

Vitamin D & Chronic Disease Risk—Causes, Consequences & Clinical Recommendations

Key Points for Self-Study CPE Program

The information below summarizes key points from the self-study Continuing Professional Education (CPE) podcast presentation, ***Vitamin D & Chronic Disease Risk—Causes, Consequences & Clinical Recommendations***. These points will assist you with note-taking as you view the podcast and serve as support materials for answering the CPE quiz.

This self-study program is based on a live CPE webinar presented in December 2008 by noted vitamin D expert, Dr. Michael H. Holick.

Biography: Michael F. Holick, MD, PhD

Dr. Michael F. Holick is Professor of Medicine, Physiology and Biophysics, Director of the General Clinical Research Center and Director of the Bone Health Care Clinic and the Heliotherapy Therapy, Light and Skin Research Center at Boston University Medical Center. Dr. Holick has made numerous contributions to the field of the biochemistry, physiology, metabolism and photobiology of vitamin D for human nutrition. He determined the mechanism for how vitamin D is synthesized in the skin and demonstrated the effects of aging, obesity, latitude, seasonal change, sunscreen use, skin pigmentation and clothing on this vital process.

This program is worth 1 level 2 CPE hour.

The following learning codes are suggested for this program, but you may use any applicable learning code: 2090, 3000, 4040

Learning Objectives

- Identify risk factors for 25-hydroxyvitamin D deficiency.
- Describe the association between low 25-hydroxyvitamin D levels and chronic disease risk.
- Describe the appropriate biochemical marker for nutritional vitamin D sufficiency, the circulating level that should be attained and current clinical recommendations.

CPE Podcast Presentation Key Points

Risks of Vitamin D Deficiency

- It's well-known that vitamin D deficiency is associated with rickets in children and osteomalacia—the painful bone disease that is the adult form of rickets.
- Emerging research associates deficiencies with diabetes, multiple sclerosis, rheumatoid arthritis, infectious diseases, hypertension, heart disease, stroke, common cancers and other health conditions.

How Vitamin D is Made

- Vitamin D is made in the skin, principally in the upper layer known as the epidermis. Solar ultraviolet radiation penetrates the epidermis and converts cholesterol, 7-dehydrocholesterol to pre-vitamin D, which rapidly converts in the skin to vitamin D.
- You cannot become vitamin D toxic from sun exposure.

Key Events Leading to the Eradication of Rickets in Children

- In 1919, Huldschinsky cured rickets in children by exposing them to radiation from a mercury arc lamp.
- In 1921, Hess and Unger cured rickets by exposing children to sunlight.
- In 1931, the US government recommended that children receive a **sensible** amount of sun exposure to make enough vitamin D without risk for excess exposure.
- Today, dermatology societies do not recommend direct exposure to sunlight. However, most of our vitamin D comes from sensible sun exposure.

Importance of Vitamin D during Pregnancy, Lactation and Infancy

- Vitamin D deficiency may be common in pregnant women.
- In one study, the vitamin D status of 40 mother/infant pairs was measured. 70% took a prenatal vitamin and drank 2.3 glasses milk/day for an average vitamin D intake of approximately 600 IU/day, which is considered adequate during pregnancy. However, 76% of mothers and 81% of infants were vitamin D deficient (25(OH)D < 20ng/mL).
- There's a strong, inverse relationship between maternal 25(OH)D at <22 weeks and risk of preeclampsia.

- Vitamin D deficiency increases risk for C-section. Potential reason: Vitamin D is important for muscle strength needed during childbirth.
- Vitamin D deficiency during the first year of life may prevent a child from reaching peak height and bone mineral density, and may increase risk for serious chronic diseases later in life.
- However, gross manifestations of rickets are still observed today in human infants because it's assumed that human breast milk provides all nutritional requirements.
- But human breast milk provides little vitamin D—typically, no more than about 25 IU/pint.

Vitamin D Intake Recommendations during Pregnancy, Lactation and Infancy

- **Pregnancy:** Dr. Holick recommends a prenatal vitamin with 400 IU vitamin D/day + 1,000 IU vitamin D supplement for the health of the pregnant woman and unborn infant.
- **Lactation:** 4,000 to 6,000 IU/day so that breast milk contains enough vitamin D to satisfy the infant's requirements.
- **Infancy:** The American Academy of Pediatrics recommends that “a supplement of 400 IU/day of vitamin D should begin within the first few days of life and continue throughout childhood. Any breastfeeding infant, regardless of whether he or she is being supplemented with formula, should be supplemented with 400 IU of vitamin D, because it is unlikely that a breastfed infant would consume 1 L (~1 qt) of formula per day, the amount that would supply 400 IU of vitamin D.”

Meeting Vitamin D Requirements

- Vitamin D is rare in foods. Sources: Vitamin D-fortified dairy products such as milk and some cheeses and yogurts; orange juice fortified with calcium and vitamin D; cod liver oil; and oily fish such as wild salmon (farm-raised contains 10-25% of the vitamin D as wild salmon), mackerel and herring.
- People can meet vitamin D requirements from sunlight exposure. However, from November through February, the skin cannot make vitamin in latitudes above Atlanta, Georgia. In areas such as Washington DC, New York and Boston, that time period extends from about mid-October through early April.
- Excessive sunlight exposure increases the risk of non-melanoma skin cancer. Sunscreen with SPF 30 reduces the skin's ability to make vitamin D by as much as 99% because sunscreen absorbs about 99% of UVB radiation.

- Skin has a huge capacity to make vitamin D. Sun exposure of 15-20 minutes on the beach in a bathing suit gives a light pinkness to skin 24 hours later, called a “minimal erythematol dose,” which is equivalent to ingesting between 10,000 and 20,000 IU of vitamin D.
- The highest blood levels of 25-hydroxyvitamin D (a measure of vitamin D status) peaks at the end of summer and is lowest at the end of the winter. It’s preferable to keep the level stable throughout the year.

Vitamin D Status and Obesity

- Obesity is associated with vitamin D deficiency because vitamin D becomes “trapped” in fat cells.
- In our lab, we gave obese and non-obese individuals a single oral dose of vitamin D or put them in a tanning bed. Following this exposure, the serum vitamin D levels of the obese subjects was about 55% lower than the levels of non-obese subjects.
- We also obtained body fat samples from women and men going for bariatric surgery and found a large amount of vitamin D stored in the fat. Losing weight does not mobilize the vitamin D and raise blood levels of 25-hydroxyvitamin D. The vitamin D gets destroyed as the fat gets destroyed.
- Dr. Holick’s recommendation: Obese patients need 2-3 times more vitamin D than normal-weight individuals, or 50,000 IU vitamin D/week.

General Recommendation for Sun Exposure

- To make vitamin D, **briefly** expose skin to sunlight without sunscreen. Then apply sun protection to prevent damaging effects from excessive sun exposure.
- For example, for a light-skinned individual in Boston, no more than about 10-15 minutes of sun exposure on arms and legs two to three times a week is recommended. Use sun protection on the face—it’s only 9% of the body’s surface, so it doesn’t make much vitamin D and is the most sun-exposed and sun-damaged area of the body.

Skin Pigment Affects Vitamin D Synthesis

- Our lab tested the effect of UVB exposure on serum vitamin D levels in white and black volunteers by exposing them to the same amount of radiation in a tanning bed. The white volunteers raised their serum vitamin D level 60-fold, while the level in black volunteers didn’t change. Blacks needed five to 10 times more exposure to barely raise their blood level of vitamin D. We now recognize that 30-50% of African-Americans in the United States are vitamin D-deficient year-round.

Vitamin D Status and Intake Recommendations

- Measure 25(OH)D (25-hydroxyvitamin D) NOT the active form, 1,25(OH)₂D (1,25-dihydroxyvitamin D). The level of the active form is normal or elevated in a vitamin D-deficient state, so it's not of value to determine a patient's vitamin D status.
- Vitamin D intoxication occurs when levels of 25(OH)D are above 150 ng/mL, but it's extremely difficult to reach that level. A low level is of greater concern. To maximize vitamin D's effect on bone health and calcium absorption, the blood level should be 30 ng/mL or more.
- The 1997 Institute of Medicine recommendations for adequate intake (AI) of vitamin D are inadequate (0-50 years = 200 IU/day; 51-70 years = 400 IU/day; 71+ years = 600 IU/day).
- Dr. Holick's recommendation: At minimum, children and adults should take 1,000 IU of vitamin D/day and a daily multivitamin containing 400 IU to reach a serum 25-hydroxyvitamin D level of 30 to 60 ng/mL. A level of 60 to 100 ng/mL is safe. People with the rare disease sarcoidosis must keep blood levels of 25-hydroxyvitamin D at around 30 to 40 ng/mL to avoid complications.

Who Is Vitamin D-Deficient (<20 ng/mL)?

- Research has uncovered vitamin D deficiency in populations of various ages and races including people over age 65; African-American women of child-bearing age; 18-29 year-old medical students and residents; 9-11 year-old white girls, and healthy adolescents.

Vitamin D, Osteoporosis and Osteomalacia

- Vitamin D deficiency will precipitate and exacerbate both osteopenia (low-bone density, but not yet osteoporosis) and osteoporosis (porous bones).
- One US study looked at the vitamin D status of women with osteoporosis who were taking osteoporosis medication. Results showed that 52% had low blood levels of vitamin D (<30 ng/mL). Thus, they were not getting the full benefit of their medication because they were not getting the full benefit of calcium and vitamin D.
- Osteoporosis does not cause bone pain until a fracture occurs. Osteomalacia, a bone disease associated with vitamin D-deficiency, is manifested with these typical symptoms: generalized bone pain, isolated bone pain, and muscle aches and pains that often occur in the fall and winter. These patients are often diagnosed with fibromyalgia, but in Dr. Holick's clinic, 40-60% are vitamin D-deficient and correcting the deficiency resolves their symptoms.

- Research supports a link between hypovitaminosis D and non-specific muscle pain in children and adults.
- Vitamin D is critically important for muscle strength. In fact, skeletal muscle has a vitamin D receptor. And higher serum 25-hydroxyvitamin D is associated with higher bone mineral density. Increasing vitamin D intake to 700 IUs/day reduced risk of non-vertebral fractures by 58% in the elderly. Thus, raising serum vitamin D above 30 ng/mL seems to increase bone mineral density, increase muscle strength and reduce risk of fracture because people are less likely to fall.

Treating Vitamin D Deficiency

- Dr. Holick's recommendation: Prescription for 50,000 IU vitamin D2 one/week for eight weeks to correct the deficiency, then maintain sufficiency with 50,000 IU every two weeks long term.
- It's difficult to become vitamin D intoxicated. Dr. Holick's research showed healthy blood levels and no toxicity in patients who received 50,000 IU of vitamin D every two weeks for up to six years. A review of 37 clinical studies showed that vitamin D intoxication does not occur until intakes are more than 10,000 IU/day.
- Studies show that vitamin D2 and vitamin D3 are equally effective in raising serum levels of 25-hydroxyvitamin D. In addition, Dr. Holick just completed a study showing that the vitamin D in fortified orange juice (100 IU/cup) is as bioavailable as the vitamin D in milk.

Vitamin D and Disease Risk

It's well-known that the active form of vitamin D regulates calcium metabolism. But it appears to play a role in preventing several chronic diseases.

Cancer. Epidemiological studies suggest that living in higher latitudes (i.e., with less sunlight) is associated with higher risk of dying of colon cancer. Research also shows that taking at least a 1,000 IU of vitamin D/day reduces risk of developing colon cancer by as much as 50%. Women taking more than 400 IU vitamin D/day who raised their blood levels above 48 ng/mL reduced their risk of developing breast cancer by 50%. A study of 47,800 male physicians showed that those who increased their vitamin D intake had reduced risk of pancreatic, esophageal and colorectal cancer.

People who receive more sun exposure may be less likely to die of cancer. One study showed that girls age 10-19 with the most sunlight exposure had a 69% reduced risk for breast cancer and women age 20-29 had a 51% reduced risk; no benefit was shown for women age 45-54.

There's an inverse relationship between vitamin D status and risk of developing many common cancers. However, findings from the Women's Health Initiative suggested that taking calcium and vitamin D did not reduce risk of colorectal cancer. But women who were severely vitamin D-deficient and followed for the next eight years had a 253% increased risk of developing colorectal cancer. A 2007 study showed that women taking 1,100 IU vitamin D/day for four years reduced their risk of developing all cancers by 60%.

Diabetes. A Finnish study showed that children who received 2,000 IU vitamin D/day during their first year of life reduced their risk of getting type 1 diabetes by 78% after 31 years, and children with rickets had a 2.4-fold increased risk for type 1 diabetes. The beta islet cells that make insulin respond to the active form of vitamin D and make more insulin, suggesting that type 2 diabetes is associated with vitamin D deficiency. A review study found that taking more than 800 IU vitamin D/day and 1,200 mg calcium/day reduced risk of type 2 diabetes by about 33%.

Multiple Sclerosis and Rheumatoid Arthritis. People in latitudes above Atlanta, Georgia, have a 100% increased risk of developing multiple sclerosis. A Harvard study showed that women taking more than 400 IU of vitamin D/day reduced their risk of multiple sclerosis by 41%. Vitamin D intake also is inversely related to rheumatoid arthritis in women.

Vitamin D deficiency has been associated with several other conditions including osteoarthritis, hypertension, peripheral vascular disease, and heart failure. Low serum vitamin D is associated with increased risk for myocardial infarction and cardiovascular and all-cause mortality.

Adequate Vitamin D Intake

- Adequate vitamin D is critically important from birth until death. Vitamin D deficiency is a disease of neglect. A significant amount of scientific evidence links vitamin D deficiency to many serious chronic diseases.
- Everyone's serum 25-hydroxyvitamin D level should be greater than 30 ng/mL. For every 100 IU ingested, the blood level is raised by 1 ng/mL.
- Dr. Holick's recommendation: Children and adults not exposed to adequate sun in the spring, summer and fall, should receive at least 1,000 IU of vitamin D/day for good health.
- Dr. Holick advises **sensible** sun exposure: Exposure of arms and legs for 5 to 30 minutes (depending on time of day, season, latitude, and skin pigmentation) between the hours of 10 a.m. and 3 p.m. twice a week is often adequate. Then, apply sunscreen with SPF 30.

Selected References

1. Holick MF. The vitamin D epidemic and its health consequences. *J Nutr.* 2005;135:2739S-2748S.
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3. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, Benjamin EJ, D'Agostino RB, Wolf M, Vasan RS. Vitamin D deficiency and risk of cardiovascular disease. *Circulation* 2008; 117(4):503-511.
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8. Holick MF, Biancuzzo RM, Chen TC, et al. Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D. *J Clin Endocrinol Metab* 2008; 93(3):677-681.
9. Moore CE, Murphy MM, Keast, DR, Holick MF. Vitamin D intake in the United States. *J Am Diet Assoc.* 2004;104:980-983.
10. Moore CE, Murphy MM, Holick MF. Vitamin D intakes by children and adults in the United States differ among ethnic groups. *J Nutr.* 2005;135:2478-2485.

Additional Resources

- VitaminDHealth.org—Dr. Michael F. Holick on Vitamin D. Available at: <http://www.vitaminhealth.org>.

- Institute of Medicine. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (1997). Available at: www.nap.edu/books/0309063507/html/index.html.
- National Institutes of Health/Office of Dietary Supplements. Dietary supplement fact sheet: Vitamin D. Available at: <http://ods.od.nih.gov/factsheets/vitamind.asp>.
- Vitamin D: Benefits for Bone Health and Beyond—A Conversation with Dr. Michael F. Holick. Available at: http://www.beverageinstitute.org/healthcare_professionals/vitamin_d_qa.shtml.
- Client handout: Straight Facts about Vitamin D. Available at: <http://www.beverageinstitute.org/vitamind/files/vitamin-d-straight-facts.pdf>.

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