VITAMIN D IN SCLERODERMA
By Arnold Postlethwaite, MD

Vitamin D Deficiency/Insufficiency and How to Correct It

Vitamin D is produced in the body by a series of chemical reactions, including ultraviolet B light from the sun, which is necessary to generate pre-vitamin D in the skin. An active form of vitamin D that regulates calcium absorption from the gastrointestinal (GI) tract is known as 1,25(OH)D_3. Measurements of serum levels of 25(OH)D most accurately reflect vitamin D status.

Vitamin D Serum Concentration
The American Endocrine Society defines vitamin D status by serum 25(OH)D concentration as follows:

Concentration	*Measurement*
Deficiency	<20 ng/ml
Insufficiency	21-29 ng/ml
Sufficiency	>30 ng/ml
Ideal	40-60 ng/ml
Safe upper limit	100 ng/ml

Vitamin D deficiency/insufficiency is very common. Chances are your vitamin D is low, unless you eat a lot of vitamin D-rich foods, such as wild salmon, sardines, mackerel, tuna or sun-dried mushrooms, or are exposed to sunlight on a frequent basis.

Some medications interfere with vitamin D metabolism and may promote deficiency of vitamin D, including antiepileptic drugs, HIV protease inhibitor drugs (e.g. ritonavir and saquinavir) and taxol.

Shopping Guide

Visit the USP website (http://www.usp.org/usp-verification-services/usp-verified-dietary-supplements/verified-supplements) to view vitamin D supplements with or without calcium, brands, and where you can purchase them.

If 25(OH)D is very low, it is common to prescribe vitamin D_2 (ergocalciferol) 50,000 units once a week for 6 to 8 weeks to rapidly replenish body stores. After that time, daily maintenance vitamin D_3 (cholecalciferol) supplements are taken. Vitamin D supplements are best absorbed when taken with a large meal. If over-the-counter rather than prescription vitamin D supplements are used, make sure they carry “USP” (U.S. Pharmacopeia) on the label, which attests to content and purity.

There is little difference in absorption of vitamin D supplements that are in powder form (tablet) or dissolved in an oil carrier (gel capsule) as long as there is no GI disease. In one study of patients with malabsorption due to cystic fibrosis, oil-based vitamin D supplements were absorbed as well as those in tablet form.

The Institute of Medicine (IOM) and the Endocrine Society offer different vitamin D recommendations, with the former recommending lower daily requirements for vitamin D than the latter. A summary of recommendations by these entities can be reviewed online.[1,2] The Endocrine Society considers the daily requirement to be 400 to 1000 international units (IU) for children and 1500 to 2000 IU of vitamin D for adults to attain vitamin D sufficiency, in other words to keep 25(OH) D levels above 30 ng/ml.

Scleroderma patients with GI involvement may require higher doses of supplemental vitamin D due to poor absorption. Maintaining optimal vitamin D levels in scleroderma patients with reduced kidney function may require management by a nephrologist. Excessive intake of vitamin D can raise levels of calcium in the blood, which can cause a number of serious problems including heart and kidney damage or failure.

Vitamin D and Human Diseases

Originally recognized as essential for bone health and prevention of rickets (a softening of bone) and osteomalacia (defective bone mineralization), vitamin D is now thought to be important for proper functioning of virtually all organs of the body. Numerous epidemiological studies demonstrate low levels of vitamin D are associated with worse outcomes of a wide spectrum of human diseases including stroke, heart attack, heart failure, cancer, asthma, Alzheimer's disease, Parkinson's disease, macular degeneration, infectious diseases, and major autoimmune diseases including rheumatoid arthritis, lupus, multiple sclerosis, psoriasis, inflammatory bowel disease, antiphospholipid syndrome, type I diabetes, autoimmune thyroid disease, undifferentiated connective tissue disease and systemic sclerosis.

Association of low vitamin D with worse outcome in these diseases does not establish a cause-and-effect relationship. However, animal models of some of these diseases including lupus, rheumatoid arthritis, multiple sclerosis, Alzheimer's disease, inflammatory bowel disease and type I diabetes are significantly improved by high-dose vitamin D therapy. Randomized clinical trials need to be conducted to determine whether certain doses of vitamin D given for prolonged periods of time would be safe and improve outcome of these diseases.

Vitamin D and Scleroderma

[1] Dr. Postlethwaite suggests searching online using the search term "drholic.com/table-of-recommended-dosages/."

[2] A full discussion of reasoning behind The Endocrine Society recommendations can be viewed online. Use the search term "endo-society.org/guidelines/final."

Several studies show 25(OH)D levels are lower in patients with scleroderma and associated with higher degrees of skin fibrosis, elevated pulmonary artery pressure, lower diffusing capacity for carbon monoxide and elevated inflammation markers. Patients with scleroderma are also at increased risk for osteoporosis, which can be improved with appropriate intake of vitamin D and calcium. Patients with scleroderma should have their 25(OH)D levels measured, and if below the ideal range of 40-60 ng/ml, should take, with the guidance of a physician, a vitamin D supplement to raise the level to the ideal range.

There is reason to suspect from animal models that vitamin D could improve autoimmunity and fibrosis in patients with scleroderma. Vitamin D has direct anti-fibrotic properties inhibiting collagen production by both cultured fibroblasts and in some animal models of heart and kidney fibrosis. Our recent report in the *Journal of Investigative Dermatology* demonstrates 1,25 $(OH)_2D_3$ and an analog of vitamin D, 17,20$(OH)_2$pD, discovered by Dr. Andrzej Slominski at the University of Tennessee, Memphis, which does not cause elevated calcium in the blood, inhibits TGF-β1 stimulated collagen and hyaluronan production by cultured scleroderma fibroblasts. Furthermore, we show in the same study that non-calcemic 17,20(OH)pD protected mice from developing experimental scleroderma.

Conclusion

If you have scleroderma, you are at increased risk for having vitamin D insufficiency/deficiency. Unless contraindicated by other conditions, such as sarcoidosis or lymphoma, raising your 25(OH)D level to greater than 30 ng/ml should be done under the supervision of a qualified health professional. Also, use only over-the-counter vitamin D_3 supplements with “USP” on the label. Finally, clinical trials are needed to determine whether high-dose vitamin D supplements improve fibrosis and other complications of scleroderma.

About the Author

Arnold Postlethwaite, M.D., is a board certified rheumatologist from The University of Tennessee Health Science Center. He also is a member of the Scleroderma Foundation’s National Medical Advisory Board. Earlier in 2012, he was named the organization’s “Doctor of the Year.” Dr. Postlethwaite and his wife are active volunteers with the Foundation’s Tennessee Chapter.