vitamin D for Cancer Prevention: Global Perspective

Annals of Epidemiology
Volume 19, Issue 7, July 2009, Pages 468-483

Cedric F. Garland Dr PH, Edward D. Gorham MPH, PhD, Sharif B. Mohr MPH, Frank C. Garland PhD.
This article has 144 references.

KEY POINTS FROM DAN MURPHY

1) Higher serum levels of vitamin D3 are associated with substantially lower incidence rates of colon, breast, ovarian, renal, pancreatic, aggressive prostate and other cancers.

2) Raising the minimum year-around serum vitamin D3 level to 40 to 60 ng/mL (100–150 nmol/L) would prevent approximately 58,000 new cases of breast cancer and 49,000 new cases of colorectal cancer each year, and three fourths of deaths from these diseases in the US and Canada. This would also reduce fatality rates of patients who have breast, colorectal, or prostate cancer by half.

3) Raising serum vitamin D3 level 40 to 60 ng/mL would require supplemntation with about 2,000 IU of vitamin D3 per day. "There are no unreasonable risks from intake of 2,000 IU per day of vitamin D3."

4) High sun exposure reduces both the incidence of and mortality from breast and prostate cancers.

5) Higher sun exposure in childhood and adolescence reduce the lifetime incidence of prostate cancer by about 50%.

6) "Approximately 220,149 new cases of breast cancer and 254,105 new cases of colorectal cancer would be prevented annually in the world by raising serum vitamin D3 concentrations to approximately 40 to 60 ng/mL, which is, in general, associated with oral intake of 2,000 IU of vitamin D3 per day."

7) Vitamin D3 serum level of 40 to 60 ng/mL would prevent three fourths of deaths from breast and colorectal cancer in the US and Canada. **[Wow!]**

8) There are ten separate mechanisms by which vitamin D3 and calcium reduce cancer incidence and mortality.

9) Preventing the spread of cancerous cells is dependent upon intercellular adherence. Intercellular adherence is requires extracellular calcium ions. Low calcium levels thus allow the spread of cancer cells.

10) Intercellular adherence is also degraded by omege-6 vegetable oils. "Unfortunately, omega-6 linoleic acid is the most common polyunsaturated fatty acid consumed in the Western diet (median intake 15 g/day)."

11) The "National Academy of Sciences–Institute of Medicine recommended adequate intake [of vitamin D3] should be revised upward to at least 2,000 to 4,000 IU/day. Adoption of the new adequate intake [of vitamin D3] would substantially reduce the incidence of cancer, and there are no consistently established adverse effects of vitamin D3 intake in the range below 4,000 IU/day that would be sufficient to justify a lower adequate intake [of vitamin D3]."

12) "The upper limit [of vitamin D3] should be increased to at least 5,000 IU/day, based on expected benefits compared to anticipated minor risks." Some knowledgeable vitamin D scientists and physicians have recommended a higher upper limit of 10,000 IU/day.

13) Vitamin D3 (cholecalciferol) should replace vitamin D2 (ergocalciferol) because vitamin D3 is more effective in humans.

14) "The preventive effects of higher vitamin D3 intake have led 16 vitamin D scientists and concerned physicians in the US and Canada to disseminate a call to action recommending universal daily intake of 2000 IU of vitamin D3."

15) Low vitamin D levels also increase the incidence of myocardial infarction, type-1 diabetes, multiple sclerosis, and falls.

16) "Populations living at or higher than 30° latitude in either the northern or southern hemisphere, or who have a mainly indoor lifestyle, should be considered at high risk of breast, colon, ovarian, and many other types of cancer as a result of highly prevalent vitamin D deficiency."

17) Vitamin D should be used to "reduce incidence and mortality from cancer, and substantially increase treatment success."

COMMENT FROM DAN MURPHY

For a couple of years now I have been recommending that most of us and our patients supplement with 2,000 IU vitamin D3 per day. This article certainly supports that recommendation.

Vitamin D intake and incidence of multiple sclerosis

NEUROLOGY, January 13, 2004;62:60-65

K. L. Munger, MSc, S. M. Zhang, MD ScD, E. O,Reilly, MSc, M. A. Hernán, MD DrPH, M. J. Olek, DO, W. C. Willett, MD DrPH and A. Ascherio, MD DrPH

KEY POINTS FROM DAN MURPHY

1) The incidence of multiple sclerosis (MS) is low in the tropics and increases with distance from the equator in both hemispheres. Sunlight exposure and the resulting increase in vitamin D may exert a protective effect against MS.
2) Vitamin D intake may be more important for women living in regions at high latitude where winter sunlight is insufficient.

3) Individuals with MS tend to have insufficient vitamin D levels.

4) Periods of low vitamin D precede the occurrence of high MS lesion activity, and periods of high vitamin D precede low MS lesion activity, as detected by MRI.

5) This study found that women who used supplemental vitamin D had a 40% lower risk of MS than women who did not use vitamin D supplements.

6) Taking vitamin D supplements for more than 10 years lowered the risk of developing MS by 59%.

7) There was no reduced risk of MS with increased vitamin D intake from food. It had to be in the form of supplements.

8) Vitamin D supplements in the first year of life, reduces the risk of type-1 diabetes.

9) Vitamin D has strong immunoregulatory effects.

10) These results support a protective effect of vitamin D supplement intake on risk of developing MS.

[Recent studies are advocating that we all supplement with 1000 IU of vitamin D per day.] Dan

Serum 25-Hydroxyvitamin D Levels and Risk of Multiple Sclerosis

Journal of the American Medical Association
December 20, 2006 pp. 2832-2838

Kassandra L. Munger, MSc; Lynn I. Levin, PhD, MPH; Bruce W. Hollis, PhD; Noel S. Howard, MD; Alberto Ascherio, MD, DrPH

This study was performed at the Harvard School of Public Health

KEY POINTS FROM DAN MURPHY

1) High levels of vitamin D, a potent immunomodulator, decrease the risk of multiple sclerosis.

2) High circulating levels of vitamin D are associated with a lower risk of multiple sclerosis.

3) "Multiple sclerosis (MS) is among the most common neurological diseases in young adults."

4) "MS is an autoimmune disorder whereby an unknown agent or agents triggers a T cell–mediated inflammatory attack, causing demyelination of central nervous system tissue."

5) MS increases significantly with increasing latitude, both north and south, of the equator.

6) "A protective effect of vitamin D on MS is supported by the reduced MS risk associated with sun exposure and use of vitamin D supplements." **[Important]**

7) "Among whites, there was a 41% decrease in MS risk for every 50-nmol/L increase in 25-hydroxyvitamin D."

8) "MS risk was highest among individuals in the bottom quintile and lowest among those in the top quintile of 25-hydroxyvitamin D levels."

9) "The risk of MS decreased with increasing serum levels of 25-hydroxyvitamin D."

10) "Nutritional vitamin D status could be key in innate immune response." **[Important]**

11) "Vitamin D levels earlier in life may be critical in conferring protection for MS."

12) "Vitamin D supplementation in infancy seems to exert a strong protective effect against the autoimmune disease type 1 diabetes, and vitamin D levels in early childhood could also have an impact on the risk of MS."

13) Half of white and two thirds of black adults in the United States have 25-hydroxyvitamin D levels below 70 nmol/L. "The best serum 25-hydroxyvitamin D concentrations are between 90 and 100 nmol/L."

14) "Increasing the vitamin D levels of adolescents and young adults could result in an important reduction in MS incidence. Such an increase could be achieved by using vitamin D supplements." **[Very Important]**

15) Vitamin D supplementation is safe at levels several-fold higher than 2000 IU/d for adults.

On the Aetiology of Autism

Acta Paediatrica
August 2010, Vol. 99, No. 8, pp. 1128–1130

John J Cannell

BACKGROUND FROM DAN MURPHY

The world standard for blood levels of vitamin D uses nmol/l, while US standard uses mg/dl.

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For vitamin D, to convert nmol/l to mg/dl, just multiply by 2.5.

In 2008, this author, John Cannell, published an article in the journal Medical Hypothesis, titled:

Autism and Vitamin D
Medical Hypotheses
Volume 70, Issue 4, 2008, Pages 750-759

I reviewed this article; it is Article 18-10. In this newer article, Cannell updates his hypothesis of the link between low levels of vitamin D3 and the incidence of autism, reviewing the studies that have appeared in the literature since his 2008 publication.

KEY POINTS FROM THIS ARTICLE:

1) "The primary environmental trigger for autism is not vaccinations, toxins or infections, but gestational and early childhood vitamin D deficiency."

2) An article in Scientific American (2009) and two articles in Acta Paediatrica (2010) support the evidence that "vitamin D deficiency – either during pregnancy or early childhood – may be an environmental trigger for the genetic disease of autism."

3) Currently there is an epidemic of gestational vitamin D deficiency. Prenatal supplementation with 400 IU of vitamin D3/day "is virtually irrelevant in preventing" this gestational deficiency. "The Canadian Paediatric Society cautioned pregnant women they may require not 400 IU / day but 2000 IU / day, or more, to prevent gestational vitamin D deficiency."

4) The increased incidence of autism in the children of richer college-educated, wealthy parents might be explained by noting that such parents are more likely to "practice sun avoidance and use of sun block."

5) The melanin found in darker skin is an effective sun block. Consequently, dark skinned people have a higher incidence of autism.

6) Environmental toxins are more likely to damage the genome of those who are deficient in vitamin D. Vitamin D "protects the genome from damage by toxins."

7) A 2008 study (*Journal of Autism and Developmental Disorders*) found that boys with autism have reductions in metacarpal thickness; this is consistent with a deficiency of vitamin D during a stage of development.

8) A 2008 study (Archives of Pediatric and Adolescent Medicine) [My review Article 26-10] indicated that autism rates are higher in regions with more rainy/cloudy days. "Clouds and rain retard vitamin D-producing ultraviolet B light from penetrating the atmosphere."

9) Autism is more prevalent in cities than in rural settings. "City life affords less vitamin D because of tall buildings, indoor occupations and increased air pollution, all of which block ultraviolet B light from penetrating the atmosphere."

10) Studies published in the journal *Neurology* (2008 and 2009) indicate increased autism in the children of mothers who took antiepileptic drugs. "Antiepileptic drugs are one of the few classes of drugs that consistently and significantly interfere with vitamin D metabolism, lowering vitamin D3 levels."

11) Autism rates are higher in children born in the winter, when vitamin D from sun exposure is low.

12) Autism has a genetic contribution. The current epidemic maternal and early childhood deficiency of vitamin D may "allow the genetic tendency for autism to express itself."

13) Theoretically, prevention and perhaps treatment of autism with physiological doses of vitamin D3 "is so simple, so safe, so inexpensive, so readily available and so easy, that it defies imagination."

14) "Children with chronic ilinesses such as autism, diabetes and/or frequent infections should be supplemented with higher doses of sunshine or vitamin D3, doses adequate to maintain their 25(OH) D levels in the mid-normal of the reference range [65 ng/mL {USA} or 162 nmol/L {global}] – and should be so supplemented year round.'

15) "To some real but unknown extent, autism is an iatrogenic disease, caused by governments, organizations, committees, newspapers and physicians who promulgated the current warnings about sun exposure for pregnant women and young children without any understanding of the tragedy they engendered."

THE Vitamin D CURE

James Dowd, M.D.

Diane Stafford

2008

WILEY

John Wiley & Sons, Inc.

THE VITAMIN D SOLUTION

A 3-Step Strategy to Cure Our Most Common Health Problems

MICHAEL F. HOLICK, Ph.D., M.D.

Foreword by ANDREW WEIL, M.D.

2010

A PLUME BOOK

Chronic Pain Syndrome
And
Vitamin D

Humans evolved outdoors, in the sunshine. Exposure to the sun's ultraviolet radiation produces a hormone known as "vitamin D". Vitamin D is critical for human health. The nucleus of all of our cells have vitamin D receptors. There is evidence that vitamin D influences the expression of about 10% of human genes.

With very rare exceptions, humans cannot achieve optimal levels of vitamin D through diet alone. Although some foods are fortified with vitamin D, consumption of large amounts of such foods will not achieve optimal levels. To achieve and maintain optimal levels of vitamin D, we must either use vitamin D supplements or use the sun.

The sun showers onto earth a large range of radiation, including ultraviolet radiation (UV). UV radiation has three wavelengths, as follows:

Ultraviolet A (UVA): 320-400 nm

UVA has the longest wavelength and therefore it penetrates deepest into the skin. The most superficial layer of skin cells is the squamous cells. Deeper to the squamous cells are the basal cells. Below the basal cells are the melanocytes. Because UVA penetrates deepest into the skin, it is the primary UV influence on the melanocytes. Melanocytes produce the dark colored skin pigment melanin. This means that it is UVA that is primarily responsible for skin tanning. Sadly, damage to these same melanocytes increases the risk of the deadly skin cancer melanoma. UVA radiation is also primarily responsible for skin wrinkles.

Ultraviolet B (UVB): 280-319 nm

UVB should be subcategorized: 280-289 nm and 290-319 nm

- 280-289 nm UVB radiation is absorbed by the atmosphere and therefore does not influence human physiology, neither positively nor negatively.

- 290-319 UV radiation is most important. This range of UVB is primarily responsible for burning of the skin with excess sun exposure. Because of its shorter wavelength (as compared to UVA), it is less likely to affect the deeper melanocytes, and therefore is less associated with deadly melanoma.

Older sunscreens (UVB blockers only) and contemporary non-broad-spectrum sunscreens (UVB and UVA blockers) only blocked the skin burning UVB radiation, allowing the user to spend more time in the sun without burning. Ironically, this increased the sunscreen user's exposure to the dangerous wrinkle and melanoma producing UVA radiation.

To add to the irony, it is UVB radiation in the 290-319 nm wavelength that starts the production of vitamin D, as detailed below.

Consequently, older sunscreens (UVB blockers only) reduced skin burning, reduce the skin production of vitamin D, increase skin wrinkles, and increase deadly melanomas.

Ultraviolet C (UVC): 200-280 nm

UVC has the shortest wavelength and therefore it does not penetrate well. In fact, it is unable to penetrate the earth's atmosphere, where it is 100% absorbed.

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James Dowd, MD, is an Associate Professor of Medicine at Michigan State University. He is also the founder and director of both the Arthritis Institute of Michigan and the Michigan Arthritis Research Center. He is board certified in internal medicine, adult rheumatology and pediatric rheumatology.

In 2008, Dr. Dowd published a book titled The Vitamin D Cure: Five Steps to Heal Your Pain and Improve Your Mood.

Dr. Down states that the optimal level of vitamin D is between 50-70 ng/ml.

PAIN

In his book, Dr. Dowd states:

"Research tells us that a lack of vitamin D makes us ache. Symptoms that point to vitamin D deficiency are muscle spasms, bone pain, and joint pain."

"Doctors often mistake vitamin D deficiencies for fibromyalgia, rheumatoid arthritis, and lupus."

"Because I'm a rheumatologist, people come to me because they want solutions for the pain they're experiencing in their joints, tendons, ligaments, muscles, and bones. They typically have at least one disease involving muscles, ligaments, joints, and bones, but all of the aches and pains they have are actually connected to their vitamin D levels and what they eat."

Dr. Dowd explains how joint cartilage integrity is dependent upon the quality of the bone the cartilage sits upon, stating:

"The bone that lies under the joint cartilage keeps the cartilage stable, functioning, and durable." "You will speed up the rate of your cartilage breaking down when anything destabilizes the bone below the cartilage, such as poor bone development or increased bone turnover caused by vitamin D deficiency."

Dr. Dowd notes that there is a 2-3 fold faster rate of osteoarthritis progression in those with the lowest 20% of vitamin D levels compared to those with the highest levels.

Dr. Dowd notes that adequate vitamin D supplementation can eliminate chronic back pain symptoms in nearly all patients, stating:

"Those who took vitamin D supplements saw dramatic resolution of pain, muscle fatigue and muscle cramps."

MAGNESIUM

Dr. Dowd emphasizes that there is an important relationship between vitamin D and magnesium, stating:

1) Magnesium is critical for one's body to produce the active form of vitamin D.

2) The receptor that vitamin D uses in the nuclear membrane is poorly expressed when one is magnesium deficient.

3) Magnesium is required for vitamin D to function properly.

Dr. Dowd further explains that magnesium is low when the body becomes acidic. He notes that the two main causes of an acidic body are the consumption of grains and dairy products, so he discourages both. He states that the most abundant and absorbable source for magnesium is the consumption of green leafy vegetables.

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The world's leading authority on vitamin D is Michael F. Holick, PhD, MD. Dr. Holick is a professor at Boston University Medical Center and the director of the university's General Clinical Research Unit, Bone Health Clinic, and the Heliotherapy, Light, and Skin Research Laboratory. A search of the National Library of Medicine using the PubMed search engine identified 345 articles using the key words "holick mf AND vitamin d".

Dr. Holick is the discoverer of the active form of vitamin D (1,25, dihydroxy vitamin D). In his 2010 book titled The Vitamin D Solution: A 3-Step Strategy to Cure Our Most Common Health Problems, Dr. Holick details these steps to the formation of the active form of vitamin D:

STEP #1
Our skin cells contain a molecule called
7-dehydrocholesterol = provitamin D3
which absorbs ultraviolet light B (UVB, wavelength 290-319 nm)

STEP #2
The absorption of UVB by provitamin D3
produces
pre-vitamin D3
within the skin cells

STEP #3
Our body heat
converts
pre-vitamin D3
into
vitamin D3
within the skin cell
(this is the same molecule as supplemental vitamin D3)

STEP #4
Vitamin D3
exits the skin cell into the blood stream
and
travels to the liver
where
25-hydroxy vitamin D (calcidrol) is produced

STEP #5
25-hydroxy vitamin D
leaves the liver
into the blood stream
to the kidney

STEP #6
The kidney makes the active form of vitamin D
1, 25 dihydroxy vitamin D
(this is the active form of vitamin D that was discovered by Dr. Holick)

STEP #7
This active form of vitamin D (1, 25 dihydroxy vitamin D)
circulates throughout the body
binding to receptors in the nucleus of the cell
influencing gene expression

Dr. Holick discusses the following FACTS pertaining to vitamin D:

1) Humans evolved in a manner as to be dependent upon sunshine for life and health.

2) There has been a 22% reduction of vitamin D levels in the US population in the last 10 years.

3) In the United States vitamin D insufficiency occurs in:

70% of Whites
90% of Hispanics
97% of Blacks

4) The activated form of vitamin D that is found in your blood is produced in the kidneys. However, some other tissues also make the activated form of vitamin D. These include the prostate, breast, lungs, colon and brain. The activated vitamin D formed in these tissues does not enter the blood stream, but remains in those specific tissues.

5) "You could easily consume 5,000 IU of vitamin D a day, probably forever," without overdosing.

6) The assay for 25-vitamin D is the most ordered assay in the United States. This is the form of vitamin D that exists after the liver but before the kidney.

8) It is more difficult to synthesize the active form of vitamin D as one ages. A 70-year old person is 75% less efficient in synthesizing vitamin D as compared to a 20-year old person.

9) Neither calcium levels nor activated vitamin D levels (1, 25 dihydroxy vitamin D) levels are indicative of one being vitamin D deficient or not. The only acceptable measure for vitamin D deficiency is 25-vitamin D (made in the liver). Dr. Holick states:

"Do not accept any other marker no matter what your doctor tells you."

Dr. Holick discusses the following MYTHS pertaining to vitamin D:

1) It is a myth that one can wash vitamin D off from the skin shortly after being in the sun. Dr. Holick says this is not true because vitamin D3 is

actually produced inside the skin cell itself, and therefore cannot be washed off.

2) Vitamin D2 does not work or is inferior to vitamin D3. Dr. Holick says it is now proven and understood that vitamin D2 works just as well as vitamin D3.

3) One can obtain adequate activated vitamin D from eating a good diet. Dr. Holick disagrees with this. He is adamant that one can only achieve adequate levels of vitamin D by being exposed to sufficient sunshine or by supplementation. He further notes that one cannot obtain optimal levels of vitamin D by consuming vitamin D fortified foods or by taking a multiple vitamin supplement, as the levels of vitamin D are too low.

PAIN

In 2007, Dr. Sota Omoigui states:

"The origin of all pain is inflammation and the inflammatory response."

"Irrespective of the type of pain, whether it is acute or chronic pain, peripheral or central pain, nociceptive or neuropathic pain, the underlying origin is inflammation and the inflammatory response."

"Activation of pain receptors, transmission and modulation of pain signals, neuroplasticity and central sensitization are all one continuum of inflammation and the inflammatory response."

"Irrespective of the characteristic of the pain, whether it is sharp, dull, aching, burning, stabbing, numbing or tingling, all pain arises from inflammation and the inflammatory response."

Dr. Holick details how vitamin D has substantial anti-inflammatory properties.

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Dr. Holick notes that osteomalacia is a known widespread chronic pain syndrome that is caused by vitamin D deficiency. Dr. Holick states:

> **"Osteomalacia is characterized by vague but often intense bone and muscle aches and is frequently misdiagnosed as fibromyalgia, chronic fatigue syndrome, or arthritis."**

Dr. Holick estimates that 40 – 60% of those diagnosed with fibromyalgia or chronic fatigue syndrome are actually suffering from osteomalacia subsequent to a massive vitamin D deficiency.

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Dr. Holick notes that when a patient has a deficiency of vitamin D, there also exists a deficiency of calcium mineralization in the bones. Poorly mineralized bones consist of a "Jell-O-like" collagen matrix that expands with pressure, abnormally stretching the highly innervated periosteal coverings. The result is a throbbing, aching bone pain. Dr. Holick states:

> **"When people are sitting with aches in their hips or lying in bed with throbbing aches in their bones, it can be very hard for physicians to immediately think of vitamin D deficiency. But often that's exactly what's causing the problem."**

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Dr. Holick notes that 93% of those suffering from nonspecific muscular and skeletal aches and pains are shown to be vitamin D deficient.

RECENT SUPPORTIVE STUDIES

In 2009, Gerry Schwalfenberg, MD from the Department of Family Medicine, University of Alberta, Canada, published an article in the ***Journal of the American Board of Family Medicine***, titled:

Improvement of Chronic Back Pain or Failed Back Surgery with Vitamin D Repletion: A Case Series

In this study, Dr. Schwalfenberg describes 6 cases of improvement/resolution of chronic back pain or failed back surgery after vitamin D repletion in a Canadian family practice. He notes that vitamin D insufficiency is common; repletion of vitamin D to normal levels in patients who have chronic low back pain or have had failed back surgery may improve quality of life or, in some cases, result in complete resolution of symptoms. In this report, there were 4 patients who had chronic back pain

for more than a year and 2 patients who suffered for more than 3 years from failed back surgery.

In this study, Dr. Schwalfenberg makes the following key points:

"Back pain is the most common neurological complaint in North America, second only to headache."

"Low back pain (LBP) and proximal myopathy are common symptoms of vitamin D deficiency and osteomalacia."

"Vitamin D is required for the differentiation, proliferation, and maturation of cartilage cells and for the production of proteoglycan synthesis in articular chondrocytes."

"Patients who have chronic, nonspecific LBP or have had failed back surgery may have an underlying vitamin D insufficiency/deficiency."

"All patients had tried various pain treatments, including physiotherapy, visiting a chiropractor, acupuncture, or visit to a pain management clinic, all without much benefit."

"Repletion of inadequate vitamin D levels demonstrated significant improvement or complete resolution of chronic LBP symptoms in these patients."

Physicians should have a high index of suspicion for low vitamin D levels in patients with LBP.

"The patients in this study who responded best used between 4000 and 5000 IU of vitamin D3/day."

"This case series supports information that has recently become apparent in the literature about vitamin D deficiency and its influence on back pain, muscle pain, and failed back surgery. Doses in the range of 4000 to 5000 IU of vitamin D3/day may be needed for an adequate response."

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In 2009, (Straube) a study was published in the journal ***Pain***, titled:

Vitamin D and Chronic Pain

The authors reviewed 22 studies that indicated a strong association between vitamin D deficiency and chronic pain.

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In 2010, JoAnn Manson, MD from the Division of Preventive Medicine, Brigham and Women's Hospital, Harvard Medical School, published an article in the journal ***Metabolism***, titled:

Pain: sex differences and implications for treatment

In this study, Dr. Manson found that women have a higher prevalence than men of several clinical pain conditions and of inflammation-mediated disorders. Given the important role of inflammation in mediating pain, nutritional factors that modulate the inflammatory response offer a promising and exciting new avenue for the prevention and treatment of chronic pain disorders. Of particular interest is the potential role of moderate- to high-dose vitamin D and omega-3 fatty acid supplements, both of which have powerful anti-inflammatory effects. These nutritional interventions, which influence cytokine, leukotriene, and prostaglandin pathways, may be of particular benefit to women due to their higher prevalence of inflammatory chronic pain disorders.

In this study, Dr. Manson makes the following key points:

Inflammation increases the incidence of pain. Both vitamin D and omega-3 fatty acids "have powerful anti-inflammatory effects."

"Women tend to have a heightened inflammatory response compared with men. This enhanced inflammatory response may contribute to the substantially higher risk of painful inflammatory autoimmune conditions in women compared with men, including rheumatoid arthritis, lupus and other collagen vascular disorders, and osteoarthritis."

Two very promising nutritional interventions for pain management are moderate- to high-dose vitamin D and the marine omega-3 fatty acids (eicosapentaenoic acid + docosahexaenoic acid).

Vitamin D and omega-3 fatty acids "reduce levels of circulating pro-inflammatory cytokines, decrease chronic joint pain, and may reduce the risk of autoimmune diseases."

"Vitamin D, in addition to its role in calcium homeostasis, has powerful effects on the immune system, inhibiting proinflammatory cytokines such as interleukin-6 and tumor necrosis factor–alpha and reducing C-reactive protein."

Vitamin D deficiency increases chronic widespread pain and/or fibromyalgia, especially in women.

A high level of vitamin D reduces knee and hip osteoarthritis and pain.

Given the important role of inflammation and cytokines in mediating and modulating pain, there is a "promising role of moderate- to high-dose vitamin D and omega-3 fatty acid supplementation in preventing and treating inflammation and chronic pain disorders. These nutritional interventions may be of particular benefit to women due to their higher prevalence of inflammatory chronic pain disorders."

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In October 2010, (Heidari) a study was published in the journal ***International Journal of Rheumatic Disease***, titled:

Association between nonspecific skeletal pain and vitamin D deficiency

The authors detail the evidence on how deficiency of vitamin D is reported in patients in many types of musculoskeletal pain. Their study evaluated 276 chronic skeletal pain sufferers and 202 control subjects to add to the evidence that vitamin D deficiency is associated with chronic nonspecific skeletal pain.

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In November 2010 (Bhatty) a study published in the journal ***Journal of the Pakistan Medical Association***, titled:

Vitamin D Deficiency in Fibromyalgia

The authors assessed 40 female patients diagnosed with fibromyalgia from Karachi, Pakistan. They found that 100% of these woman had suboptimal levels of vitamin D. Specifically, they found that 80% had vitamin deficiency (averaging about 15 ng/ml) and 20% had vitamin D insufficiency (below 30 ng/ml). The authors concluded that vitamin D deficiency is frequently seen in patients with fibromyalgia and nonspecific musculoskeletal pain syndromes.

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In April 2011, (Arnson) an editorial appeared in the journal ***Israeli Medical Association Journal***, titled:

Is Vitamin D a New Therapeutic Agent in Auto-inflammatory and Pain Syndromes?

The authors note that "hypovitaminosis D is a worldwide epidemic, due to insufficient intake and inadequate sunlight exposure," estimating that worldwide 40-90% of older persons are vitamin insufficient. They recommend that all chronic pain persons be assessed for vitamin D levels.

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In September 2011, Tague and colleagues from the University of Kansas Medical Center published a study in the ***Journal of Neuroscience***, titled:

Vitamin D deficiency Promotes Skeletal Muscle Hypersensitivity and Sensory Hyperinnervation

The authors note that "musculoskeletal pain affects nearly half of all adults and most of them are vitamin D deficient." They also know that nociceptors express vitamin D receptors, and that a lack of vitamin D can cause nociceptive hyperinnervation of skeletal muscles, contributing to muscular hypersensitivity and pain.

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In 2011, the editorial of the ***Scandinavian Journal of Primary Health Care*** (Kragstrup) is titled:

Vitamin D Supplementation for Patients with Chronic Pain

In this editorial Dr. Kragstrup reviews the epidemiological studies that link low levels of vitamin D to chronic pain. He advocates both testing for and supplementing of vitamin D in chronic pain sufferers.

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Also in 2010, Joseph Pizzorno, ND, the Editor in Chief of the journal ***Integrative Medicine***, published an editorial in his journal titled:

What We Have Learned About Vitamin D Dosing?

In this article, Dr. Pizzorno makes the following key points:

1) "Over the past several years, the surprising prevalence of vitamin D deficiency has become broadly recognized."

2) Vitamin D deficiency is linked to:
Osteoporosis
Cardiovascular disease
Cancer
Autoimmune diseases
Multiple sclerosis
Pain
Loss of cognitive function
Decreased strength
Increased rate of all-cause mortality

3) "Deficiency of vitamin D is now recognized as a pandemic, with more than half of the world's population at risk."

4) Approximately 50% of the healthy North American population and more than 80% of those with chronic diseases are vitamin D deficient.

5) 80% of healthy Caucasian infants are vitamin D deficient. [And the rate of vitamin D deficiency tends to be greater in African American and Hispanic children].

6) Those with vitamin D deficiency experience 39% higher annual healthcare costs than those with normal levels of vitamin D.

7) The minimum blood levels of vitamin D [25(OH)D3] is 32 ng/ml; the optimal level is 50-70 ng/ml.

8) Prolonged intake of 10,000 IU of supplemental vitamin D3 "is likely to pose no risk of adverse effects in almost all individuals."

9) The recommended loading dose of supplemental vitamin D3 should be about 20,000 IU/day for 3 - 6 months with a maintenance dose of 5,000 IU/day. Those taking this amount of supplemental vitamin D3 should periodically have their serum 25(OH)D3 levels measured.

SUMMARY POINTS FROM DAN MURPHY:

- All chronic pain patients should have their 25 hydroxy vitamin D levels checked.

- If a patient's 25 hydroxy vitamin D levels are below 50 ng/ml, and especially if they are below 30 mg/ml, the patient needs more UVB sun exposure without sunscreen, or they need to supplement with 5,000 IU of vitamin D3 per day until optimal levels are achieved.

Dan Murphy, DC

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Vitamin D Supplement Doses and Serum 25-Hydroxyvitamin D in the Range Associated with Cancer Prevention

Anticancer Research
February 2011; Vol. 31; No. 2; pp. 617-622

Cedric F. Garland, Christine B. French, Leo L. Baggerly and Robert P. Heaney;
Dr. Garland is from my Alma mater, the University of California, San Diego

KEY POINTS FROM THIS STUDY:

1) The vitamin D testing done in this study was a blood spot D3 test kit manufactured by ZRT Laboratory (Beaverton, OR).

2) This study evaluated the vitamin D intake in a community-based cohort of 3,667 persons, mean age 51.3.

3) Serum D3 concentration of 60-80 ng/ml may be needed to reduce cancer risk.

4) The supplemental dose of vitamin D3 ensuring that 97.5% of this population achieved a serum D3 of at least 40 ng/ml was 9,600 IU/d.

5) Serum D3 concentration above 200 ng/ml are considered to be toxic.

6) Intakes of up to 40,000 IU vitamin D per day are unlikely to result in vitamin D toxicity.

Minimum Value of serum D3	**30 ng/ml**	**40 ng/ml**	**50 ng/ml**
Daily amount of supplemental Vit D required to ensure everyone in the group reached this value of serum Vit D, assuming everyone obtained 3,300 IU Vit D from sun exposure	6,100 IU	9,600 IU	14,100 IU
Daily amount of supplemental Vit D required to ensure everyone in the group reached this value of serum Vit D with no sun exposure	9,400 IU	12,900 IU	17,400 IU
Mean Vit D values in those with this degree of Vit D intake	**65 ng/ml**	**75 ng/ml**	**85 ng/ml**

COMMENT FROM DAN MURPHY:

Apparently, we all need much more D3 from the sun and supplements.

Low Vitamin D Status and Suicide: A Case-Control Study of Active Duty Military Service Members

Public Library of Medicine One
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John Umhau, David George, Robert Heaney, Michael Lewis, Robert Ursano, Markus Heilig, Joseph Hibbeln, Melanie Schwandt

KEY POINTS FROM THIS ARTICLE:

1) "Considering that epidemiological studies show that suicide rates in many countries are highest in the spring when vitamin D status is lowest, and that low vitamin D status can affect brain function, we sought to evaluate if a low level of 25-hydroxyvitamin D [25(OH)D] could be a predisposing factor for suicide."

2) "This is the first study to examine the relationship between vitamin D status and suicide risk."

3) Vitamin D {25(OH)D} levels were measured in serum samples drawn within 24 months of the suicide. Each verified suicide case (n = 495) was matched to a control (n = 495) by rank, age and sex.

4) "More than 30% of all subjects had 25(OH)D values below 20 ng/mL."

5) "Risk estimates indicated that subjects in the lowest octile of season-adjusted 25(OH)D (<15.5 ng/mL) had the highest risk of suicide, with subjects in the subsequent higher octiles showing approximately the same level of decreased risk [by about 51%]"

6) "Low vitamin D status is common in active duty service members. The lowest 25(OH)D levels are associated with an increased risk for suicide."

7) "Among the United States military, suicide has become a critical issue. The increased risk of suicide in areas with less sun exposure, and during the spring when 25-hydroxyvitamin D [25(OH)D] levels are at their lowest, suggests that some seasonally determined factor could increase the risk for suicide."

8) More than 90% of vitamin D is produced by the effect of sunlight.

9) "25(OH)D is 1-α-hydroxylated in the brain and other tissues [primarily the kidney] to produce an active form, 1,25-dihydroxyvitamin D, which serves as the ligand for vitamin D receptors found in both the cell membrane and nucleus."

10) Optimal brain function might require a threshold level of 25(OH)D.

11) Vitamin D influences brain function. "Transcription of more than 1,000 genes is known to be under the control of vitamin D, potentially contributing to neurotrophic and neuroprotective effects which could influence suicidal behavior. These transcriptional effects are mediated by nuclear vitamin D receptors (VDR) found in many areas of the brain."

12) These variables were found not to be a significant suicide risk:

- Experiences during deployment (i.e., danger of being killed, witnessing death, or engaged in direct combat)
- Feeling detached
- Feeling down
- Feeling depressed
- Having thoughts about hurting oneself
- Feeling loss of control
- Experiencing nightmares
- Being constantly on guard
- Intention to seek help for mental health related problems
- Receiving a referral for mental health treatment

13) "We found that the risk for suicide was increased in the lowest octile of 25(OH)D levels, all the members of which had seasonally adjusted levels of 25(OH)D below 20 ng/mL."

14) "Vitamin D deficiency is often defined as a level of 25(OH)D below 20 ng/ml, a level not always associated with clinically evident symptoms, but rather with histological evidence of osteomalacia."

15) "Our finding that more than 30% of active duty personnel had 25(OH)D levels below 20 ng/ml is cause for concern."

16) Low vitamin D status has been associated with reduced cognitive performance, psychotic-like symptoms, and the subsequent development of depression. Depressive illness is a major risk factor for suicide.

17) Vitamin D deficiency may increase brain inflammatory cytokines, which can reduce serotonergic activity, and which have been associated with suicide.

18) "Military service requirements for protective clothing and night time operations may reduce the opportunity for normal sunlight exposure."

19) "In a recent study, 25(OH)D levels fell in new recruits after eight weeks of combat training in South Carolina, even though it was summer."

20) This study shows that many military service members have inadequate levels of 25(OH) D levels.

21) Eliminating vitamin D deficiency in the military may reduce stress fractures and might also have the additional benefit of reducing the risk of suicide.

22) "Studies are urgently needed to develop an appropriate strategy to insure that service members do not suffer ill effects from a preventable deficiency of vitamin D."

23) "Our findings are observational in character, and hence do not establish a causal role for vitamin D deficiency and suicide. It is possible that sunlight may exert beneficial effects that are independent of vitamin D, as suggested by the fact that light therapy can reduce suicidal ideation in patients with seasonal affective disorder."