Vitamin D:
An Old Vitamin With New Health Implications

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. At the same time, vitamin D status is declining in this country due to lower intakes and reduced sunlight exposure. This monograph will provide the practicing health professional with an in-depth understanding of this growing public health dilemma, as well as practice points to optimize the vitamin D status of individuals and the population.

Basics of vitamin D synthesis

Vitamin D is the only vitamin the human body makes itself in any significant amounts. Vitamin D_3 is synthesized in the skin following exposure to UV-B sunlight. The "storage form" of vitamin D, called 25-hydroxyvitamin D_3 [25(OH)D], is then synthesized in the liver and circulates in the blood. Finally, $1,25(OH)_2D$, 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 is being liberalized by the American and Canadian Cancer Societies.[1,2] Depending on one's location, time of year, amount of melatonin in his or her skin, and age, generally about 10-15 minutes of sun exposure at least twice a week on one's face, hands and arms may be adequate to produce at least some of the vitamin D the body needs. Since it is a fat-soluble vitamin, it 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; sunscreen SPF 8 blocks UVB; and clothing, being indoors, skin pigments and age reduce synthesis.

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 50-100% higher than the current recommendation, could prevent about one-quarter of all hip and nonvertebral fractures in both ambulatory and institutionalized older persons.[3] There is evidence that higher concentrations of serum 25(OH)D may also contribute to peak bone mass in younger adults, which could protect against fractures at an older age.[4]

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.[5] In the past few years, nutritional rickets has re-emerged in the U.S. as a public health concern. A recent 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.[6] Many other children and adolescents are suspected to have borderline or undetected deficiencies.

Experts believe the cause for this resurgence in cases of rickets is multifactorial 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.
- Breast milk has typically low levels of vitamin D.
- Dark-skinned individuals don't absorb sunlight as easily as whites 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 and prostate cancer; some experts believe this is the result of marginal vitamin D status.

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.[7]

The strongest evidence for a protective effect of vitamin D against cancer is with colorectal cancer. Not only do rates of colorectal cancer rise with increasing distance from the equator,[8,9] but higher serum 25(OH)D and higher vitamin D intakes are independently associated with lower risk.[10,11]

Cognitive Performance

Emerging evidence suggests vitamin D may play a role in cognitive performance. Cross-sectional studies in older adults show vitamin D deficiency is associated with low mood and worsened cognitive performance, as well as greater severity of dementia.[12]

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_3, 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.

Vitamin D insufficiency may also impair development of regulatory T cells, increasing the risk of autoimmune diseases such as multiple sclerosis (MS) and type I diabetes. Evidence to this effect is that rates of MS 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 MS.[13]

Periodontal Disease

There is some evidence that poor vitamin D status is linked to higher risk of periodontal disease, a common chronic inflammatory disease leading to tooth loss. A recent study found that supplementation with vitamin D and calcium reduced tooth loss in older persons over a 3-year period.[14] It is believed that vitamin D may also reduce periodontal disease through its anti-inflammatory effect.[15,16]

Vitamin D recommendations

The Adequate Intake (AI) for vitamin D was established in 1997 with the first set of Dietary Reference Intakes (DRIs) released by the Institute of Medicine.[17] The AIs, which were set assuming no sunlight exposure, are as follows:

Age (yr)	IU (µg)/day
0-50	200 (5)
Pregnant/lactating	200 (5)
51-70	400 (10)
>70	600 (15)

Factors considered in setting these requirements include:

- Age—older individuals lose some ability to synthesize vitamin D from sunlight exposure and to metabolize it to its active form
- Obesity—adipose tissue may serve as an irreversible sink to vitamin D storage
- Type of vitamin D—D_2 is less well-utilized by the body than D_3
- Amount of sun exposure—determined by latitude, season, skin pigmentation, use of sunscreen, clothing and outdoor activities

Recommendations up for revision?

Since 1997, when the AIs for vitamin D were established, new studies have provided data challenging what was determined as the optimal range of serum 25(OH)D. There are also increasing concerns about the reliability of sun exposure in different groups, making it more critical than ever for people to consume adequate dietary vitamin D.

When the current recommendation is revised, the new level will likely be based on the intake needed to achieve a desirable serum concentration of 25(OH)D greater than 75 nmol/L, considerably higher than the previous level of 27 nmol/L. This higher level is associated with lower rates of hip fracture and reduced risk of falling.[18] Intakes needed to maintain this higher level of 25(OH)D are estimated to be up to 2,000 IU per day for individuals receiving little sun exposure.[19] Thus, we will likely see considerably higher recommendations for vitamin D intake in the future in order to optimize its various health effects.

The Upper Level (UL) level, currently set at 2,000 IU/day, was considered the level above which may lead to high blood and urine calcium levels and the commensurate kidney stones, kidney failure and deterioration of muscle and bone mass. Some experts, however, believe this value could be much higher, as the published study upon which it was based may have been misinterpreted.[20] New studies show intakes as high as 10,000 IU/day may be safe in adults.[21] Thus, UL levels may also be adjusted upward once the committee reconvenes.

Meeting vitamin D recommendations

Vitamin D is not plentiful in the diet. Fortified milk is the 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.

Although average intakes in the U.S. are within the current recommended range for individuals younger than 50, older individuals' intakes fall well below age-appropriate values. Data from NHANES III indicate the average intake of adults from food alone falls in the range of 160-240 IU/day, [22,23] and average intake from foods plus supplements is 220-380 IU/day. [24,25]

Multivitamin supplements generally provide between 200 and 400 IU per tablet; single vitamin D supplements can provide up to 1,000 IU. Fish liver oils contain up to 1,300 IU but are also high in vitamin A, carrying risks of vitamin A toxicity. Relying on supplements for vitamin D, however, raises concerns of long-term compliance as well as an incomplete "package" of nutrients for health benefits—for example, calcium, phosphorus and other nutrients needed for bone health.

Thus, although supplements are not the ideal means of meeting vitamin D recommendations, for those at risk of deficiency—people living in the northern third of the U.S. and Canada, those with dark skin, those who are housebound or institutionalized, and those who consume no milk or other fortified foods—supplementation may one way to meet their needs. If and when vitamin D recommendations increase, we will likely see introduction of more fortified food products in the marketplace in an attempt to help consumers meet their requirements through foods.

Below is a chart of vitamin D content of some common food sources (adapted from ref. 26).

	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
Egg (1 whole)	20

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, identifying marginal or deficient intakes and in some cases warding off clinical symptoms of deficiency before they occur. In evaluating vitamin D status in clients:

- Consider skin pigmentation, use of sunscreen, time spent outdoors and latitude in assessing vitamin D status. 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.
- Listen for complaints of bone or muscle pain (which may indicate osteomalacia).
- Recommend a vitamin D test [serum 25(OH)D] if there is uncertainty as to intake or status.
- 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.
- 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. Even with a healthy diet, older individuals 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 process of updating recommendations for vitamin D over the next few years so that you will be prepared to help clients incorporate the possibly higher levels into individualized dietary plans developed to meet their needs.

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