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Importance of Vitamin D for Adult Health

By Michael F. Holick, PhD, MD

VITAMIN D IS TAKEN FOR GRANTED AND ITS ROLE IN HEALTH IS underappreciated by both physicians and patients. Health care practitioners may be aware that vitamin D is associated with bone health in growing children, but little attention has been paid to the important role that vitamin D plays in maximizing and maintaining bone health in adults. Additionally, vitamin D ingestion may have implications for the prevention of many common cancers, hypertension, and Type 1 diabetes.[1]

Unlike most fat-soluble and water-soluble vitamins that are plentiful in a healthy diet, very few foods naturally contain vitamin D. Consumption of oily fish, such as salmon or mackerel, three to four times a week, or ingestion of cod liver oil on a daily basis provides vitamin D from natural sources. Some foods, including milk, some breads, and some cereals, also are fortified with vitamin D. A majority of our vitamin D requirement (80-95%) comes not from dietary sources but from sunlight exposure.[1,2]

Prevalence of Vitamin D Deficiency

Vitamin D deficiency is extremely common in the U.S. adult population.[1-7] In the epidermis, concentrations of provitamin D_3 are inversely related to age. Not surprisingly, more than half of elders (both free-living and those in nursing homes) are deficient in vitamin D. It has been assumed that young and middle-aged adults are not at risk for vitamin D deficiency. However, the lifestyle of many young and middle-aged adults is such that they are constantly at work indoors.

In addition, heightened awareness about sun exposure and skin cancer has resulted in the use of a sunscreen before exposure to sunlight. A sunscreen with an SPF of 8 will reduce vitamin D synthesis by 97.5%.[8] The CDC recently reported that 41% of African-American women ages 15-49 years throughout the United States were vitamin D deficient at the end of the winter.[9,10] Thirty-two percent of medical students and residents at our hospital were found to be vitamin D deficient at the end of the winter.[6]

VOLUME 5 • NUMBER 1 • JANUARY 2003 • PAGES 1-8

INSIDE

Consequences of Vitamin D Deficiency

Chronic vitamin D deficiency has subtle and insidious consequences for both bone health and overall health and well-being. Vitamin D deficiency results in decreased efficiency of intestinal calcium absorption. The body responds by increasing the production of parathyroid hormone, which in turn mobilizes precious calcium stores from the skeleton. Thus, vitamin D deficiency can precipitate and exacerbate osteoporosis. In addition, vitamin D deficiency causes osteomalacia, a mineralization defect of the skeleton. Unlike osteoporosis, which is a silent disease, osteomalacia often presents as isolated or generalized muscle aches, muscle weakness, and bone pain. It has been estimated that upward of 60% of patients with symptoms consistent with fibromyalgia (i.e., muscle and bone aches and pains) actually may have vitamin D deficiency.[1,11,12]

Exposure to tanning bed radiation resulting in a more than 100% increase in circulating concentrations of 25-hydroxyvitamin D [25(OH)D] was effective in treating hypertension.[13] It now is recognized that 1,25-dihydroxyvitamin D (the biologically active form of vitamin D) can down-regulate the renin-angiotensin system. It also is recognized that most organs in the body have vitamin D receptors (VDRs),[11-16] and that $1,25(OH)_2D$ is a potent down-regulator of cell growth. Furthermore, the prostate, colon, and breast, as well as other tissues, can make $1,25(OH)_2D_3$; the most likely purpose is for regulating cell growth.[17-19] There is strong evidence that vitamin D deficiency, especially in those who live at higher latitudes, increases the risk of death from many common cancers, including colon, breast, prostate, and ovarian cancer.[20-22] Garland et al observe that the risk of death from colon cancer was reduced by 50% if 25(OH)D was greater than 20 ng/mL.[20]

Vitamin D deficiency may predispose children to diabetes. The ß-islet cells of the pancreas have VDRs, and a recent study reported that the risk of developing Type 1 diabetes decreased by 80% in children who received vitamin D supplementation.[23]

The best method to determine vitamin D deficiency is to measure circulating concentrations of 25(OH)D. Patients who are vitamin D deficient will have a normal serum calcium due to their secondary hyperparathyroidism. Thus, the only measure of vitamin D status is a 25(OH)D level. $1,25(OH)_2D$ is of no value and indeed can be low, normal, or even elevated in a vitamin D insufficient patient.[1]

Treatment of Vitamin D Deficiency

The best method to treat vitamin D deficiency is to fill the vitamin D tank quickly by giving the patient 50,000 IU of vitamin D once a week for eight weeks.[8] A repeat 25(OH)D after the therapy often shows an increase of at least 100%. However, if this does not occur, the treatment should be repeated for an additional eight weeks. For those who cannot absorb vitamin D due to chronic malabsorption syndromes (e.g., chronic liver disease, cystic fibrosis, Crohn's disease, Whipple's disease, sprue), exposure to natural sunlight or tanning bed radiation[24,25] that has a component of ultraviolet-B radiation is suggested.[26,27]

The National Academy of Sciences recently recommended that the adequate intake of vitamin D be increased in middle-aged adults and elders. Current recommended dietary allowances are 200 IU for ages 1-50, 400 IU for ages 51-70, and 600 IU for those older than 70 years. We, and others, have estimated that in the absence of exposure to sunlight, the requirement is closer to 1,000 IU of vitamin D daily.[1,28-31] The goal is to maintain circulating concentrations of 25(OH)D of at least 20 ng/mL and preferably, between 30 and 50 ng/mL.

Because vitamin D deficiency is so common, I have recommended that as a preventive health measure, similar to measuring blood lipids, it is reasonable to check

Alternative Therapies in Women's Health, ISSN 1522-3396, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

VICE PRESIDENT/PUBLISHER: Brenda L. Mooney.

EDITORIAL GROUP HEAD: Lee Landenberger.

MANAGING EDITOR: Paula L. Cousins.

GST Registration Number: R128870672.

Periodical rate postage pending at Atlanta, GA.

POSTMASTER: Send address changes to *Alternative Therapies in Women's Health*, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $42. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Education guidelines, physicians have reported the following relationships with companies related to the field of study covered by this CME program. Ms. Ball, Dr. Cates, Dr. Fugh-Berman, Dr. Greenwood, Dr. Hardy, Dr. Keegan, Dr. Kronenberg, Dr. McKeown, and Dr. Massion have reported no relationships with companies related to the field of study covered by this CME program. Dr. Low Dog is a consultant for the Materia Medica Group. Dr. Pan is a researcher for Chitosan, Green Foods Inc., and BioCrave. Dr. Holick is a consultant for Nichols Institute/Quest Diagnostics and is on the speaker's bureau for Merck.

25(OH)D annually. This will ensure that patients are vitamin D sufficient, thus maximizing their bone health, as well as their overall health and well-being.[1,32,33] ❖

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The Role of Whole-Grain Foods in Chronic Disease

By Nicola M. McKeown, MD

RECENT OBSERVATIONAL STUDIES HAVE FOUND THAT diets rich in whole-grain foods appear to protect against several chronic diseases, including cardiovascular disease,[1,2] stroke,[3] Type 2 diabetes mellitus,[4,5] and certain cancers.[6,7] Whole-grain breads and breakfast cereals often are the major food contributors to whole-grain intake; however, other sources of whole grains include popcorn, cooked oatmeal, wheat germ, brown rice, whole-wheat pasta, and crackers.[2,4,8,9] Yet despite dietary recommendations to "choose a variety of grains daily, especially whole grains,"[10] current intakes remain low in the United States, with less than 8% of women consuming more than three servings of whole grains per day.[11]

Whole grains contain most of the intact or cracked kernel, which consists of the fiber-rich bran and germ layer. During the grain-refining process, the bran and germ layer are removed, leaving behind the starchy endosperm, which is ground into flour.[12,13] Refined grain foods contain lower amounts of vitamin E, fiber, and magnesium than whole-grain foods, but enrichment of refined flour with thiamin, riboflavin, niacin, iron, and folic acid has improved the nutritional value of refined grains.[13,14] Despite enrichment, however, there appears to be no evidence of a protective association between refined grain intake and risk of heart disease[1] or Type 2 diabetes.[4,5]

The exact mechanism by which whole grains may play a causal role in health remains unknown. It may depend on the presence or interaction of several biologically active nutrients found in whole grains, such as dietary fiber, folate, potassium, magnesium, and vitamin E, among other measured and unmeasured nutrients.[15] Current evidence suggests that the health benefits of whole grains are not attributed solely to a single nutrient, but rather to the synergistic effect of several constituents found in whole grains. In this review, emphasis will be placed on the observational data linking whole-grain intake to risk of chronic diseases among women, although similar health benefits have been observed in men.[16-18]

Cardiovascular Disease

The first prospective study to comprehensively examine the relationship between whole-grain intake and heart disease was conducted among 34,492 postmenopausal women in the Iowa Women's Health Study.[1] After controlling for age and dietary and cardiovascular risk factors, the relative risk (RR) of ischemic heart disease mortality was approximately one-third lower (RR 0.70, 95% confidence interval [CI] 0.5-0.98; P = 0.02 for trend) among those women eating three or more servings of whole-grain foods per day, compared to those women who rarely ate whole-grain foods.

Liu and colleagues also found that whole-grain intake was protective against coronary heart disease (CHD) in the Nurses Health Study.[8] In this cohort of 75,521 middle-aged women, 761 cases of CHD occurred over the period of 10 years. After adjustment for potential confounding factors, the multivariate adjusted RR of CHD was 0.75 (95% CI 0.59-0.95; P = 0.01 for trend) when the highest category was compared with the lowest category of whole-grain intake. In both prospective cohorts, the Iowa Women's Health Study and the Nurses Health Study, refined grain intake was not associated with coronary disease risk.

Liu and colleagues also examined the effects of reported whole-grain intake and risk of ischemic stroke among middle-aged women in the Nurses Health Study.[3] After adjustment for factors known or suspected to increase the risk of ischemic stroke, the authors found a strong inverse association between whole-grain intake, but not refined grain intake, and risk of ischemic stroke. The RR for ischemic stroke in the highest category of whole-grain intake (with a median intake of 2.7 servings/d) in comparison to the lowest category (median intake of 0.13 servings/d) was 0.69 (95% CI 0.50-0.98; P = 0.04 for trend).

Type 2 Diabetes

Whole-grain foods also may protect against the development of Type 2 diabetes, a disease that affects

approximately 600,000 Americans each year.[19] In the Iowa Women's Health Study, women consuming an average of three servings of whole grains per day had a 21% lower risk (RR 0.79, 95% CI 0.65-0.96) of developing diabetes than those with the lowest intake of whole grains.[4] Similarly, daily consumption of whole grains was associated with a lower risk of Type 2 diabetes in the Nurses Health Study.[5] In this study, the multivariate adjusted RR of Type 2 diabetes among women with the lowest (< 1 serving/d) to the highest (2.7 servings/d) intake of whole grains were 1.0, 0.84, 0.82, 0.72, 0.75 (P = 0.005 for trend).

Metabolic Risk Factors

The influence of whole grains on Type 2 diabetes and cardiovascular disease risk may be mediated through multiple pathways such as reducing blood lipids[20,21] and blood pressure,[22] enhancing insulin sensitivity, and improving blood glucose control.[23] Randomized clinical trials[20] and metabolic studies[21] have shown that oats and oat bran reduce total blood cholesterol. Jacobs et al found that serum total cholesterol and systolic blood pressure were reduced slightly among Norwegian women who consumed approximately three slices of whole-grain bread per day.[17] In the Framingham Offspring Study of 2,941 men and women, total cholesterol and LDL concentrations were significantly lower in the highest quintile category of whole-grain intake.[9]

Insulin sensitivity, as measured by a hyperinsulinemic euglycemic clamp, improved in overweight adults after six weeks on a whole-grain diet compared to a refined grain diet, independent of body weight.[24] In the Coronary Artery Risk Development in Young Adults Study (CARDIA) there was a mean difference of 1.0 uU/mL (7.18 pmol/L) in concentrations of fasting insulin between the least (< 2 servings/wk) vs. the most frequent consumers (> 9 servings/wk) of whole grains.[25] In the Framingham Offspring Cohort, fasting insulin concentrations were lower in those with a higher intake of whole-grain foods, comparing the lowest with the highest quintile of intake, (207 and 198 pmol/L, P = 0.002 for trend) after controlling for body mass index and other risk factors.[9]

Cancer

To date, there are few prospective studies examining the association between whole-grain intake and cancer risk. One prospective study found no significant association between whole-grain intake and risk of endometrial cancer among middle-aged women overall, although a moderate association was found among women who had never used hormone replacement therapy.[26] Among this subgroup, the RR of endometrial cancer was lower among women with the lowest (mean 1.8 servings/wk) to the highest (mean 25 servings/wk) intake of whole grains; RR were 1.0, 0.77, 0.70, 0.66, and 0.63 (P = 0.05 for trend). These findings need to be confirmed in future prospective studies.

In a review of 40 case-control studies,[6] dietary exposures associated with whole-grain intake (such as whole-grain bread or pasta, whole-meal bread, brown bread, or high-fiber cereal products) appeared to be protective against various cancers, particularly colon, stomach, and endometrial cancer.

Potential Mediating Nutrients in Whole Grain

Several nutrients found in whole grains may contribute to the lower risk of cardiovascular disease and Type 2 diabetes. Dietary fiber has been shown to reduce blood lipids and improve postprandial glycemic response and circulating insulin concentrations both in normal subjects and those with Type 2 diabetes.[27-30] Chandalia et al demonstrated that Type 2 diabetics consuming a high-fiber diet, compared with a low-fiber diet, had significantly lower fasting glucose and insulin concentrations at the end of the study.[31] Furthermore, epidemiological evidence suggests that fiber intake is associated inversely with fasting insulin[32] and that insoluble and cereal fiber intake significantly reduces the risk of Type 2 diabetes.[4,16,33]

Magnesium, a nutrient found in the outer bran of whole grains, has been linked to Type 2 diabetes. Clinical studies have reported that low plasma concentrations of magnesium are associated with insulin resistance and that supplementation with magnesium improves insulin sensitivity.[34,35] Furthermore, observational studies have found that high intakes of magnesium are associated with lower risk of Type 2 diabetes.[16,33]

Vitamin E, manganese, antioxidants, and lignans, among other measured and unmeasured nutrients, are integral factors of whole grains that may independently or synergistically contribute to disease prevention. Notably, the inverse association between whole-grain intake and coronary risk could not be attributed solely to nutrients found in whole grains.[1,8]

Glycemic Index

Due to their physical form, whole-grain foods are less easily digested and absorbed compared to refined grain products.[36] This elicits a much smaller postprandial response and consequently exerts less insulin demand on the pancreatic β-cells. The glycemic index (GI) was proposed to measure a carbohydrate's ability to raise blood glucose concentrations.[37] A low GI is characteristic of most whole-grain foods such as whole-grain breakfast cereals, brown rice, and oat-bran products.[38] Evidence is

accumulating to suggest that dietary glycemic load (the product of the GI value of a food and its carbohydrate content) is associated with risk factors for cardiovascular disease[39,40] and increased risk of coronary heart disease among women.[41]

Conclusion

Lack of consumer knowledge of the health benefits of whole grains and the difficulty encountered by consumers in identifying whole-grain products may explain, in part, the low whole-grain intake in the United States.[42] The current dietary guidelines for Americans include a table that specifies key ingredients to help identify whole-grain foods.[10] Given that whole-grain intake is one modifiable dietary risk factor that may lead to substantial health benefits, greater emphasis should be placed on increasing consumption of whole-grain foods. This could be achieved easily simply by substituting refined grain foods for whole-grain alternatives. For example, brown rice could be substituted for white rice, whole grain for white bread, wheat for white pasta, and popcorn for potato chips or other refined grain snacks. From a public health point of view, the current recommendation to increase whole-grain consumption is warranted and, based on the findings of several prospective studies, may lead to a reduction in the risk of several chronic diseases. ❖

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2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients; and
4. offer guidance to patients based on the latest science and clinical studies regarding alternative and complementary therapies.

CME Questions

1. Adequate vitamin D ingestion may prevent:
a. many common cancers.
b. hypertension.
c. Type 1 diabetes.
d. All of the above

2. What percentage of our vitamin D requirement comes from sunlight exposure?
a. 40-55%
b. 60-75%
c. 80-95%
d. 100%

3. Sources of whole-grain foods include:
a. popcorn.
b. cooked oatmeal.
c. brown rice.
d. All of the above

4. Which of the following foods confers a protective effect on the risk of heart disease and Type 2 diabetes?
a. Whole-grain foods
b. Refined grain foods
c. Enriched, refined grain foods
d. All of the above

With Comments by Mary Hardy, MD

Nutritional Status and Characteristics of Vegetarians

Source: Larsson CL, Johansson GK. Dietary intake and nutritional status of young vegans and omnivores in Sweden. *Am J Clin Nutr* 2002;76:100-106.

Objective: To compare the dietary intake and nutritional status of young Swedish vegans and omnivores.

Design: The dietary intakes of 30 vegans (15 males and 15 females; mean age 17.5 ± 1.0 years) and 30 sex-, age-, and height-matched omnivores were assessed with the use of a diet-history interview and validated by the doubly labeled water method and by measuring nitrogen, sodium, and potassium excretion in urine. Iron status and serum vitamin B_{12} and folate concentrations were measured in blood samples.

Outcomes: Vegans had higher intakes of vegetables, legumes, and dietary supplements and lower intakes of cake, cookies, candy, and chocolate than did omnivores. Vegans had dietary intakes lower than the average requirements of riboflavin, vitamin B_{12}, vitamin D, calcium, and selenium. Intakes of calcium and selenium remained low even with the inclusion of dietary supplements. There was no significant difference in the prevalence of low iron status among vegans (20%) and omnivores (23%). Two vegans with low intakes of vitamin B_{12} had low serum concentrations.

Conclusion: The dietary habits of the vegans varied considerably and did not comply with the average requirements for some essential nutrients.

Source: Larsson CL, et al. Lifestyle-related characteristics of young low-meat consumers and omnivores in Sweden and Norway. *J Adolescent Health* 2002;31:190-198.

Objective: To compare the lifestyle-related characteristics of low-meat consumers and omnivore adolescents in Sweden and Norway.

Methods: A total of 2,041 students, with a mean age of 15.5 years, completed a questionnaire. Information was collected about physical characteristics, and health; family situation; and social, exercise, alcohol, and tobacco habits. The response rate ranged from 83-95%. Statistical analyses included chi-square and Mann-Whitney U tests.

Results: There was no reported difference between low-meat consumers and omnivores with respect to alcohol use, smoking, weight, or amount of exercise. Female low-meat consumers more frequently used smokeless tobacco, reported having more sick days during the last year, attached less importance to "being healthy," and had been depressed more often than female omnivores. Male low-meat consumers reported, to a greater extent than male omnivores, having been tired without reason, having often had headaches, and having been depressed. Female low-meat consumers had parents with a higher average level of education than did female omnivores and more often spent time with friends after school.

Conclusion: In this study, vegetarianism or low-meat consumption is mainly a female phenomenon among adolescents. Adherence to a low-meat diet may not correlate with other health promotion practices among adolescents in Sweden and Norway.

Comments: Given the high rates of chronic cardiovascular disease and cancer in women, as well as the increasing rates of obesity in the United States, strategies that would start healthy life habits early would be of great interest to health care providers. The need for this is made more urgent by the emergence of chronic metabolic diseases such as Type II diabetes and hyperlipidemia in an increasingly obese adolescent population.

These two articles give us insight into the health risks and benefits of this practice as well as its ability to predict other healthy habits. First, most adolescents chose this diet for ethical or ecological, not health reasons. Thus, these subjects still were very likely to make typical food choices such as pizza, white bread, and other snack foods. In addition, other healthy habits, such as abstinence from alcohol or smoking or increasing exercise, were not more likely in these vegetarians.

On the positive side, these subjects were more likely to have a lower weight and body mass index (especially males) and have much higher intake of key foods such as fruits, vegetables, and legumes. In fact, a survey in the United States of 4,746 adolescents showed that the vegetarian teens were more likely than their omnivorous counterparts to actually meet the Healthy People 2010 objectives.

Much has been made of the inadequacy of vegetarian diets, especially the more restrictive or vegan version, for key nutrients. In this study, vegans had lower intake of riboflavin, vitamin B_{12}, vitamin D, calcium, and selenium. Iron intake was generally adequate. Supplementation did not fully correct these deficits. It would be important to encourage careful dietary planning and adequate supplementation for vegetarian or vegan teens and pregnant women to ensure adequate micronutrients.

Although teens do not choose this diet for their health, it is important to educate them about the benefits of this diet as a life-long choice. Diets high in these foods have been associated with lower risks of heart disease, stroke, and cancer (including breast cancer). Low-fat vegetarian diets also have been suggested for rheumatoid arthritis and fibromyalgia, two diseases more common in women. We therefore recommend that if you are seeing an adolescent or young woman who has made this lifestyle choice, educate her to ensure proper micronutrient consumption and re-enforce the health benefits that can accrue over a lifetime. ❖