Refresher Course Vitamin D - Post Graduate Level

Reproduced below is an extract taken from:
(with my parenthetical commentary in italics where the need is found to amplify and clarify)

James M. Orten, Otto W. Neuhaus Human Biochemistry, The C. V. Mosby Company – Tenth Edition, 1982. ISBN 0-8016-3730-9

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Relation of radiant energy

"Interesting recent observations suggest that the rate of synthesis of cholecalciferol from 7-dehydrocholesteril in the skin (stratum granulosum) is regulated by the amount of pigmentation and keratinization in the overlying stratum corneum. This regulates the amount of solar ultraviolet radiation, especially at 290 to 320 nm, that penetrates into the stratum granulosum and forms vitamin D. Thus white skin, which contains little pigment and keratin, allows maximal ultraviolet penetration. Yellow skin, which contains more keratin, permits less ultraviolet penetration, whereas black skin, which is more pigmented, permits still less. These differences are apparently a genetic adaptation to climate. Hair or fur in animals is a still further regulatory mechanism. Vitamin D synthesis is thus maintained within physiological limits estimated to be 0.01 to 2.5 mg of cholecalciferol per day. Skin pigmentation also may correct for seasonal variations, e.g., tanning in the summer months in northern latitudes."

(Note: What is noteworthy here is that skin pigmentation, being different in various geographical regions, plays an important role. It is also one of the mechanism in the human body that ensures that excessive exposure to sunlight does not in any way cause vitamin D toxicity. With more exposure to sunlight the skin also begins to tan to a darker shade, thereby regulating the production of vitamin D. Besides this, other feedback loops exist in the body that when coupled with the body's ability to store excess vitamin D for later use, ensures that sunshine does not create any toxicity in the human body).

Occurrence

"Cod liver oil and other fish liver oils are the best natural sources of vitamin D. The edible portions of oily fish, e.g., sardines, salmon, herring, are also excellent sources. Egg yolk and liver of the commonly slaughtered animals contain amounts that depend on the food of the animal from which they are derived, but mammalian liver is not very rich in this vitamin D. Milk contains little vitamin D unless enriched in one of several ways, and vitamin D milk is now a common article or the American dietary. Many ordinary foods, among them the green plants, contain small quantities, and mushrooms contain slightly greater amounts. In general, this vitamin is not widely distributed, but the fact that it can be provided in three ways should make its deficiency rather uncommon, These three ways of providing vitamin D are (1) by furnishing the vitamin as it occurs naturally in foods or by enriching the food by the additions of vitamin D, (2) by irradiating foods containing precursors of the vitamin, and (3) by irradiating the skin of the individual with ultraviolet light or sunshine."

(Note: Different types of eggs will have varying amounts of vitamin D based on the conditions under which the eggs were produced and the way the poultry were fed and bred. For example, hens that were not allowed to roam around and were cooped up in little cages will not have the same amount of vitamin D as their counter parts who were free range and pasture fed hens. Three ways to increase vitamin D include: 1) consuming enriched foods; 2) consuming irradiated foods; and 3) irradiating the skin with ultraviolet rays or by direct exposure to sunshine. A possible fourth way would be by topical applications of creams or gels enriched with therapeutic doses of vitamin D).

Absorption

"Absorption of vitamin D from the intestinal tract requires the presence of bile salts. Here again mineral oil acts as a hindrance because the vitamin is soluble in it and consequently is carried through the intestine into the feces. After absorption, cholecalciferol is apparently transported in the plasma, tightly bound to an α_2-globulin."

(Note: If you have a liver with a poor liver function test (LFT) and borderline liver enzymes, it is most probable that the flow of bile will be less efficient. In addition, if you had your gall bladder removed, suffer from gallstones, or have a partial blockage of gall bladder duct, you will have a poor supply of bile. For efficient absorption of vitamin D, the enzymes (AST, ALT and Gamma GT) in the LFT Test must ideally be maintained in the 15 to 20 U/L range.

Liver insufficiency in terms of poor bile flow into the intestines will itself result in poor levels of serum vitamin D.

There are two other situations which need to be highlighted here that cause vitamin D malabsorption. One is the use of drugs like orlistat which block the digestion and the absorption of fats in the digestive tract and the other is the poor

flow of enzymes especially lipase, from the pancreas. Lipase helps in digestion of fats. In both these situations the absorption of vitamin D is compromised.

The correlation of magnesium and vitamin D is the case of which came first - the chicken or the egg,. Excessive vitamin D causes depletion of magnesium and low magnesium levels in turn cause malabsorption of vitamin D.[1] So monitoring serum and RBC or erythrocyte magnesium levels from time to time while on vitamin D supplementation is highly recommended.

To counteract all the above mentioned situations you will end up taking abnormally large doses of vitamin D to achieve appropriate serum vitamin D levels. It would however be far safer to achieve normal serum vitamin D levels through natural rather than artificial means).

(Serum values of vitamin D are no indication of the total amount of vitamin D stored in the body. When vitamin D levels go very low (say below 10 ng/mL) it is a good indication that the total vitamin D stores in the body has also been depleted. When mega doses of vitamin D (typically 50,000 IUs once a week for six to eight weeks) are administered for a short while to quickly correct this deficiency and the serum levels just start showing sufficiency, it does not mean that the depleted body fat levels of vitamin D have been replenished. It may take additional months of much lower therapeutic doses of vitamin D to correct the deficiency of vitamin D stores. Do not confuse serum levels with total amount of vitamin D stored in the body. Again measuring serum levels of vitamin D are best attempted 7 days after discontinuing the intake of vitamin D. This allows the body to normalize vitamin D serum levels and show more realistic values.

Sunshine is capable of producing large amounts of vitamin D in one hour of skin exposure. (Individuals exposed to excessive sunlight may have concentrations of 25(OH)D up to 370 nmol/L / 150 ng/mL without adverse effects on calcium metabolism)[2]. However, don't be disappointed if after a month or two of regular exposure to sun your serum levels do not show very high levels. The reason for this could be that the vitamin D being produced is being utilized for replenishing depleted vitamin D stores in the body. This is especially true if your vitamin D levels were 10 ng/mL or lower to begin with).

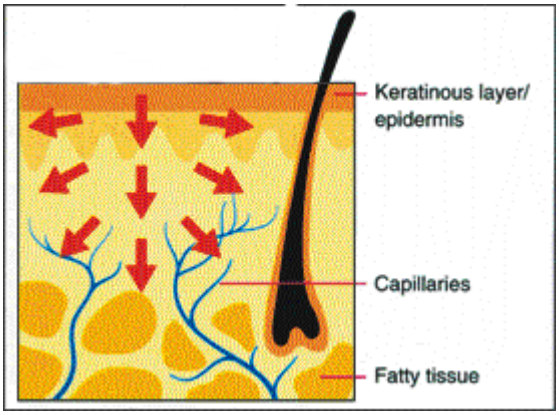
Effects of deficiency

"Another clinical condition indirectly associated with a lack of cholecalciferol is celiac disease, also know as idiopathic steatorrhea, gluten-sensitive enteropathy, and nontropical sprue, discussed later in this chapter. Here, as in osteomalacia, there is an impaired mineralization of the bones, which may result in deformities of dwarfism. Here, too, a low serum calcium and low serum phosphorus are found, with possible manifestations of tetany. Celiac disease is indirectly a vitamin D deficiency because the primary abnormality seems to be, in part, a fatty diarrhea. The fatty acids in the intestinal lumen are not absorbed normally and carry with them into the stools calcium soaps and vitamin D."

(Note: Celiac disease results in poor absorption of vitamin D from the intestines. So again, abnormally large doses of vitamin D may have to be orally administered to achieve satisfactory serum levels. A better option would be go for topical application of vitamin D through a transdermal delivery system or go for ultraviolet irradiation of the skin).

"In all the conditions mentioned the administration of vitamin D in therapeutic doses, or ultraviolet irradiation, or both, produce good result."

(Transdermal method is the preferred method as it does not increase the load on the excretory organs. I will try to further explain the route to transdermal delivery.



Approximately 80% of all nutrition taken orally is excreted from the body. This creates a load on the excretory organs. The effective part retained in the body is approximately only 20%. So when we want to convert oral doses to transdermal ones, we need to only use 20% dose for topical application. If we were to assume a RDA for oral administered vitamin D to be 400 IUs, it means that you only need to apply approximately 80 IUs topically to the body. So if presently your Vitamin D daily dose is 4000 IUs then it would translate to 800 IUs topically or most probably much lower, since you may be have started off with malabsorption issues to begin with. This is a strong possibility in view of having to take such large doses [4,000 to 8,000 IUs] orally.

So the question arises how do we go the transdermal route?).

(1 teaspoon of cod liver oil can have approximately 400 to 1,000 IUs of Vitamin D. Apply one teaspoon of cod liver oil topically at late evening or before going to bed but after a bath. If you don't like the smell of cod liver oil, add a drop or two of aromatherapy oils like lavender, geranium, jasmine, etc. Apply to your legs, thighs or arms. Rotate the area of application each day. Oil typically gets absorbed within 15 to 20 minutes and does not get messy. Leave on overnight and you will be able to get past any malabsorption problem and put in enough vitamin D to get your levels above 30 ng/mL or 40 ng/mL, what ever you choose, so long as this level does not cause your magnesium levels to go below an optimum level of 2.4 mg/dL / 1.0 mmol/L (serum) and 6.0 mg/dL / 2.5 mmol/L for

RBC or erythrocyte (intracellular) magnesium. At these levels of magnesium, the risk of osteoporotic fractures is minimized mainly due to increased bone flexibility. Remember bone flexibility is more important than bone density.

The second route to get therapeutic transdermal vitamin D is to use a specially formulated vitamin D gel containing 4,000 IUs of Vitamin D per gram of gel. Applying a pea size quantity (0.25 g) will result in 1,000 IUs topically into the body. This is equivalent to an oral dose of 5,000 IUs. The beauty of a transdermal dose of vitamin D is that it does not cause any spikes of serum vitamin D levels through out the day and is gradually delivered into the blood stream over a 24 hours period. One application after a bath in the morning will help to maintain your vitamin D levels in a very steady manner and allow its proper storage in the body fat for use months later when sunshine is inadequate, as in winter).

Mechanism of action

"Vitamin D has a regulatory influence on calcium and phosphorus metabolism. Both calcium and phosphorus must be present in the diet to have the complex calcium salt deposited in bone. However, no matter how great an amount of these minerals is available, normal calcification does not take place in the absence of this vitamin. On the other hand, even if the supply of calcium and phosphorus is practically at starvation levels, an optimum amount of cholecalciferol can enable them to be utilized and deposited in a nearly normal manner."

"In the first place, vitamin D causes an increased absorption of calcium and phosphorus from the intestinal tract. In studies on the transfer of ^{45}Ca across the membrane of everted segments of small intestine of rats, vitamin D greatly increased the rate of passage of ^{45} Ca across the intestinal mucosa. There was an active transport (i.e., against a concentration gradient) in the proximal portion of the small intestine that was dependent on the energy of oxidative metabolism. Vitamin D also increased the rate of facilitated transfer of calcium along the entire length of the small intestine. Using the same technique, investigators have found that ergocalciferol likewise increases the absorption of phosphate."

(Note: *High levels of Vitamin D and excessive intake of vitamin D over a prolonged period is known to cause depletion of magnesium levels in the body.*[1] *Magnesium is very important for the treatment of numerous chronic diseases such as osteoporosis, high blood pressure and type 2 diabetes. Again, adequate levels of magnesium are required in the body to aid proper absorption of vitamin D. So it is a never-ending downward spiral in which the body can go into, if proper evaluation of RBC / Erythrocyte and serum magnesium levels are not done periodically, when taking vitamin D supplementation. Again, if you are on magnesium supplementation, discontinue magnesium for 7 days before drawing a blood sample to ensure that the serum levels have returned to normal and show the true retained values.*

Human requirements

"The vitamin D requirements of normal infants and children are especially important and depend partly on the amount of ultraviolet light to which they are exposed. Remember that the effective ultraviolet rays do not penetrate ordinary glass. Therefore exposure to sunshine coming through window glass is of little value. Smoke also impedes the penetration of these rays, and consequently city sunshine is not always beneficial. For this and other reasons some vitamin D should be included in the food of younger individuals. The Food and Nutrition Board (1980; Table 21-4) recommends 10 ug / 400 IUs of cholecalciferol daily for infants, children, and young adults up to the age of 19 years. The same amount is advised for women during pregnancy and lactation. The 1980 RDA for both males and females, ages 19 to 22 years, is 7.5 ug cholecalciferol per day (table 21-4). Therefore the RDA is 5 ug cholecalcigerol per day for both sexes, The minimal requirement for vitamin D is difficult to determine because of the variability of environmental factors such as sunshine. However, the RDA provides an adequate margin of safety over a minimal value. Ten ug of pure crystalline vitamin D_3 is equivalent to the biological activity of 400 IU formerly used."

(Note: The author supports a RDA not, exceeding 10 μg / 400 IUs of vitamin D for most adults when administered orally. Recent studies have shown that 600 IUs to 800 IIUs could be used for a period of one year to safely remove a state of deficiency). [3]

Toxic effects

"After administration of an excess of vitamin D to a mammal the vitamin can be found in the circulating blood for months. Thus the use of enormous doses of vitamin D is not without danger. Severe and even fatal effects have been noted. The toxic manifestations caused by excess dosage include nausea, anorexia, weakness, headache, digestive disturbances, and polyuria. Irreversible damage to the kidneys, as well as calcification of other soft tissues, results. The threshold of toxicity seems to be about 500 to 600 ug cholecalciferol per kilogram of the body weight per day. Such doses are not ordinarily employed."

"The reason for the toxicity of vitamin D is the difficulty of excretion of this vitamin rather than its storage in the liver. Any excretion is gradual, by way of the bile. Excess cholecalciferol injected into animal remains in the circulation for several months. In contrast, the water-soluble vitamins, if given in excess, are excreted promptly in the urine and are therefore relatively nontoxic."

(*Note: What we need to understand here is that serum vitamin D tests are incapable of measuring vitamin D stores in the human body. They only measure the vitamin D in circulation in the blood. Since vitamin D is stored in the liver and also in the fat of the body, it means that if you were to indeed have sufficient exposure to sunlight in spring, summer and fall, you could technically have some reserves left over for winter when sunshine may be scarce in some parts of the world.)*

(Since there is no further evolution of the human body during the last 100 years, the standards of vitamin D toxicology have not changed during this period. The serum ranges and doses given in standard medical textbooks like Harrison's Principles of Internal Medicine therefore need to be adhered to.[2] Here they have defined the upper safe serum upper limit of 80 ng/dL.

Again supplements as the word indicates are to be used to supplement natural sources of vitamin D like adequate sunshine and diet and should not to be used as drugs for life. This will ensure minimum risk of overdose and accidental toxicity.)

References:

1. Seelig MS, Magnesium deficiency with phosphate and vitamin D excess: Role in pediatric cardiovascular nutrition. Cardio Med *3(1978), 637-650*"

2. Harrison's Principles of Internal Medicine 12th Edition. 1991.

3. Gallagher JC, Sai A, Templin T 2nd, Smith L., Dose response to vitamin D supplementation in postmenopausal women: a randomized trial. Ann Intern Med. 2012 Mar 20;156(6):425-37. Erratum: Ann Intern Med. 2012 May 1;156(9):672. PMID: 22431675