



DOSE YOUR D3

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Dr. Miller started practice in Internal Medicine in 1985, then went on to become board certified in Diagnostic and Interventional Radiology. He left his hospital-based practice in 1995 and started a private office practice of Integrative Medicine. His practice is based on preventing disease by encouraging health, and when problems do arise, treating the root of the problem to bring a cure.

Vitamin D3 supplements are recommended for most of his clients, and Dr. Miller has been amazed how rare colds and flu have been in his office practice for the last 12 years since he began suggesting Vitamin D3 supplements.

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CHAPTER ONE

Vitamin D3 Can Protect You From Flu and the COVID-19 Virus

Maintaining an elevated Vitamin D3 blood level is one of the most effective things you can do to protect yourself from infection from the flu virus or the current coronavirus. In this age of the COVID-19 pandemic, one would think that doctors and public health officials would be screaming from the rooftops about the usefulness of everyone doing whatever it takes to keep their Vitamin D status at an optimal level. For most people, all this means is regularly taking a supplement. In the time of the current COVID-19 pandemic, we recommend taking Vitamin D3 supplements year-round.

A compelling body of evidence demonstrates the safety and effectiveness of D3 supplementation as a means to increase immunity against colds, flu, and even novel viruses like the COVID-19 virus. This short paper will discuss peer-reviewed literature, dosing recommendations, and safety data on Vitamin D3 supplementation, and provide a short discussion of the biology of Vitamin D3 in human beings.

Vitamin D3 is cheap, easy to use, safe, and it works. Even if you already take adequate Vitamin D3, this short paper provides valuable background and useful recommendations.

When considering a treatment, doctors are always balancing the risks versus the benefits. When few or no treatments are available, and there is a treatment that is less than 100% proven, but which has zero risk, then it is prudent to use that treatment.

CHAPTER TWO

The Science That Shows the Connection Between Vitamin D3 Deficiency and Epidemic Viruses Like Flu And Coronavirus

The material in this chapter summarizes material from several articles published in respected peer-reviewed medical journals. If you would like to read the full text of these articles, we include links to all of them in APPENDIX-A. They can also be found on OrganicMD.com, just search for "Vitamin D3".

Much of the research discussed in this paper concerns study of the behavior of the influenza virus. This research is very relevant for the current coronavirus pandemic. The influenza virus and the coronavirus are different viruses, but the way that human beings respond to these two viruses (which enter our bodies through mucosal surfaces) is similar. Therefore, what we have learned about increasing human resistance to the influenza virus also likely applies to the coronavirus.

A 2008 study published in Virology Journal¹ is our starting point. Epidemiologists have noted for decades that the influenza virus does not obey the textbook rules for an infectious disease. Some of the behaviors that epidemiologists and virologists have struggled to explain include:

- Why is influenza both seasonal and ubiquitous, and where is the virus between epidemics?
- Why are the epidemics so explosive?
- Why do they end so abruptly?
- What explains the frequent coincidental timing of epidemics in countries of similar latitude?
- Why does experimental inoculation of non-vaccinated and

¹ Virology Journal 2008, 5:29

non-immune humans fail to cause illness in all volunteers?

- Why has influenza mortality in the elderly not declined as their vaccination rates have increased?

Recent discoveries indicate that our immune cells have receptors for Vitamin D3 and that Vitamin D3 serves to upregulate the increase the natural ability of these cells to fight infection and kill invading viruses. These newly understood functions that Vitamin D3 serve to significantly improve our immunity suggest that the incongruities described above may be secondary to the epidemiology of Vitamin D deficiency.

Vitamin D is actually a hormone, and most tissues in the human body have receptors for Vitamin D. The major circulating form of Vitamin D in the blood is 25-hydroxyVitamin D, which is an inactive form. To convert this form to the active form, 1,25 dihydroxy Vitamin D, for the most part, requires sunlight.

"The physiological basis of the protective effect of Vitamin D lies in its ability to stimulate innate immunity and to moderate inflammation. The active form of Vitamin D, 1,25-dihydroxy Vitamin D stimulates the genetic expression of antimicrobial peptides in human monocytes, neutrophils, and epithelial cells."²

This hypothesis that vitamin D3 deficiency makes us more prone to infections from epidemic viruses has not been proven, but this hypothesis does address some of the difficult questions about why the annual influenza epidemics are so seasonal, and why the affected populations live mostly in latitudes above 20 degrees. The hypothesis about the connection between Vitamin D3 deficiency and the epidemiologic patterns of influenza in communities has been tested and confirmed in some interesting studies. In one

² Epidemic Influenza and Vitamin D, Epidemiology and Infection, October 2007, Vol.135, No.7, pp.1095-1098

type of study, researchers look at a population of people living in the same geographic area (population studies). Researchers look at thousands of people living in the same city over the course of the flu season. They look at everyone's Vitamin D status using a simple blood test, and correlate Vitamin D status with the likelihood of getting the flu. Again, the results are clear. People with a mid to high range of Vitamin D in their blood don't get the flu or colds. People with a low or low normal level of Vitamin D in their blood are those who get colds and flu.³

Conclusion:

You need high blood levels of D3 to protect you from viruses. You're not going to get D3 from the food you normally eat, and you're not going to receive adequate sun exposure in the winter months to make sufficient Vitamin D3. We'll discuss just a bit more about why you cannot get adequate Vitamin D3 from sunlight in the next section, and then we will discuss the recommended dose of Vitamin D3 to take.

So, Dose your D3. Taking supplemental Vitamin D3 in adequate amounts on a regular basis is the only way to ensure that you have an adequate blood level of D3. Period.

³ Multiple references. Please see APPENDIX-A

CHAPTER THREE

Sunlight does Not Make Enough Vitamin D3

The chemistry that allows human beings to make Vitamin D3 requires sunlight. Not just sunlight, but the ultraviolet radiation from bright sunlight. In the winter when the sun is lower in the sky, virtually all of the ultraviolet radiation needed to allow us to make Vitamin D3 is absorbed by the atmosphere.⁴ Bottom line: if you live above latitude 20 in the northern or southern hemispheres, you could stand outdoors all day in the sun and you might not make sufficient—or even any—Vitamin D. Moreover, Vitamin D is not found in significant amounts in any of the foods we routinely eat, and the Vitamin D that is used to fortify some foods is in the form of Vitamin D2.⁵ Vitamin D2 also requires sunlight to transform it into Vitamin D3. No sunlight, no synthesis or conversion, and large populations of people who live above latitude 20 degrees end up deficient in Vitamin D. So please, Dose your D3. During the current COVID-19 pandemic, we recommend taking Vitamin D3 supplements year-round.

⁴ **The seasonality of pandemic and non-pandemic influenzas: the roles of solar radiation and vitamin D,**
<https://doi.org/10.1016/j.ijid.2010.09.002>

⁵ Much of the fear that many doctors have about taking larger doses of Vitamin D comes from the collective memory of all of the harm that was done when foods were first fortified with Vitamin D2. The amount originally added to foods in the 1950's was too high, and many children were poisoned. Vitamin D2 can be toxic, but it is almost impossible to overdose on Vitamin D3.

DOSING:

CHAPTER FOUR-Part A

Dosing of Vitamin D3 Supplements

We recommend using supplemental Vitamin D3 at higher doses than some doctors recommend. An article entitled *Vitamin D Deficiency* from the **New England Journal of Medicine**⁶ in 2007 includes an excellent chart about dosing.

In general, we find that all human beings over the age of one-year-old require about 10,000 IU (international units) of Vitamin D3 per day on average to maintain a therapeutic blood level. It's "on average," because since Vitamin D3 is partially fat-soluble, it does not run through the body the way that Vitamin C or the B Vitamins do. If the recommended dose of Vitamin D3 is 10,000 IU per day, and you take 70,000 IU once a week all at the same time, we find that this works to maintain a healthy blood level. Divide up this recommended dose of 70,000 IU per week in whatever manner works for you. (Note: Most multivitamins contain only 400 IU of Vitamin D, and it is often D2, when what you want, again, is Vitamin D3.)

If you have not been taking any Vitamin D3 supplementation, we recommend taking 50,000 units per day for three days in a row as a loading dose, and then take 70,000 units per week to maintain a therapeutic blood level.

We encourage regular dosing of Vitamin D3, at least during the winter months. If you discover that you are low in Vitamin D3 from a blood test, please do not make the mistake many make when they take Vitamin D3 supplements for a week to get their level up, and then forget about taking them. A couple of months later they get re-tested, and once

⁶ Holick(MF.((Vitamin(D(deficiency.(N(Engl(J(Med.(2007,(357(3):266581

again find that their levels are low. We are low in the winter because we need Vitamin D3 supplements, so please do take them.

The dosage for Vitamin D3 is not guesswork. There is an inexpensive and simple blood test that can be used to monitor your own serum Vitamin D3 level if you are concerned that you're taking too little or too much. We recommend getting tested at first to find the dose you need to maintain a serum level that is in the high normal reference range as reported by your laboratory.⁷ For instance, in the lab we use, the reference range is 30 to 100 nmol/ml. We aim to have our clients have a value of 80, not 36, even though both of these would be considered normal for this lab.

Also, please note that the "Reference Level" for a Vitamin D3 test (and every other lab test) is not an ideal level, but simply the average level for patients of similar gender in your community. Since research shows that much of the population in the United States is chronically low in Vitamin D, reference levels for most labs are skewed low. And remember, even if you are a bit over the upper limit, you are still in a safe zone.

A dose of 10,000 units per day over the entire year is safe. There are many articles that confirm this. See the footnote below for two of them.⁸

Single nucleotide polymorphisms (SNPs) in the Vitamin D binding protein (DBP)⁹, as well as in enzymes related to activation or degradation of Vitamin D and its metabolites,

⁷ The test you want is for Vitamin D3 (1-25 dihydroxy Vitamin D) rather than the test for Vitamin D2 (25 hydroxy Vitamin D). Vitamin D3 is the active form, and the form you are needing in the winter months, and it is the status of Vitamin D3 in your blood that you want to monitor.

⁸ Vieth R. Why the optimal requirement for Vitamin D3 is probably much higher than what is officially recommended for adults. *J Steroid Biochem Mol Biol* 2004; 89-90:575-9.

Markestad T, Halvorsen S, Halvorsen KS, Aksnes L, Aarskog D. Plasma concentrations of Vitamin D metabolites before and during treatment of Vitamin D deficiency rickets in children. *Acta Padiatr Scand* 1984;73:225-31.

⁹ *European Journal of Endocrinology* (2013) 169 559–567

are as important for serum 25(OH)D levels as the effects of season. If you have one of the common genetic polymorphisms that can affect your body's handling of Vitamin D3, you may need to take much higher doses to maintain a healthy blood level. If so, do indeed take higher doses, and use lab testing to figure out what dose you need on a regular basis to keep your blood level up.

CHAPTER FOUR-Part B

Dosing for Children

While children are obviously smaller than adults, their actively growing bodies and higher metabolisms actually require proportionately more Vitamin D3 than adults. For children over the age of one, the recommended dose is almost the same as for an adult.

To be safe, if children over one year have not been taking Vitamin D3 supplements, start them with a loading dose of 50,000 units on the first day, then 5,000 IU per day (35,000 IU per week) as a maintenance dose for children under 10 years. For children over 10 years, take 10,000 IU per day (70,000 to 75,000 IU per week), which is an adult dose.

For children under one year, 1,000 to 2,000 IU per day of Vitamin D3 is recommended, and has been shown by multiple studies to be safe.

The above dosing recommendations come from the article *Vitamin D Deficiency* in the **New England Journal of Medicine**.¹⁰ See this reference for more information, including the many references that document the safety of these recommendations.

¹⁰Holick(MF.((Vitamin(D(deficiency.(N(Engl(J(Med.(2007,(357(3):266581. The reference can be found at organicmd.com

CHAPTER FIVE

The Biology of Vitamin D3 in Human Beings

Next, we'll discuss a bit about the biology of Vitamin D and why you need to use supplements that contain only Vitamin D3, and not Vitamin D2.

This section will be kept short. You can find some nice graphics and descriptions of how the human body processes Vitamin D in the New England Journal of Medicine article "Vitamin D Deficiency."¹¹

The take-away lesson for this section is that the active form of Vitamin D is Vitamin D3, and that is the form you need to take it in if you are taking a Vitamin D supplement. Doctors prescribe Vitamin D2 which, but it can be toxic and needs to be converted to the active form of Vitamin D3 by sunlight. Lack of sunlight exposure, especially in the winter, is the cause of the rampant Vitamin D deficiency we see in all age groups, so taking Vitamin D2 does not really help.

As mentioned earlier, the body needs sunlight to make Vitamin D3 from cholesterol. Not just sunlight, but sunlight containing adequate amounts of ultraviolet rays. Most people, even when they are in good sunlight, are covered with hats, clothing and sunscreen, all of which block ultraviolet rays. Smog and air-pollution also block the ultraviolet rays. If you have dark skin because your ancestors came from more southerly places, then your skin naturally blocks a good deal of the sun's ultraviolet rays. Finally, if you live in the middle or upper latitudes, above latitude 20 degrees, then during the winter months the sun is lower in the sky so sunlight travels through more atmosphere, thus blocking ultraviolet rays.

¹¹ N Engl J Med 2007;357:266-81. Text and some of the graphics from this article can be found at organicmd.com

The active form of Vitamin D, Vitamin D3, is partially water soluble, and the dosing discussion reviews some research that showing that daily dosing with large amounts of Vitamin D3 is quite safe.

Vitamin D3 provides many health benefits, such as decreasing the risk of many chronic illnesses, including many common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease.

"The physiological basis of the protective effect of Vitamin D lies in its ability to stimulate innate immunity and to moderate inflammation. The active form of Vitamin D, 1,25-dihydroxy Vitamin D stimulates the genetic expression of antimicrobial peptides in human monocytes, neutrophils, and epithelial cells."¹²

CHAPTER SIX

Vitamin D3 Is Very Safe

The current recommendations for supplementation are almost all for Vitamin D3.

NOTE: Prescription Vitamin D2 products like Vitamin D2 (ergocalciferol), in a 50,000 IU/capsule, and Drisdol (Vitamin D2) liquid supplements, are not recommended by us.

¹² RE: Epidemic Influenza and Vitamin D, Epidemiology and Infection, October 2007, Vol. 135, No. 7, pp. 1095-1098

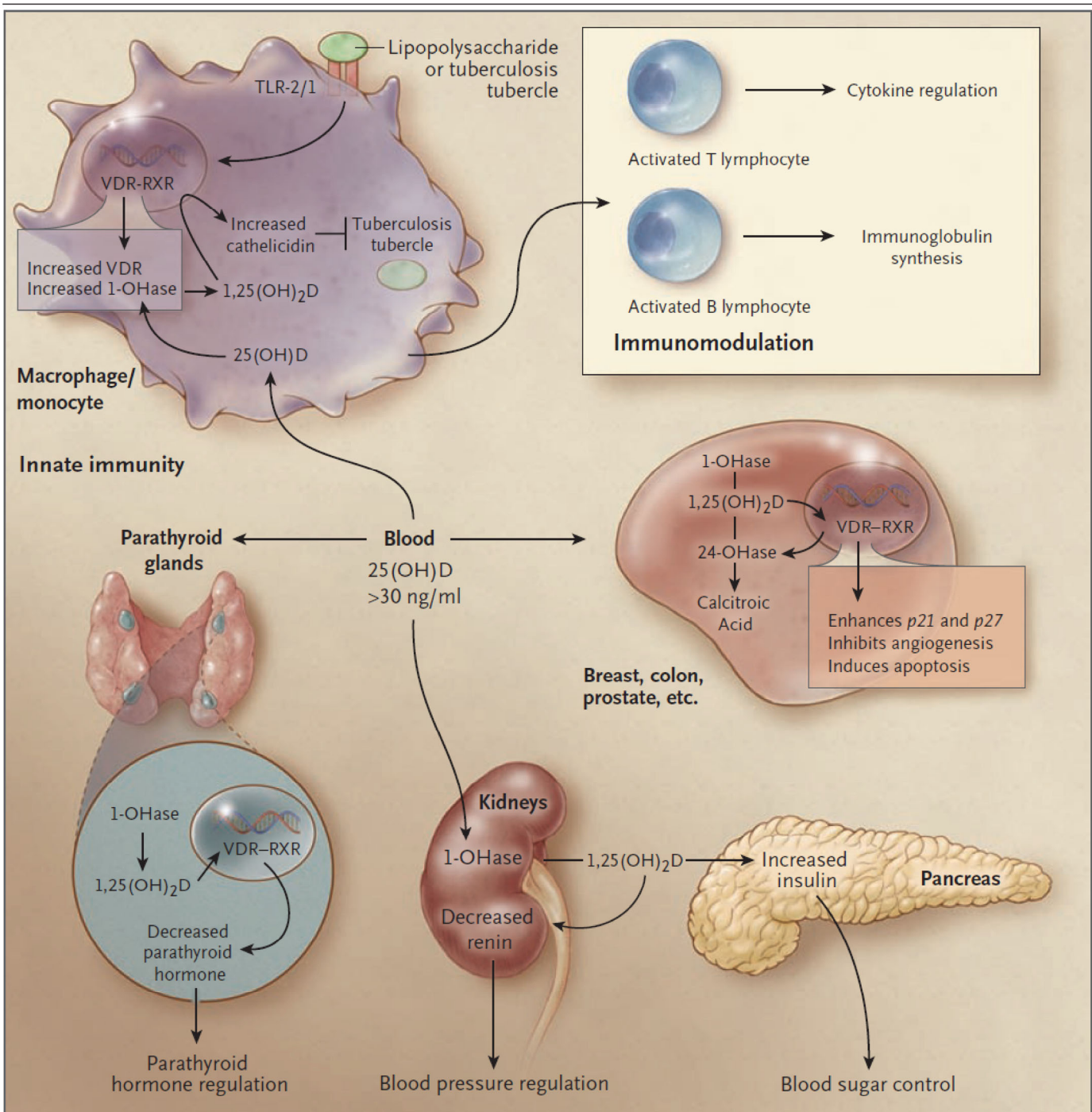


Figure 2. Metabolism of 25-Hydroxyvitamin D to 1,25-Dihydroxyvitamin D for Nonskeletal Functions.

When a macrophage or monocyte is stimulated through its toll-like receptor 2/1 (TLR2/1) by an infectious agent such as *Mycobacterium tuberculosis* or its lipopolysaccharide, the signal up-regulates the expression of vitamin D receptor (VDR) and 25-hydroxyvitamin D-1 α -hydroxylase (1-OHase). A 25-hydroxyvitamin D [25(OH)D] level of 30 ng per milliliter (75 nmol per liter) or higher provides adequate substrate for 1-OHase to convert 25(OH)D to its active form, 1,25 dihydroxyvitamin D [1,25(OH)₂D]. 1,25(OH)₂D travels to the nucleus, where it increases the expression of cathelicidin, a peptide capable of promoting innate immunity and inducing the destruction of infectious agents such as *M. tuberculosis*. It is also likely that the 1,25(OH)₂D produced in monocytes or macrophages is released to act locally on activated T lymphocytes, which regulate cytokine synthesis, and activated B lymphocytes, which regulate immunoglobulin synthesis. When the 25(OH)D level is approximately 30 ng per milliliter, the risk of many common cancers is reduced. It is believed that the local production of 1,25(OH)₂D in the breast, colon, prostate, and other tissues regulates a variety of genes that control proliferation, including *p21* and *p27*, as well as genes that inhibit angiogenesis and induce differentiation and apoptosis. Once 1,25(OH)₂D completes the task of maintaining normal cellular proliferation and differentiation, it induces expression of the enzyme 25-hydroxyvitamin D-24-hydroxylase (24-OHase), which enhances the catabolism of 1,25(OH)₂D to the biologically inert calcitroic acid. Thus, locally produced 1,25(OH)₂D does not enter the circulation and has no influence on calcium metabolism. The parathyroid glands have 1-OHase activity, and the local production of 1,25(OH)₂D inhibits the expression and synthesis of parathyroid hormone. The 1,25(OH)₂D produced in the kidney enters the circulation and can down-regulate renin production in the kidney and stimulate insulin secretion in the beta islet cells of the pancreas.

CHAPTER SEVEN

Dose Your D3, Please

Maintaining an elevated Vitamin D3 blood level is one of the most effective things you can do to protect yourself from infection from the flu virus or the current coronavirus. A compelling body of evidence demonstrates the safety and effectiveness of D3 supplementation as a means to increase immunity against colds, flu, and even novel viruses like the COVID-19 virus.

Vitamin D3 supplements are inexpensive, very safe, and widely available without a prescription. 10,000 IU per day on average is a sufficient dose for most people. Their value in helping human beings defend against viral infection is proven. No one disputes these facts.

If you already take adequate Vitamin D3, please keep dosing yourself.

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Summary:

- There are irregularities in how influenza and other epidemic viruses like the current COVID-19 pandemic virus behave, when compared with the textbook behavior expected of infectious diseases.
- The hypothesis that these irregularities are due to Vitamin D3 deficiency does not prove but does offer a good explanation for the seasonality of epidemic viral infections, and the variations in how the epidemics favor certain latitudes.
- Research now shows that Vitamin D3 deficiency is itself epidemic, and studies show a correlation between a person's Vitamin D3 blood level and their vulnerability to getting influenza and other epidemic viruses.
- Research has also recently shown how Vitamin D3 acts to dramatically improve the ability of our immune cells to produce the proteins needed to protect us from and actually kill invading viral cells.
- Sunlight exposure does not work to provide an adequate blood level of Vitamin D3 for people who live above latitude 20 degrees.
- Vitamin D3 is remarkably safe, inexpensive, widely available and taken as a supplement has the potential if used widely to reduce deaths during the current pandemic. Because the recommendation (take a Vitamin D3 supplement at a dose sufficient to maintain a blood level in the mid to upper level) is so safe, the level of proof we have offered is enough to support this recommendation.
- Take Vitamin D3 as a supplement. Dose Your D3 at 10,000IU per day on average for adults and children over the age of one year.
- When getting a blood test to check your Vitamin D3 blood level, make sure you include the test for 1-25 dihydroxy vitamin D, which tests specifically for Vitamin D3.

APPENDIX-A

Links to the References

On The Epidemiology of Influenza (PDF Download):

<https://link.springer.com/article/10.1186/1743-422X-5-29>

Other article that cite this article if you want more data:

https://scholar.google.com/scholar?cites=8418928550997412034&as_sdt=2005&sciodt=0,5&hl=en

Related Articles, if you want more data:

https://scholar.google.com/scholar?q=related:wkiYZ-KKlnQJ:scholar.google.com/&scioq=&hl=en&as_sdt=0,5

Vitamin D Supplementation Does Cut Respiratory Infections, New Study Suggests

<https://www.bmj.com/content/356/bmj.j847.full>

Vitamin D Supplementation to Prevent Acute Respiratory Tract Infections: Systematic Review and Meta-Analysis of Individual Participant Data

<https://www.bmj.com/content/356/bmj.i6583>

Epidemic Influenza and Vitamin D-4621170

https://www.jstor.org/stable/4621170?seq=1#metadata_info_tab_contents

The Seasonality of Pandemic and Non-Pandemic Influenzas: The Roles of Solar Radiation and Vitamin D

<https://www.sciencedirect.com/science/article/pii/S1201971210024975>

Vitamin D for Prevention of Respiratory Tract Infections: A Systematic Review and Meta-Analysis

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3543548/>

Vitamin D Deficiency. (An excellent review article, with good material on the biology of Vitamin D in human beings, causes of Vitamin D deficiency, the dosing chart we used for the recommendations in this paper, and materials and additional references on the safety of using Vitamin D3 supplements on a regular basis over a long period of time.

Holick, MF, N Engl J Med 2007;357:266-81. Text and some of the graphics from this article can be found at organicmd.com

And finally, below is a letter to the editor about this New England Journal of Medicine article:

(november 8, 2007, n engl j med 357;19)

To the Editor:

Holick proposes a minimum target level of 30 ng of 25-hydroxyvitamin D per milliliter in a healthy population. Many of his references cite a high incidence of vitamin D deficiency in at-risk populations. We have been measuring 25-hydroxyvitamin D levels in unselected outpatients in an affluent suburb of sunny South Florida. Data are available for 170 women and 76 men (age range, 18 to 85 years) between 2005 and 2007. A total of 22 women (12.9%) had levels under 15 ng per milliliter, and 110 women (64.7%) had levels under 30 ng per milliliter. Sixteen men (21.1%) had 25-hydroxyvitamin D levels under 15 ng per milliliter, and 50 (65.8%) had levels under 30 ng per milliliter.

The majority of our vitamin D-deficient patients have been treated with 50,000 IU of vitamin D3 weekly for up to 2 years, without clinical evidence of toxicity or hypercalcemia or elevated serum levels.

We believe that 25-hydroxyvitamin D screening should be included in standard screening laboratory batteries, and replacement doses of 50,000 IU weekly are well tolerated for up to 2 years without toxicity.

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