Nutrition *News and Views*

July/August 2012 **Vol.16, No.4** **For health professionals**

VITAMIN D – THE KNOWN AND (AS YET) UNKNOWN

By Judith A DeCava, CNC, LNC

Vitamin D is a hot news item. It's previously under-recognized importance to health is being revealed in an explosion of research reports. Plus we are told that most people have inadequate or deficient levels. Vitamin D supplements are current superstars. But there is much more to the story than the headlines.

It has long been known that vitamin D is made in your skin when you're exposed to sunlight, but it was only in the 1970s that understanding increased regarding its complexity and bodily journey. The form made by your skin is inactive; it must undergo changes. First it goes to your liver to get hydroxylated—modified into 25(OH)D, the major circulating form—which is also inactive. The 25(OH)D then goes to your kidneys where it is modified again into its active form, 1,25(OH)2D. It's this active form that 'tells' your intestines to absorb calcium more efficiently, for example, to make sure there's enough calcium in your blood and for your bones. All participants in this journey must be in good working order—skin, liver, kidneys—or you won't be able to activate vitamin D. Eventually it was realized that vitamin D is needed for much **more** than regulation of calcium and bone health. It was also learned that, though the kidneys are the major activators of vitamin D, the prostate, breast, colon, and other tissues in the body were capable of activating it. It is now known that **every** tissue and cell in your body has a vitamin D receptor, indicating that every tissue and cell has some use for vitamin D. The sun's ultraviolet B waves act on a cholesterol derivative in the skin to induce the formation of cholecalciferol, vitamin **D_3**. Vertebrate animals, fatty salt-water fish, and eggs make D_3 too. Certain plants (mushrooms, some algae, bacteria, diatoms) and crustaceans, when exposed to sunlight, produce ergocalciferol, vitamin **D_2**. Both of these natural forms of D_3 and D_2 can be absorbed and converted into 25(OH)D. Also, vitamin D made by your body is not truly a vitamin. It's a **hormone**. By definition, a hormone is made in one organ, goes into the blood and has an effect on another organ system. In the case of vitamin D, the skin makes the pro-hormone which gets into the bloodstream, goes to the liver and kidneys to get activated, then acts on specific receptors on cells. Production is increased or decreased in response to the body's needs. That's a hormone. Vitamin D is stored in body fat as 25(OH)D (inactive form) which is also the circulating form with a long half-life. [1]

DEFICIENCY. The publicity surrounding vitamin D includes warnings that most everyone is deficient. One study found the amount of vitamin D in people's blood serum was lower in 2000-2004 than in 1988-1994. But changes in the way vitamin D levels are measured "accounted for much of the difference." Data from the National Health and Nutrition Examination Survey from 2001-2008 found that 24% of adults and children were "at risk of inadequacy"—defined by the Institute of Medicine (IOM) as 30-49 nmol/L. Only 8% of North Americans were found to be actually "deficient" (less than 30 nmol/L). The IOM reviewed nearly 100 studies. According to their report, the majority of people in the US and Canada are getting enough vitamin D. Yet **many** studies have concluded that the prevalence of low vitamin D is "epidemic." Confusion reigns.

Part of the confusion is due to a lack of agreement on how to define adequate, inadequate or deficient blood serum levels. Some scientists advocate higher levels as thresholds for deficiency than do others. Some laboratories use reference values above 30 nmol/L as the cut off point for adequacy; others use lower values. There's "wide variability in the assay [analysis]—values can be off by 15% to 20%." There's an "urgent need" to standardize the assay and develop a **consensus** for reference values. Plus, sun exposure and dietary intake aren't always reflected in serum levels. Another question is what form of vitamin D to measure. Dr Michael Holick, a vitamin D researcher, says to measure 25(OH)D, **not** the active form—1,25(OH)2D. (The active form is normal or elevated with vitamin D deficiency because, as you become deficient, production of parathyroid hormone increases, telling your kidneys to activate vitamin D. Blood levels increase but target tissues may still not be getting enough.) The **active** form circulates at 1000 times less concentration than 25(OH)D. The active form has a half life in circulation of 2 to 4 hours; 25(OH)D has a half life of 2 to 3 weeks. Although 25(OH)D may be the best test at this time, it's **not** a reliable indicator of vitamin D status (except at extreme toxicity or severe deficiency). That's because, explains Alan Gaby, MD, 25(OH)D is "just one of more than 50 vitamin D metabolites in the body, and an individual's vitamin D nutritional status might be a function of complex interactions between various vitamin D metabolites." Individuals may have different 25(OH)D "set points." And,

since serum 25(OH)D levels decline when there is inflammation, it may not be a reliable indicator of vitamin D status in people who are experiencing inflammation. Elevation of serum parathyroid hormone may suggest vitamin D deficiency, but an overactive parathyroid gland for other unrelated reasons can also be the reason.

Many labs have increased their reference range for serum 25(OH)D; thus many more people are now told they have vitamin D deficiency. The increases were based on associations between 25(OH)D, indicators of vitamin D status such as serum parathyroid hormone levels, and percent absorption of an oral calcium load. The validity of using such indicators to assess vitamin D status has been called into question. The 25-hydroxylation of vitamin D takes place primarily in the liver, but there's evidence that it also occurs in other tissues including the testes and ovaries. Liver enzymes that hydroxylate vitamin D are also involved in phase 1 detoxification pathways. So an 25(OH)D level may indicate gonadal function or the liver's ability to detoxify xenobiotics. Widespread 25(OH)D testing without specific symptoms of deficiency "is unhelpful" and may not be accurate. [2]

BENEFITS. Vitamin D's well-known function is in **calcium** metabolism. For example, it's needed to prevent rickets, a disease affecting children causing abnormal bone structure and strength due to inadequate cartilage and bone mineralization. Vitamin D helps maintain bone mineral density and strength, prevent and treat osteoporosis, reduce incidence of stress fractures, and preserve muscle strength and physical function. Musculoskeletal weakness and pain, bone disease, and gait abnormalities are aided by vitamin D. It's now being learned that vitamin D's importance is far more **extensive**, that it participates in numerous bodily processes and functions, and impacts a vast array of systems beyond the musculoskeletal system including: the heart and blood vessels, pancreas, skin, hair, hearing, respiratory tract, eyes, cell formation and longevity, digestion and nutrient absorption, carbohydrate and fat metabolism, aging processes, immune function, sleep patterns, reproductive organs, pregnancy, athletic performance, moods, and more.

Deficiencies have been found in people with cardiovascular disorders (heart disease, stroke, peripheral artery disease, hypertension); immune and inflammatory reactions (colds, flu, asthma, pneumonia, other respiratory conditions, lupus, fibromyalgia, psoriasis, rheumatoid arthritis, tuberculosis, and more); many types of cancer (breast, ovary, prostate, esophageal, pancreatic, oropharyngeal, gastric, colon, lymphoma); brain and nervous system ills (Alzheimer's, Parkinson's, depression, poor cognition, autism, seizures, multiple sclerosis); eczema; kidney disease; hormonal imbalances; endometriosis; polycystic ovary syndrome; Crohn's disease; metabolic conditions (insulin resistance, high blood sugar, diabetes types 1 and 2); cavities; periodontal disease; hearing loss; eye diseases; infertility; preeclampsia; fetal risks (nervous and musculoskeletal systems); sudden infant death syndrome; food allergies; non-alcoholic fatty liver disease; migraines; septicemia; increased risk of death; and more. So is vitamin D a cure-all? It's not known yet. A deficiency is found in many diseases and conditions, but the **question** is whether the deficit contributes to these problems or whether the problems contribute to a vitamin D deficiency. Plus the definition of vitamin D deficiency depends on the opinion of the researchers. Most studies have been **epidemiological**—focused on the distribution of a disease or condition among certain populations and attempts to find links to diet, lifestyle, or other factors. Such studies are helpful, but seldom prove cause and effect. Numerous variables come into play. In this case, age, skin color, obesity, health status, season, amount of outdoor activity, location, and diet can make a difference. More randomized **clinical trials** have been called for, but they have problems too. For instance, people can't be kept out of the sun and their vitamin D levels "are hard to control," explains Dr Bruce Hollis. Still, research performed so far indicates a need for vitamin D throughout the body and that we're probably not getting enough. [3]

CAUSES OF DEFICIENCY. The foremost cause of D deficiency is a lack of sufficient exposure to sunlight, specifically ultraviolet-B (UVB) radiation. Other contributors are kidney or liver diseases, severe burns (which destroy the skin's ability to make vitamin D), organ failure, malabsorption syndromes (inflammatory bowel disease, celiac disease, etc.), poor dietary intake, and side-effects from some medications. Pregnant women with inadequate vitamin D have deficient babies. Deficient Moms have little if any vitamin D in their breast milk. When you build up your vitamin D level from sunshine, some is stored in fat cells and released when you need it. If you're overweight, you're prone to deficiency because vitamin D is absorbed into fat cells and then has difficulty getting out. Overweight, particularly obese, people have lower circulating levels of vitamin D, and with supplementation will have smaller increases in 25(OH)D. Losing excess weight improves vitamin D levels. Vitamin D production and function require normal cholesterol metabolism. Statin drugs "poison this," says Dr

Sherry Rogers. Plasticizers from plastic products also poison cholesterol metabolism. Diuretics and proton-pump inhibitors may interfere with the body's usage of vitamin D. Many anticonvulsant drugs induce liver enzymes to inactivate vitamin D. Antibiotics can result in abnormal intestinal bacteria which can interfere with secretion of pancreatic enzymes needed to assimilate vitamin D. Corticosteroids (prednisone, cortisone) create D deficiency. Heavy metals damage the kidneys where vitamin D conversion occurs. Receptors on cell membranes must be healthy too, but refined, trans and other altered fats and oils as well as various nutritional deficiencies can contribute to unhealthy cell membranes. 'Diet' foods containing Olestra® damage absorption of fat-soluble vitamins (A, E, K and D), so little or no vitamin D from supplements gets into the bloodstream. Pollution in urban areas filters ultraviolet rays, decreasing synthesis of vitamin D in the skin. [4]

SUNLIGHT. The best source of vitamin D is the sun. For decades we were told to avoid sun to reduce risk of skin cancer. Many scientists now criticize this approach as overkill. The benefits of moderate sun exposure have become **obvious**. Even cancer advocacy groups like the American Cancer Society have softened their stance and say that some sun exposure is good for us. Government experts advise that we expose our face, arms, hands, legs, or back to the sun at least twice a week for 10 to 15 minutes. Other professionals say we need up to 30 minutes a few days a week. Still others say we need even more. Moderate sun exposure has been shown, so far, to reduce cancer risk at more than 16 body sites. What about **skin cancers**? Ultraviolet A (UVA) radiation, which penetrates to the lower epidermis of the skin, is thought to cause skin damage and cancer. It's not blocked by most sunscreens (though a few do so). But sunscreens reduce your skin's ability to make vitamin D. The incidence and death rates from melanoma, a deadly type of skin cancer, have actually increased since sunscreens were introduced in the 1960s. Dr David Holick says "…there's very little evidence in my opinion that sensible, moderate sun exposure increases your risk of the most deadly form of skin cancer, melanoma. In fact, there's good evidence to suggest that it may decrease your risk."

Ultraviolet light from the sun comes in two main wavelengths: UVA and UVB. Your skin needs **UVB** to produce vitamin D. UVA waves are basically constant during daylight, but UVB waves are low in the morning and evening and high during the middle of the day (roughly between 10 AM and 2 PM). For optimum vitamin D production, we should go outside in the sun around the middle of the day (without sunscreen). Stay out only long enough for your skin to just begin to get a little pink. This may be only a few minutes for people with pale skin. Each individual needs to learn how long he/she can spend outside before risking sunburn. Often gradual increases are needed. **How much** vitamin D does your skin make when exposed to sunlight? Estimates vary widely because the amount made is triggered by the season, time of day, latitude, skin color, age (older people tend to produce less) and other conditions. About 10,000-25,000 IU of vitamin D can be generated by 10-15 minutes of direct whole-body sun exposure, depending on sun intensity and your skin pigmentation. A short period of exposure between 10 AM and 2 PM results in as much vitamin D production as a longer period of exposure before 10 AM or after 2 PM. It's possible to make vitamin D under clouds—just not as much as in full sunlight. Sitting under a shade tree delivers about half as much UVB as sitting in direct sun but can be more comfortable in summer. All glass filters out UVB rays, so the windows in your car, house, etc., block UVB.

In humans and animals, vitamin D is formed in **sebum**, the fat the skin produces. That's why most vitamin D_3 supplements are made from lanolin or sebum-like material from the skin of sheep or cows. Oils on your skin absorb UVB light from the sun. Only if those oils are reabsorbed into the skin does the body receive the vitamin D—it can take up to 48 hours before most of it is absorbed. If you wash the oil from your skin by showering with soap before going out into the sun, vitamin D can't be formed. If you shower with soap after being in the sun before it's absorbed, you wash away much of the vitamin D your skin produced. Usually you only need to use soap under your arms, in your groin area, and on your feet. If you must use soap elsewhere at least use a gentle oil-based soap. But, if possible, **avoid** soaping larger areas of your body that are exposed to the sun.

Most tanning beds don't give you UVB rays, only UVA rays. There are some medium-pressure lamps that put out UVB rays. Still, natural sunlight is the best source of full-spectrum light and needed ultraviolet rays. The sun has more wavelengths than only UVA and UVB. It's best to get all the wavelengths for maximum health benefits. No doubt all the other frequencies and waves have health benefits that haven't been discovered yet. Dr Stephanie Seneff says that when your skin is exposed to sunshine, it makes not only vitamin D_3, but also vitamin D_3 **sulfate**. Your sulfur levels are intricately tied to your cholesterol levels and play important health

roles. The sulfated vitamin D formed in your skin is water soluble, unlike vitamin D_3 supplements that are nonsulfated. The water-soluble form can travel freely in your bloodstream; the nonsulfated form needs LDL (so-called "bad" cholesterol) as a vehicle of transport. Dr Seneff suspects that nonsulfated supplements may not provide all the benefits as the sulfated form because they can't be converted to vitamin D sulfate. [5]

FOODS, SUPPLEMENTS. A few foods contain vitamin D. Salmon, mackerel, tuna, sardines, other fatty cold-water fish, shrimp, beef liver, egg yolk, and sun-dried (or sun-exposed) mushrooms are primary sources. Cod liver oil is an excellent source unless it has been processed to remove toxins, as are most cod liver oil supplements, resulting in the elimination of most of the vitamins A and D. On average, free-range/pastured eggs contain 3-6 times more vitamin D than commercial eggs. Raw milk from pasture-fed animals supplies some D in the milk fat. The plant sterol, ergosterol, in mushrooms makes vitamin D_2 from sunlight. Commercial milk products, margarine, butter substitutes, ready-to-eat cereals, soy milk, and orange juice are usually "fortified" with vitamin D, but it's often synthetic and not as useful in the body.

Which form of **supplement** is best: D_2 or D_3? D_3 may be better absorbed than D_2, but in "high enough dosages vitamin D_2 can be effective." Both forms are converted by the liver and kidneys to the active form but D_3 may do it faster. D_2 produces 25(OH)D_2 which has less affinity for vitamin-D binding protein, resulting in a shorter circulating half-life. Although it's commonly believed that D_2 is about 30% less potent in the body than D_3, the variables in studies make it "extremely difficult to make comparisons and draw accurate conclusions," writes Dr Tori Hudson. Studies have had inconsistent results. D_2 is vegetable-based (from fungus or plant matter); D_3 is animal-based (from lanolin or skin sebum). Could people respond differently due to the source or whether the supplement is synthetic or natural? Very possible. Yet people taking **either** type of vitamin D supplement (especially those prone to deficiency) often do not experience the rise in blood and tissue levels that would be expected. There must be more to this story. Considering what we know about other nutrients and hormones, isolated or synthetic compounds are not the same as whole complexes of naturally-produced nutrients and hormones. Synthetic means imitation, not the real deal. This is especially disconcerting when it comes to vitamin D since we don't yet know everything about the real vitamin D. It performs as a hormone and its conversion, distribution, actions and effects are very complex. Shouldn't we explore more natural approaches?

In addition to sulfur, vitamin D needs other co-workers. Taking a substantial amount of vitamin D can create a relative deficiency of other nutrients needed to process and act with vitamin D. For example, research reveals that vitamins **A**, **E**, and **K** work synergistically with vitamin D. It is known that "if you're deficient in vitamin A, vitamin D cannot function properly either." Vitamin A helps to protect against vitamin D (supplement) toxicity and to balance production of vitamin D-dependent proteins. Without vitamin A, vitamin D produces an excess of defective vitamin-K dependent proteins. Vitamin D increases the level of vitamin K-dependent proteins; they work together to increase Matrix GLA Protein, for instance, which helps protect blood vessels from calcification. All fat-soluble vitamins (A, D, E and K) need to be present; they balance and enhance each other, are intricately bound through shared receptors, and, as a group, work together. The liver and kidneys, for example, need vitamins A, D, E, and K for optimal function. Natural fats in your diet can improve the efficacy of vitamin D supplements while consumption of refined, altered fats may reduce supplement effectiveness. Fully activated 1,25(OH)2D is vital to **calcium** absorption and regulation. Without enough vitamin D, blood calcium can drop too low. Excess D supplementation may raise calcium levels too high. Yet people who work outdoors during the summer (and make lots of vitamin D through their skin) don't absorb too much calcium despite high serum concentrations of vitamin D. Vitamin A helps regulate the ability of vitamin D to boost calcium metabolism. Vitamin K helps prevent calcium from being deposited in soft tissue and arteries. Vitamin D requires **magnesium** and vise versa. Some children with rickets don't respond to huge doses of vitamin D, but when given magnesium too, will rapidly improve. There are reports of people with low blood calcium whose calcium levels would not return to normal after vitamin D 'treatment.' But their calcium levels return to normal after they were given magnesium. Magnesium deficiency can be improved by vitamin D supplementation. All the enzymes that metabolize vitamin D require magnesium. A molecule of **zinc** is present in the interface of vitamin D receptors throughout the body. **Boron** is involved with vitamin D interaction with cell walls. **Iron** deficiency impairs fat and vitamin A absorption so may also impair vitamin D absorption. Getting vitamin D the way Nature intended (sunshine, nutrient complexes) does not lead to imbalances. High doses of isolated and human-made nutrients can and do lead to imbalances which can be worse than deficiencies. [6]

SUPPLEMENT DOSAGE. The 'proper' dose is another highly controversial issue. Recommendations vary all over the place—from 400 IU to 100,000 IU daily, for example—and should be dependent on a number of factors. There is no consensus on minimum, optimal, or toxic levels. There is no widely accepted upper limit. Other disagreements involve oral versus intramuscular dosing, and intermittent versus daily dosing (daily vs. weekly vs. monthly). Scientific trials have used many different doses. Some used D2; others used D3; a few tried active forms. Some used oral supplements; others used intramuscular. Most used a pharmacological approach, so "vitamin D is the drug the doctor ordered." Actually vitamin D requirements are highly **individual**. Your need depends on your unique body, on specifics like extent of sun exposure, location, season, age, skin color, health status, and more—all taken together. It's impossible to make a blanket recommendation.

Vitamin D is known to be toxic when taken in **high** doses. Symptoms include constipation, vomiting, fever, loss of appetite, weight loss, excessive urination, dehydration, weakness, fatigue, disorientation, and pain. Kidney stones and gastrointestinal complaints are regularly reported as more likely in study participants getting vitamin D than in those getting placebo. High doses may increase calcium retention from diuretics; increase activity of calcium-channel blockers; increase absorption of aluminum from aluminum-containing antacids and statins. Large doses can cause imbalances of other nutrients. But excessive sun exposure has **never** been reported to cause vitamin D toxicity. Researcher Mary Frances Picciano, PhD, says: "When you take in vitamin D from the sun, there is a feedback mechanism, so you will never get an excess amount from the sun. Now, we don't have a similar feedback mechanism for vitamin D that is ingested, so you could possibly get too much vitamin D. We know there are toxic levels, and we don't have very good data on what those toxic amounts are. We don't have a long-term history on the use of these very high levels that people are currently recommending." Sun exposure results in many biochemical and physiological effects that don't occur with D supplements. As there are still many unidentified factors about vitamin D, its modulation and functions, **care** should be used especially with synthetic or isolated supplements. Since D_3 may be more potent than D_2, high doses of D_3 could be potentially more toxic than D_2. For deficiency, it may be safer to use **moderate** doses initially (600 to 1200 IU/d) followed by a lower maintenance dose. Professor Alan N Peiris, MD, PhD, says there is much individual variation in how people respond to different doses, so he recommends lower doses and monitoring. "Individual customization of the dose based on clinical experience and patients' characteristics is mandatory."

The safety of high doses has not been adequately studied. Animal studies indicate that high doses increase the severity of atherosclerosis, for example. It's not known if it may do the same in humans. So far, explains Alan R Gaby, MD, the available evidence "does not support the idea that more vitamin D is better," and **does** indicate that modest doses are usually preferable to higher pharmacological doses. A study of postmenopausal women with low bone mass found a trend toward better outcomes with 800 IU per day than with 6500 IU per day. In another study, vitamin D supplementation appeared to improve strength and hip bone mineral density in elderly women, but 1600 IU per day was not more effective than 880 IU per day. An analysis of the Women's Health Initiative study found that modest doses reduce the risk of developing cancer, but high doses provide no additional benefit and may negate the benefit of lower doses or increase risk of cancer. Improving the vitamin D status in children appeared to help prevent flu; 150 IU per day was sufficient; an additional 1200 IU per day provided no further benefit and may have had a deleterious effect. Using different doses of vitamin D to investigate their influence on inflammatory cytokines and muscular strength in young adults found that low doses increase and maintain adequate serum 25(OH)D and cytokines, and that muscular strength doesn't improve by higher doses. Vitamin D can reduce the inflammation biomarker C-reactive protein (CRP) in people with low levels of the vitamin, but this beneficial effect disappears and may increase CRP levels in high doses.

"[R]ather than a pharmacological model (one nutrient isolated from others)," says Stephen Levine, PhD, "we need a nutritional model that takes into account the diet and lifestyle…" as well as the way our body responds. Studies can be "inconsistent if they isolate a single factor without taking into account the tight synergy among nutrients." We **don't** yet know the optimal blood level of vitamin D, which form to test to best determine vitamin D levels, whether supplements that increase blood levels are actually functioning as naturally-made vitamin D or whether blood levels just reflect the presence of the compound without performing as bodily-made or food-obtained vitamin D. We don't know all potential adverse effects from large doses of vitamin D supplements, the extent of these doses to affect levels of other nutrients, or the effects on bodily systems and functions. Actually, little is known about the quantity or location of vitamin D in the human body. We need to **learn** much more.

If supplementation is needed, keep it low—150 to 1200 IU per day has been shown to be helpful in preventing osteoporosis, falls, flu, colds, cancer, MS, and more. It's not known whether taking more would improve results. So get some sunshine and take modest oral doses if needed. [7] If there is evidence of vitamin D deficiency, the following can be considered (for an adult):

With Two Meals:

2 or 3 Calcifood Wafers (chew) OR 1½ teaspoons Calcifood Powder – for calcium, magnesium, boron, zinc
2 Chlorophyll Complex – for vitamins A, E, and K, magnesium
1 Cruciferous Complete – for vitamin K, sulfur

With One Meal:

1 Cataplex D (break in mouth) – for 6 months only, then 2 Tuna Omega-3 Chewable with two meals
1 Cataplex A (break in mouth) – for 6 months only

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