

# The Whitehall-Robins Supplement

## A selection of recent findings in the field of nutrition

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### **Vitamin D deficiency and risk of cardiovascular disease.**

Vitamin D deficiency is highly prevalent in North America and worldwide. Measuring 25-hydroxyvitamin D (25-OH D) levels provides the best way to assess vitamin D nutritional status, as it is the principal storage form of vitamin D. One third to one half of otherwise healthy adults have low levels of 25-OH D. The main reasons for the low levels are limited synthesis by the skin due to limited sun exposure or pigmented skin and inadequate dietary intake of vitamin D. Although the role of vitamin D for the musculoskeletal system is well known, there is growing evidence that low levels of vitamin D may adversely affect the cardiovascular system. Vitamin D receptors are distributed in many tissues which includes vascular smooth muscle, endothelium, and cardiomyocytes. Several studies reported an association between lower vitamin D levels and renin activity, blood pressure, coronary artery calcification, and cardiovascular disease. Ecological studies have reported higher rates of heart disease and hypertension the further a population is away from the equator. This phenomenon could partially be explained by the higher prevalence of vitamin D deficiency in areas with less exposure to sunlight. The association between vitamin D status and the incidence of cardiovascular events was investigated prospectively, in a large, ambulatory, all white, community-based sample of individuals free of cardiovascular disease at baseline. Vitamin D status was assessed by measuring 25-OH D levels and prespecified thresholds were used to define degrees of deficiency [ $< 15$  ng/mL (37.5 nmol/l),  $< 10$  ng/mL (25 nmol/L)]. In this study, vitamin D deficiency was associated with an increased risk of cardiovascular disease. The higher risk was particularly strong among individuals with hypertension, in whom 25-OH D levels  $< 15$  ng/mL were associated with a 2-fold risk of cardiovascular events. The authors conclude "Vitamin D deficiency is associated with incident cardiovascular disease. Further clinical and experimental studies may be warranted to determine whether correction of vitamin D deficiency could contribute to the prevention of cardiovascular disease."

[Wang TJ, et al. *Circulation* 2008;117:503-511]

### **Calcium supplementation and bone mineral accretion in adolescent girls: an 18-mo randomized controlled trial with 2-y follow-up.**

The risk of osteoporosis could be reduced by increasing bone mass or decreasing the rate of bone loss with aging. Calcium supplementation of the diet can lead to greater bone mass and this can reduce the risk of fracture later in life. A recent meta-analysis cast some doubt as to whether calcium supplementation in children can benefit bone mineral density (BMD) in the spine and hip. This study investigated whether girls (mean age 12 years) with low calcium intake (mean intake 636 mg/day) benefited from taking a calcium supplement. The study was an 18 months randomized trial of calcium supplementation (providing 792 mg/day) with follow-up 2 years after supplement withdrawal. The main outcome measure was change in total-body, lumbar spine, and total hip bone mineral content (BMC) during supplementation and 2 years after supplement withdrawal. In this study, the supplemented group showed significantly greater gains in BMC over the 18 months study period. BMD change was significantly greater for all skeletal sites. Supplementation had most marked effects on rates on bone mass accretion during the first 6-12 months. In the 2 years after withdrawal of the supplement, the skeletal gains were no longer evident. The authors conclude "Calcium supplementation enhances bone mineral accrual in teenage girls, but the effect is short-lived. The likely mechanism for the effect of the calcium is suppression of bone turnover, which is reversed upon supplement withdrawal".

[Lambert HL, et al. *Am J Clin Nutr* 2008; 87:455-462]

### **Vitamin K and Vitamin D status: Association with inflammatory markers in the Framingham Offspring Study.**

Cardiovascular disease and osteoporosis are major contributors to morbidity and mortality particularly in the elderly. Inflammation is one of the characteristics of both conditions, and several proinflammatory cytokines are involved in vascular calcification and the regulation of bone remodeling. This may partially explain the simultaneous manifestation of bone loss and vascular calcification. Vitamins K and D have been implicated in cardiovascular and bone health as well as in the activity of proinflammatory cytokines. Vitamin K is a recognized cofactor in the  $\gamma$ -carboxylation of vitamin K-dependent proteins and a role for vitamin K in cardiovascular and bone health has been reported. The role of vitamin D for bone health is well-recognized, and there is growing evidence of a role for vitamin D in reducing the risk of cardiovascular disease. The investigators hypothesized that vitamin K and vitamin D status are inversely associated with measures of inflammation. This hypothesis was investigated in older men and women participating in the Framingham Offspring Study, an ongoing community-based cohort study. The investigators examined the associations between dietary and biochemical measures of vitamin K and vitamin D status and a panel of circulating proinflammatory biomarkers. In this study, there was an inverse association between vitamin K status (measured by plasma Phylloquinone level and Phylloquinone intake) and overall circulating markers of inflammation. Vitamin D status (measured by plasma 25-hydroxyvitamin D level) was not consistently associated with systemic inflammatory markers. The authors conclude "The observation that high vitamin K status was associated with lower concentrations of inflammatory markers suggests that a possible protective role for vitamin K in inflammation merits further investigation".

[Shea MK, et al. *Am J Epidemiol* 2008; 167:313-320]

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### **Egg Consumption in relation to cardiovascular disease and mortality: the Physicians' Health Study.**

Coronary artery disease (CAD) is the leading cause of death in the United States and Canada. Elevated LDL cholesterol is a risk factor for CAD, therefore, dietary guidelines recommended a reduction in dietary cholesterol intake to <300 mg/day to reduce the risk of CAD. Egg is a major source of dietary cholesterol and an average egg contains approximately 200 mg cholesterol. On the other hand, eggs contain other nutrients such as some minerals, folate, B vitamins, proteins, and monounsaturated fatty acids that could reduce the risk of CAD. Therefore, it is important to determine the net benefit or harm of egg consumption as a whole food instead of focusing on an individual component of eggs such as cholesterol. Limited and inconsistent data have been reported on the association between egg consumption and CAD. There is a large variability in individual response to dietary cholesterol. The investigators assessed prospectively whether egg consumption was associated with a greater risk of myocardial infarction (MI), stroke, and all-cause mortality in a cohort of 21,327 participants from Physician's Health Study I. In addition, the influence of type 2 diabetes and history of hypercholesterolemia as a possible effect modifiers of these associations was also assessed. In this cohort, infrequent egg consumption ( $\leq 6$  eggs/week) was not associated with MI, stroke, or total mortality, however, consumption of  $\geq 7$  eggs/week was associated with a modest but significantly greater risk of total mortality in this cohort. Egg consumption was associated with a greater risk of all cause-mortality in a dose response fashion among physicians with diabetes. There was a suggestive evidence for a greater risk of MI and stroke with egg consumption among male physicians with diabetes. In this cohort, baseline hypercholesterolemia status did not influence the relation between egg consumption and cardiovascular disease (CVD) mortality. The authors conclude "Infrequent egg consumption does not seem to influence the risk of CVD in male physicians. In addition, egg consumption was positively related to mortality, more strongly so in diabetic subjects, in the study population."

[Djousse L, et al. *Am J Clin Nutr* 2008; 87:964-969]

### **Suggested Readings**

#### **Dietary and supplementary betaine: acute effects on plasma betaine and homocysteine concentrations under standards and postmethionine load conditions in healthy male subjects.**

[Atkinson W, et al. *Am J Clin Nutr* 2008;87:577-585]

#### **Surrogate endpoints and emerging surrogate endpoints for risk reduction of cardiovascular disease.**

[Rasnake CM, et al. *Nutr Rev* 2008; 66:76-81]

#### **Is boron nutritionally relevant?**

[Nielsen FH. *Nutr Rev* 2008; 66:183-191]

#### **Changing dietary habits of ethnic groups in Europe and implications for health.**

[Gilbert PA, et al. *Nutr Rev* 2008; 66:203-215]

#### **Dietary intake related to prevalent functional limitations in midlife women.**

[Tomey KM, et al. *Am J Epidemiol* 2008; 167: 935-943]

#### **Dietary fat intake and risk of prostate cancer in the European Prospective Investigation into Cancer and Nutrition.**

[Crowe FL, et al. *Am J Clin Nutr* 2008;87:1405-1413]

#### **Dairy and weight loss hypothesis: an evaluation of the clinical trials.**

[Lanou AJ, et al. *Nutr Rev* 2008;66:272-279]

#### **Docosahexaenoic acid (DHA) supplementation in atopic eczema : a randomized, double-blind, controlled trial.**

[Koch C, et al. *Br J Dermatol* 2008; 158:786-792]

#### **The prevalence of folate-remedial MTHFR enzyme variants in humans.**

[Marini NJ, et al. *PNAS* 2008;105:8055-8060]

#### **Soy phytoestrogens: impact on postmenopausal bone loss and mechanisms of action.**

[Poulsen RC, et al. *Nutr Rev* 2008 ; 66 :359-3