Vitamin D:
A New Look at an Old Vitamin

New research is expanding our knowledge of the metabolic functions and physiologic needs for vitamin D, beyond its traditional role in calcium absorption and bone health. For this reason, the Institute of Medicine (IOM) recently convened a committee to examine the research and update their dietary recommendation for this all-important nutrient. This monograph will provide the health professional with an overview of the new areas of research, a summary of the recently updated recommendations and practice points to optimize the vitamin D status of patients and clients.

Basics of vitamin D synthesis

Vitamin D is the only vitamin the human body makes itself in any significant amounts. Previtamin D_3 is synthesized in the skin following exposure to UV-B sunlight. The "storage form" of vitamin D, hydroxy vitamin D [25(OH)D], is then synthesized in the liver and circulates in the blood. Finally, di-hydroxy vitamin D [1,25$(OH)_2$D], the "active form" of vitamin D (also called calcitriol), is synthesized in the kidney to support calcium balance and in other cells when and where it is needed.

Because of the sun's contribution to vitamin D status, the "completely avoid sun" message has been liberalized by the American and Canadian Cancer Societies.[1,2] Depending on location, time of year, age and amount of melatonin in one's skin, it is now encouraged to get 5 – 30 minutes of sun exposure between 10 am and 3 pm at least twice a week on the face, arms, legs or back, without sunscreen, for sufficient vitamin D synthesis.[3] Since it is fat-soluble, vitamin D can be stored for several months when people are not exposed to sunlight.

Problems in relying only on sun exposure for vitamin D, however, include that little or no synthesis takes place in winter at latitudes above 40°N (north of Columbus, Ohio) and sunscreen SPF greater than 8 blocks UV-B, as does clothing, smog, being indoors and darker skin pigments. Additionally, synthesis declines as we age.

Physiologic functions of vitamin D—Traditional

Vitamin D is best known for its role in tightly regulating serum calcium levels by enhancing calcium absorption and increasing bone resorption, as part of a process involving parathyroid hormone (PTH). Thus, classic vitamin D deficiency results in bone demineralization, which can ultimately lead to rickets in children and osteomalacia or osteoporosis in adults. As calcium also helps maintain muscle strength, vitamin D deficiency results in leg muscle weakness and an increase in falls in older people.

A recent meta-analysis indicated that intakes of 700 – 800 IU of vitamin D per day, or only slightly higher than the current recommendation, could prevent about one-quarter of all hip and nonvertebral fractures in both ambulatory and institutionalized older persons.[4] There is evidence that higher concentrations of serum vitamin D may also contribute to peak bone mass in younger adults, which could protect against fractures at an older age.[5] Higher blood levels of vitamin D are also associated with lower rates of hip fracture and reduced risk of falling.[6]

There are numerous studies showing vitamin D supplementation has positive effects on bone mineral augmentation in children and adolescents. Even maternal vitamin D status during pregnancy influences the bone growth of the offspring and their risk of osteoporosis in later life.[7] In the past few years, nutritional rickets has re-emerged in the U.S. as a public health concern. One review identified 166 cases of rickets among children four months to 4-1/2 years of age between 1986 and 2003, most of whom were African American, breastfed, and very few of whom were given supplements.[8] Rickets has also been reported in adolescents,[9] leading experts to suspect that many other children and adolescents have borderline or undetected deficiencies.

Experts believe the cause for this resurgence in cases of rickets is multi-factorial and includes the following:

- Children tend to be outdoors less, favoring indoor activities such as watching television and computer-related activities.
- Liberal use of sunscreen minimizes vitamin D synthesis in the skin.
- Living among tall buildings in urban environments results in less sunlight exposure.
- Many children have poor diets and do not consume enough dietary sources of vitamin D, such as fortified dairy products.
- Adolescents in particular often trade milk consumption for soft drinks at a time when bone mass is accumulating rapidly.
- **Dark-skinned individuals don't absorb sunlight as easily as Caucasians and are more prone to vitamin D deficiency.**

Physiologic functions of vitamin D—Emerging

Extensive research is uncovering other non-traditional functions and benefits of vitamin D in the body. Significance of nontraditional roles emerged when it was discovered that cells other than the kidney could make the active form of vitamin D for their own use. In these cells, calcitriol acts to regulate gene expression. Those areas with the most substantiation are summarized below.

Cancer

Vitamin D insufficiency affects normal cellular proliferation and differentiation and may thus affect risk of cancer. Observational evidence suggests that people who get little or no exposure to sun tend to have higher rates of breast, colon, pancreatic, ovarian and prostate cancers; some experts believe this is the result of marginal vitamin D status.

Most of the evidence showing a protective effect of vitamin D on cancer has been from observational studies. In the Health Professionals Follow-Up Study, 4,286 incident cancers (excluding prostate and non-melanoma skin cancer) and 2,025 deaths from cancer were documented between 1986 and 2000. Lower vitamin D status, estimated from intake and outdoor activity, was associated with higher risk of most cancers.[10] Epidemiological studies have found that individuals who have suboptimal serum vitamin D levels have a 30 to 50 percent greater risk of colon, prostate and breast cancers, as well as higher mortality rates from these cancers.[11]

One of the few clinical trials conducted on vitamin D and cancer risk was a 4-year randomized controlled trial of postmenopausal women given calcium alone, calcium plus vitamin D, or placebo. The calcium-only and the calcium-plus-D groups had 45 to 60 percent lower rates for all cancers compared with the placebo group; the calcium-plus-D group also had significant improvements in blood levels of vitamin D.[12]

The strongest evidence for a protective effect of vitamin D against a certain type of cancer is with colorectal cancer. Not only do rates of colorectal cancer rise with increasing distance from the equator,[13,14] but higher serum vitamin D levels and higher intakes are independently associated with reduced risk.[15,16]

Immune Function

Vitamin D insufficiency has been linked to an increased risk of tuberculosis and pneumonia, bacterial infections of the lungs and gingivitis. The active form of vitamin D, calcitriol, is believed to mediate immunological effects by binding to nuclear vitamin D receptors (VDR) present in most immune cells, which in turn increases expression of defensive genes.

A number of autoimmune diseases, such as multiple sclerosis, type 1 diabetes, systemic lupus and rheumatoid arthritis, are associated with vitamin D deficiency,[17] possibly by impairing the development of regulatory T cells. Rates of multiple sclerosis increase with distance from the equator, suggesting that populations with lower vitamin D levels are at increased risk. New research also indicates that higher levels of vitamin D in the blood may lower the risk of multiple sclerosis.[18] Finally, low vitamin D levels have been linked to an increased incidence of upper respiratory tract infections[19] and it is thought that vitamin D may play a role in maintaining innate immunity[20] and preventing infection.[21]

Most of the evidence for an effect of vitamin D on immunity, however, stems from epidemiological research and observational studies. Randomized clinical trials to provide definitive associations and quantifying optimal intake and serum levels of vitamin D are still lacking.

Insulin Resistance, Type 2 Diabetes and Metabolic Syndrome

More recently, research has focused on the association between vitamin D and insulin resistance and metabolic syndrome (MetS). Vitamin D deficiency has been shown to alter insulin synthesis and secretion in both humans and animal models, and appears to predispose to glucose intolerance, altered insulin secretion and type 2 diabetes mellitus.[22] Vitamin D may thus play an important role in the pathogenesis of type 2 diabetes.

In a recent study in middle-aged and older Chinese population, low serum vitamin D levels are associated with an increased risk of MetS and insulin resistance.[23] A similar study in Asian Indians, however, found no such association.[24] Likewise, another study found that vitamin D intake is associated with insulin sensitivity in African American, but not European American, women.[25] Such results indicate there may be population-specific associations between vitamin D status and insulin sensitivity, possibly explained by genetics, body composition, lifestyle or a combination of factors. Clinical-intervention trials are needed to confirm these provocative findings.

Vitamin D recommendations

For the first time, the IOM developed Recommended Dietary Allowances (RDAs) for vitamin D in 2010.[26] Prior to this, Adequate Intake (AI) levels—rougher estimates of people's requirements—had been set*. The new values are based on more information and higher-quality studies than were available when the previous values were established in 1997. Because the amount of sun exposure varies greatly from person to person, the recommendations assume minimal sun exposure and are as follows:

Age (yr)	IU (or ug) per day
1 - 70	600 (15)
>70	800 (20)

Pregnant and lactating women are recommended to consume 600 IU per day regardless of age.

The Upper Level (UL), set at 4,000 IU/day for everyone over 9 years of age, represents the safe boundary at the high end of the scale. Intakes consistently above this level are considered to increase one's risk for harm, such as kidney and tissue damage and other adverse health effects.

Basis for recommendations

Serum vitamin D level is considered the best indicator of vitamin D status as it represents that produced cutaneously and that obtained from the diet. However, there is no consensus in the medical community as to the level needed for optimal health. For purposes of setting the recommendation, the IOM committee considers 20 nanograms per milliliter (ng/ml) adequate for bone health—substantially lower than many groups have defined as the level for vitamin D deficiency/sufficiency.

Using the serum level of 20 ng/ml set by the IOM, blood levels of vitamin D are deemed adequate in almost all individuals, in spite of national intake surveys suggesting that most people do not consume the recommended amount of vitamin D. Data from NHANES III, for example, indicate the average intake for adults from food alone falls in the range of 160 – 240 IU/day[27,28] and intake from foods plus supplements is 220 – 380 IU/day.[29,30] It could be that sun exposure contributes meaningful amounts of vitamin D and helps most people meet their needs. Older individuals, those living in institutions and those who have dark skin preventing adequate vitamin D synthesis may still not be meeting their needs, however.

The IOM committee urges people to be cautious in getting their vitamin D status assessed through independent laboratories. Labs tend to use different cut-off points for measuring sufficiency and deficiency and often falsely categorize people as deficient. Overestimating vitamin D deficiency in this way can inappropriately lead people to assume that they need supplements, thereby increasing their risk of toxicity.

Meeting vitamin D recommendations through food versus supplements

Vitamin D is not plentiful in the American diet. Fortified milk is a major source in the U.S.; fatty fish such as salmon, tuna and sardines are also good sources. Some orange juices, margarines, and breakfast cereals are also fortified with vitamin D.

The IOM encourages people to take in vitamin D from foods rather than supplements. Not only can supplements lead to over consumption, they can result in an incomplete "package" of nutrients for health benefits—for example, calcium, phosphorus and other nutrients needed in appropriate ratio for bone health. Some groups such as the elderly, however, may require a supplement to meet their needs if their intake is inadequate and they do not get enough sun exposure. In addition, people with milk allergy, lactose intolerance and those who are strict vegetarians are at high risk for deficiency and may need supplements.[31] Finally, individuals with a body mass index (BMI) greater than 30 often have low levels of blood vitamin D, as subcutaneous fat is thought to sequester the vitamin, taking it out of circulation.[32]

Below is a chart of vitamin D content of some common food sources.[33]

Vitamin D	(IU)
Salmon, cooked (3.5 ounces)	360
Sardines, canned (1.75 ounces)	250
Tuna, canned (3 ounces)	200
Milk (1 cup)	100
Vitamin D-fortified orange juice (1 cup)	100
Soy beverage (1 cup)	100
Margarine, fortified (1 tablespoon)	60
Breakfast cereal, fortified (1 serving)	40 (varies)
Egg (1 whole)	20

Multivitamin supplements generally provide between 200 and 400 IU per tablet; single vitamin D supplements can provide up to 2,000 IU. Fish liver oils contain up to 1,300 IU but are also high in vitamin A, carrying risks of vitamin A toxicity.

The role of the practicing health professional

The health professional is in an ideal position to monitor and assess vitamin D status in clients of all ages, considering their current health and future disease risk, and to encourage appropriate sources of this important nutrient. In evaluating vitamin D status in clients:

- Consider skin pigmentation, use of sunscreen, time spent outdoors and latitude. Individuals who are dark skinned, use sunscreen liberally, are indoors much of the time and live in northern areas should be counseled to consume adequate dietary sources of vitamin D.
- Assess calcium intake simultaneously for its impact on bone health. Keep in mind that not all foods high in calcium have vitamin D, and that adequate calcium intake does not replace the need for vitamin D; both are required for optimal health.
- Recommend a vitamin D test [serum 25(OH) D] from a reputable laboratory if there is uncertainty as to intake or status. Use the IOM value of 20 ng/ml to assess status.
- Listen for complaints of bone or muscle pain (which may indicate osteomalacia).
- Encourage food and fortified food sources of vitamin D first, then supplements. Remind clients that foods provide a "package" of nutrients that is generally in the appropriate ratio needed by the body. Compliance can also be an issue when supplement use is inconsistent. Remember that even with a healthy diet, older individuals and other subgroups may need to take vitamin D supplements to meet their higher needs.

As the research matures around the various health effects of vitamin D, the consumer will increasingly seek out vitamin D-fortified food products in the marketplace. Being familiar with these sources—including milk, cheese and yogurt, soy beverages, orange juice and cereals—will assist you in making appropriate recommendations to individual clients.

Keep abreast of the research surrounding vitamin D over the next few years so that you will be prepared to answer clients' questions and concerns and help them optimize their health through individualized dietary plans developed to meet their needs.

*RDA definition: Average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97-98 percent) individuals in a life stage and gender group.
AI definition: The recommended average daily nutrient intake level based on intake of healthy people assumed to be adequate.

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