



A VITAMIN FOR ALL AGES

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It is apparent from other articles in this issue of the Journal that vitamin D does much more than just keep our bones strong. Indeed, vitamin D is not really a vitamin at all, but a steroid hormone precursor that is extremely important for multiple organ systems and at all ages. As a result, the Institute of Medicine (IOM) determined there was insufficient scientific information to establish a Recommended Dietary Intake (RDA) for vitamin D. Instead, the recommended intake is listed as an Adequate Intake (AI), which represents the daily vitamin D intake that should maintain bone health and normal calcium metabolism in healthy people. The IOM figure rises from 200 IU/day in those under 20 years, to 400 IU/day between 51-69 years, and 600 IU/day over age 70.

Ongoing studies are revealing so much new information about Vitamin D that this article will provide only a "taste" of the unfolding and exciting saga.

VITAMIN D IN THE GENERAL POPULATION

Because of Vitamin D's multiple effects, there are many who feel its AI should be increased to at least 1000 IU/day for the *general* population.

Consider the Following:

- In a 30 year cohort study of Finnish children, those who took 2000 IU/day of vitamin D had an 80% lower risk of developing Type I diabetes than those who took less.
- Hypertensive patients exposed to UVB radiation three times a week for three months experienced a 6mm drop in blood pressure, but UVA did not produce any change.
- Individuals who live above the 37°N latitudes for the first 10 years of life have a 100% increased risk of developing multiple sclerosis during their lifetime. Vitamin D at 400 IU/day reduces the risk of MS by 40%.
- Vitamin D intake is inversely associated with the risk of developing Rheumatoid Arthritis.

- There appears to be an inverse relationship between levels of 25-OH vitamin D, and the risk of colon and prostate cancer.
- Mortality from breast and prostate cancer is increased at higher latitudes. Researchers concluded from latitude variation that lack of UVB from sunlight accounts for about 25% of the breast cancer mortality rates in northern Europe.
- Vitamin D is necessary for normal cardiac function, and deficiency may be a contributing cause of heart failure.
- The depression associated with seasonal affective disorder (SAD), which responds to exposure to UVB light, may be related to Vitamin D deficiency.
- Hypovitaminosis D is associated with insulin resistance, metabolic syndrome and beta cell dysfunction in type 2 diabetes.

All of these remarkable and relatively new aspects of Vitamin D deficiency supplement our knowledge of the effects of Vitamin D on calcium and bone metabolism, including calcium absorption, parathyroid function, and osteoporosis.

What Constitutes Vitamin D Deficiency?

As detailed in the article by Reese on Vitamin D and Bone Health in this issue of the Journal, Vitamin D deficiency is defined as less than 20 ng/ml of 25-OH vitamin D, but many osteoporosis experts suggest that for bone health vitamin D levels should never be below 30 or 32 ng/ml. Indeed, any level below 20 ng/ml is considered a serious deficiency state. In addition, 25-OH D levels above 30 ng/ml maximize intestinal calcium absorption. Serum parathyroid hormone values begin to increase if 25-OH vitamin D levels are less than 30 ng/ml (Journal of Clinical Endocrinology and Metabolism Volume 90:3215, 2005). That study demonstrated vitamin D inadequacy in 52% of women already on therapy for prevention or treatment of osteoporosis!

In the elderly, there are several studies which show that levels above 36 to 40 ng/ml are required for best balance and muscle strength of the lower extremities.

Vitamin D Supplements

1. Vitamin D3 (cholecalciferol), which is found in fish oil, eggs, animal fat, and cod liver oil, and is equivalent to the vitamin D3 formed in our skin from UVB.
2. Vitamin D2 (ergocalciferol) from plants, which is found in fortified foods and some supplements, and is less biologically active than D3. Also, at higher doses D2 has greater potential for harm due to formation of toxic metabolites that D3 does not produce.

OSTEOPOROSIS IN MEN

Up to 30% of hip fractures and 20% of vertebral fractures occur in men, and in those aged 75 or older, the mortality of hip fractures is approximately 30% higher than in women! Bone mineral density is the single best predictor of fracture risk; other important risk factors include a history of fracture in a first degree relative, personal history of a fracture as an adult, cigarette smoking, and low body weight. Low blood testosterone levels, whether due to aging, medications, or surgery, substantially increase the risk of osteoporosis. People with renal disease have special risks of fracture, since parathyroid hormone levels increase as their glomerular filtration rate decreases.

At a conference of the American Society for Bone and Mineral Research, Dr. Robert Adler of Richmond, Va. reported a simple screening formula based on body weight alone, that can identify some men who are at low risk of having osteoporosis, and might not need a bone density scan:

Subtract a man's age from his *weight in kilograms*; multiply that number by 0.2; round the result to a whole number. If that number is 4 or greater, the man is unlikely to have osteoporosis, with a negative predictive value of about 97%. If the number is 3 or less, the screen's positive predictive value is about 34% – a risk of osteoporosis high enough to warrant doing bone density scans on all men with a number that low. For example, a 60 year old, 90 kg man would be

$$90 \text{ kg} - 60 \text{ years} = 30 \times 0.2 = 6$$

This calculation, based solely on weight, would make him unlikely to have osteoporosis. Add other risk factors (such as hyperthyroidism, steroid use, hypogonadism, renal or liver disease, malabsorption, smoking, hyperparathyroidism, epilepsy, myeloma, COPD, etc.), and this simple formula loses its reliability.

For a full discussion of osteoporosis in men, and prostate cancer, see the article by Sieber on this topic elsewhere in this issue.

VITAMIN D IN PREGNANCY

The official AI for pregnant women is still 400 IU, but a recent Lancet report (January 7, 2006) revealed that at age nine years, children of mothers who took vitamin D supplements during pregnancy had significantly larger bones and greater whole-body bone mineral density concentrations than children of mothers who didn't. As a result, many authorities are recommending increased amounts of vitamin D for pregnant women. Dr. Zalman Agus of the University of Pennsylvania recommends 800 IU/day of vitamin D, together with 1000 mg of calcium, during pregnancy.

Two recent articles in the American Journal of Clinical Nutrition offered differing opinions about vitamin D. The first, in May, 2004, showed that vitamin D deficiency is common; that the vitamin D "dose" in pregnancy and lactation is unknown, but is probably greater than 400 IU a day; and that some patients might even require more than 1000 IU/day to maintain normal concentrations. The second article, in December 2004, stated "there is no evidence of the benefit of supplementation during pregnancy above the amounts routinely required to prevent vitamin D deficiency." This statement seems to ignore the fact that we cannot state with certainty what constitutes "Vitamin D deficiency."

VITAMIN D IN INFANCY

In April 2003, the American Academy of Pediatrics (AAP) suggested giving Vitamin D to "all infants," particularly those who are breast fed, to help prevent abnormal bone mineralization, osteomalacia, and rickets. Of course, we should also try to increase bone density in those who don't have obvious rickets, to prepare for their mature years ahead.

All infant formulas sold in the United States contain added vitamin D, but according to the AAP, infants who drink less than 500 ml (17 ounces) of formula each day should also receive supplements. Vitamin D supplements are also recommended for children and teens who do not drink at least 500 ml each day of milk fortified with vitamin D.

In many specialties, new research is making it important to measure Vitamin D levels in a larger number of patients. The other discussions about Vitamin D in this special issue provide more insight into those considerations.

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