

# The Whitehall-Robins Supplement

## A Selection of Recent Findings in the Field of Nutrition

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### **Folate intake and the risk of incident hypertension among US women.**

Hypertension is a risk factor for cardiovascular disease and renal failure. Hypertension increases with age and the prevalence is increasing with the aging of the population. Identifying risk factors for hypertension could lead to better preventive recommendations to combat hypertension. Folate has important beneficial effects on endothelial functions, however, there is limited information about the association of folate intake and the risk of hypertension. Two small randomized trials utilizing high-dose folic acid supplementation demonstrated a reduction in systolic and diastolic blood pressure. This association was investigated in 2 large ongoing cohort studies in the USA of younger and older women who were followed up for 8 years. During this follow up period, 7,373 incident cases of hypertension were identified in younger women and 12,347 cases in older women. After adjustment for multiple potential confounders, higher (at least 1,000 mcg) total folate intake (dietary + supplementary) was significantly associated with a reduced risk of hypertension. The magnitude of the association was greater in younger women. Most of the benefit seems to be related to supplementary folic acid. Among women who did not take folic acid-containing supplements, dietary folate intake of 400 mcg /d (the current RDA) or more was not significantly associated with risk of hypertension. The authors conclude "Higher intake of folate is associated with a decreased risk of incident hypertension, especially in younger women. Supplemental folic acid appears to be independently associated with a reduction in risk, and future trials should examine folic acid supplementation as a means of lowering blood pressure and preventing hypertension in younger women. These results may have important public health implications in the United States, given the ready availability and safety of folic acid supplementation and the clinical importance of hypertension."

[Forman JP, et al. *JAMA* 2005; 293: 320-329]

### **Homocysteine as a predictive factor for hip fracture in older persons.**

There is an increased prevalence of skeletal deformities in patients with homocystinuria, including osteoporosis, which increases the risk of hip fractures. This suggests that elevated homocysteine may be associated with osteoporosis and may increase the risk of hip fractures, probably through weakening bone by interfering with collagen cross-linking, hence increasing the risk of fractures. This association was examined in a group of men and women enrolled in the Framingham Study. Plasma total homocysteine were measured for 825 men and 1,174 women, from whom blood samples had been obtained between 1979 and 1982. The participants were followed from the time that the sample was obtained through mid 1998 (median follow-up of 12.3 years) for the occurrence of incident hip fractures. The mean plasma total homocysteine was 13.4  $\mu\text{mol}$  per liter in men and 12.1  $\mu\text{mol}$  per liter in women. In this study, plasma homocysteine concentrations were associated with risk of hip fractures for men and women. The risk of hip fracture was increased by 59% in men and by 26% for women for each increase in 1 SD of total homocysteine concentration. The apparent gender differences in the gradient of risk may be explained by the lower background incidence of hip fracture in men. The authors conclude, "If the relationship proves to be one of cause and effect, this finding may have important implications for the development of interventions to prevent hip fractures, because total homocysteine concentrations can be effectively and easily modified by dietary intake of folic acid and vitamins B6 and B12. Further population-based research is needed to examine the role of homocysteine in osteoporosis and osteoporotic fracture and to determine whether nationwide folic acid fortification of food will help to reduce rates of hip fracture in the United States."

[Mclean RR, et al. *N Eng J Med* 2004; 350:2042-2049]

### **Vitamin E and respiratory tract infections in elderly nursing home residents. A randomized controlled trial.**

Respiratory tract infections are one the most common infections in the elderly and are a major cause of morbidity and mortality. Infections tend to occur more frequently in nursing home residents than among independent-living elderly. It is recognized that aging is associated with a decline in immune responses. Nutritional status is an important factor of immune function and nutritional supplementation has been shown to improve immunity in the elderly. This one-year randomized, double-blind, placebo-controlled trial investigated the effect of vitamin E (200 IU) supplementation on respiratory tract infections in elderly nursing home residents. In this study, vitamin E had no significant effect on incidence or number of days for upper and lower respiratory tract infections. However, fewer persons in the vitamin E group acquired one or more respiratory tract infections. Participants in the vitamin E group had significantly fewer common cold and 20% lower risk of acquiring a cold compared to the group who took the placebo. Vitamin E had no significant effect on antibiotic use. The authors conclude "Common colds are frequent and associated with increased morbidity in this age group, and if confirmed, these findings suggest important implications for the well-being of the elderly. Future studies in elderly individuals should assess the effect of vitamin E supplementation on the common cold and incorporate microbiological methods to allow for assessment of the impact of vitamin E on specific types of respiratory pathogens."

[Meydani SN, et al. *JAMA* 2004; 292:828-836]

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**The SU.VI.MAX Study. A randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals.** It has been suggested that the inadequate intake of antioxidant vitamins and minerals increases the risk of cardiovascular disease and cancer. There are inconsistency and/or contradictory results between observational studies and randomized studies, which did not provide clear evidence of beneficial effect of antioxidants on the incidence of these conditions. This contradiction could be partially explained by the fact that the antioxidant doses used in most clinical trials were much higher than the highest levels of these antioxidants achievable by diet. The objective of this randomized, double-blind, placebo-controlled study was to test whether an adequate and well-balanced intake of antioxidant supplements reduces the incidence of cancers and ischemic cardiovascular disease in a middle-aged general population. In this study and after a median follow-up time of 7.5 years, antioxidant supplementation lowered total cancer incidence and all cause mortality in men but not in women. There was no major effect on the incidence of ischemic heart disease in men and women. The authors speculate that the ineffectiveness of supplementation in women may be due to their better baseline antioxidant status than men. The authors conclude “Our results suggest that an adequate and well-balanced supplementation of antioxidant nutrients, at doses that might be reached with a healthy diet that includes a high consumption of fruits and vegetables, had protective effects against cancer in men. Further investigations are needed to better understand the causes of the sex differences observed in our study.”  
[Hercberg S, et al. Arch Intern Med 2004; 164:2335-2342]

### Suggested Readings

Comparison of the Atkins, Ornish, Weight Watchers, and Zone Diets for weight loss and heart disease risk reduction. A randomized trial.  
[Dansinger ML, et al. JAMA 2005; 293:43-53]

Coffee consumption and risk of Type 2 Diabetes Mellitus among middle-aged Finnish men and women.  
[Tuomilehto J, et al. JAMA 2004; 291:1213-1219]

Serum homocysteine in relation to mortality and morbidity from coronary heart disease. A 24-year follow-up of the population study of women in Gothenburg.  
[Zylberstein DE, et al. Circulation 2004; 109:601-606]

Hypovitaminosis D is associated with insulin resistance and  $\beta$  cell dysfunction.  
[Chiu KC, et al. Am J Clin Nutr 2004; 79: 820-825]

Vitamin D intake and incidence of multiple sclerosis.  
[Munger KL, et al. Neurology 2004; 62:60-65]

Homocysteine, folate, and vitamin B-12 in mild cognitive impairment, Alzheimer disease, and vascular dementia.  
[Quadri P, et al. Am J Clin Nutr 2004; 114-122]

Dairy Foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies.  
[Cho E, et al. J Natl cancer Inst 2004; 96:1015-1022]

Dietary factors and the risk of incident kidney stones in younger women. Nurses' Health Study II.  
[Curhan GC, et al. Arch Intern Med 2004; 164:885-891]

Maternal ethnicity and risk of neural tube defects: a population-based study.  
[Ray JG, et al. CMAJ 2004; 171:343-345]

Effect of age on calcium absorption in postmenopausal women.  
[Nordin BEC, et al. Am J Clin Nutr 2004; 80:998-1002]