

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

### **The influence of folate and multivitamin use on the familial risk of colon cancer in women.**

There is evidence that a history of colorectal cancer in a first-degree relative is associated with an elevated individual's lifetime risk of colorectal cancer. It is believed that while genetic factors may determine the individual susceptibility for colon cancer, environmental factors such as diet or other lifestyle factors define which genetically susceptible individuals will ultimately develop colon cancer. Low intake of folate and methionine, as well as heavy alcohol consumption, have been associated with increased risk of colon cancer. In a prospective cohort study of nearly 90,000 women, the risk of colon cancer was estimated according to a history of colorectal cancer in a first-degree relative as well as categories of folate, methionine, and alcohol intake in this large cohort. During 16 years of follow-up, colon cancer was diagnosed in 535 women. In this study, moderate to heavy alcohol consumption increased the risk associated with family history, while the inverse association of folic acid with colon cancer was greater in women with a family history. Compared with women who consumed 200 µg or less of folic acid/day, the risk of colon cancer for those who consumed more than 400 µg was 20% lower in women without a family history and more than 50% lower in women with a family history. The influence of family history was markedly diminished by use of multivitamins containing folic acid, particularly with increasing duration of multivitamin use. Individuals with a family history who use multivitamin supplements for > 5 years may decrease their risk of colon cancer by almost 50%. High levels of dietary methionine also reduced the effect of family history. Although the mechanisms by which folate modify the effect of family history are unclear, folate and methionine are important factors in DNA methylation, whereas alcohol antagonizes methylation pathway. The authors conclude, "Our results suggest that higher intake of folate and methionine, regular use of multivitamins containing folate, and avoidance of moderate to heavy alcohol consumption, may diminish the excess risk of colon cancer associated with family history."

[Fuchs CS, et al. *Cancer Epidemiol Biomark Prev* 2002;11:227-234].

### **Vitamin D insufficiency in a population of healthy Western Canadians.**

Vitamin D is important for calcium absorption and low levels of vitamin D metabolites can lead to bone loss. Although the link between vitamin D and rickets is well known, there is recent recognition that pre-clinical vitamin D deficiency (vitamin D insufficiency) increases the risk of osteoporotic fractures. Vitamin D is available either through diet or is synthesized in the skin after sun exposure. There are limited dietary sources of vitamin D, therefore, it is thought that skin synthesis is the major source for this vitamin. Populations living in higher latitudes are more susceptible to seasonal vitamin D insufficiency. For example, it was shown that in Boston (latitude 42° N), sun irradiation is inadequate to generate previtamin D from November through February. Furthermore, in Edmonton (latitude 53° 30' N) this period extends from October through March. This study also assessed levels of vitamin D in a representative sample of healthy Canadians living in Calgary (latitude 51° 07' N). The investigators evaluated the prevalence of vitamin D insufficiency, defined as 25-hydroxyvitamin D [25(OH) D] less than 40 nmol/L, and seasonal variations in [25(OH) D], parathyroid hormone, as well as other biochemical indices, among the participants in this study. As expected, there were seasonal variations in the levels of [25(OH) D] and high prevalence of vitamin D insufficiency during fall and winter in this apparently healthy population. Thirty-four percent of the participants had [25(OH) D] levels less than 40 nmol/L, however, if the 80 nmol/L proposed cutoff value for vitamin D insufficiency is used, then virtually all participants (97%) would be assessed as having vitamin D insufficiency. Ironically, Calgary receives more hours of sunshine per year than any other Canadian city, particularly in the fall and winter. Therefore, the findings from this study suggest that the prevalence of vitamin D insufficiency might be higher among other Canadians. The current dietary recommendation for vitamin D is 200 IU/d for adults in general and 600 IU/d for those over the age of 70. Many scientists, however, are currently advocating that adult requirements should be at least 800 IU/d. The authors of the study conclude, "We documented a high prevalence of vitamin D insufficiency, which warrants consideration of dietary vitamin D supplementation."

[Rucker D, et al. *CMAJ* 2002;166:1517-1524]

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### **Occurrence of Omphalocele in relation to maternal multivitamin use: a population-based study.**

Omphalocele is a congenital anomaly of the abdominal wall that affects approximately 1 in 4000 to 6000 pregnancies. Omphalocele can present either as an isolated defect or more often in association with other anomalies that include neural tube defects. This suggests that these defects might share certain pathogenetic pathways or risk profiles. Several studies demonstrated that the use of multivitamin supplements and folic acid might reduce the risk of several birth defects, however such effect was not investigated for omphalocele. This association was evaluated in a population-based case-control study of infants born from 1968-1980 to mothers residing in metropolitan Atlanta. Compared to no use of multivitamin in the periconceptual period, the use of multivitamin supplements in the periconceptual period (regular use from 3 months before pregnancy through the first trimester of pregnancy) was associated with a 60% reduction in risk of omphalocele. Most of this risk reduction appears to be explained by certain phenotypic subgroups such as isolated omphalocele or omphalocele associated with selected defects (neural tube defects, hypospadias, and bladder/cloacal exstrophy). These findings suggest that, at least in some cases, these structurally distinct anomalies might share causal or developmental factors. There was an indication that there was little benefit in reducing the risk of this condition when multivitamin use began late in pregnancy (during the second or third month of pregnancy). The findings from this study await further replication from other studies. If confirmed, this should help in substantially reducing the risk of this malformation in this population group.

[Botto LD, et al. *Pediatrics* 2002;109:904-908]

### **Dietary Antioxidants, supplements and risk of epithelial ovarian cancer.**

Several epidemiologic studies suggest that higher consumption of fruits and vegetables and foods rich in antioxidants are associated with a reduced risk of many cancers, however, only few studies have examined the relationship between antioxidants and ovarian cancers. Moreover, these studies focused mainly on dietary sources of antioxidants, and no studies examined the association between the use of antioxidants from supplements and ovarian cancer risk. This case-control study examined the association between ovarian cancer risk and reported intake of antioxidant micronutrients from diet and/or supplements. In this study, higher intake of vitamins C (> 90 mg/d) and E (>30 mg/d) from supplements was protective, while vitamin A and  $\beta$ -carotene were not related to the risk of ovarian cancer. Consumption of antioxidants from dietary sources was unrelated to risk of ovarian cancer. In an analysis combining antioxidant intake from diet and supplements, vitamin C (>363 mg/d) and E (> 75 mg/d) were associated with a 55% reduced risk of ovarian cancer. It is worth mentioning that the above-mentioned levels of intake for vitamins C and E are well above the current daily dietary recommendations for both vitamins. Based on the findings from this study, the authors conclude that, "These findings support the hypothesis that antioxidant vitamins C and E from supplements are related to a reduced risk of ovarian cancer".

[Fleischauer AT, et al. *Nutr Cancer* 2002;40:92-98]

### **Suggested Readings**

#### **Dairy Consumption, obesity, and the insulin resistance syndrome in young adults. The CARDIA Study.**

[Pereira MA, et al. *JAMA* 2002;287:2081-2089]

#### **Coenzyme Q10 improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus.**

[Watts GF, et al. *Diabetologia* 2002;45:420-426]

#### **Declining rate of folate insufficiency among adults following increased folic acid fortification in Canada.**

[Ray JG, et al. *Can J Public Health* 2002;93:249-253]

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**Mercury, fish oils, and the risk of myocardial infarction.**

[Guallar E, et al. N Engl J Med 2002;347:1747-1754]

**Pregnancy planning: a determinant of folic acid supplements use for the primary prevention of Neural Tube Defects.**

[Morin P, et al. Can J Public Health 2002;93:259-263]

**Food habits of Canadians: lutein and lycopene intake in the Canadian population.**

[Johnson-Down L, et al. J Am Diet Assoc 2002;102:988-991]

**Dietary carotenoids, serum  $\beta$ -carotene, and retinal and risk of lung cancer in the Alpha-Tocopherol, Beta-Carotene Cohort Study.**

[Holick CN, et al. Am J Epidemiol 2002;156:536-547]

**The effect of diet on risk of cancer [Review].**

[Key TJ, et al. Lancet 2002;360:861-868]

**MTHFR 677  $\rightarrow$  T polymorphism and risk of coronary heart disease. A meta-analysis.**

[Klerk M, et al. JAMA 2002;288:2023-2031]

**Heme deficiency may be a factor in the mitochondrial and neuronal decay of aging.**

[Atamna H, et al. Proc Natl Acad Sci 2002;99:14807-14812]

**Folic Acid and the prevention of Neural Tube Defects (NTDs). Challenges and recommendations for public health.**

[Reish HS, et al. Can J Public Health 2002;93:254-258]

**Effect of multivitamin and vitamin A supplements on weight gain during pregnancy among HIV-1-infected women.**

[Villamor E, et al. Am J Clin Nutr 2002;76:1082-1090]

**Safety and pharmacokinetics of purified soy isoflavones: single-dose administration to postmenopausal women.**

[Bloedon L, et al. Am J Clin Nutr 2002;76:1126-1137]

**Mercury and the risk of coronary heart disease in men.**

[Yoshizawa K, et al. N Engl J Med 2002;347:1755-1760]

**Nut and peanut butter consumption and risk of type 2 diabetes.**

[Jiang R, et al. JAMA 2002;288:2554-2560]

**Coenzyme Q10 improves blood pressure and glycaemic control trial in subjects with type 2 diabetes.**

[Hodgson JM, et al. Eu J Clin Nutr 2002;56:1137-1142]

**Relative bioavailability of calcium-rich dietary sources in the elderly.**

[Martini L, et al. Am J Clin Nutr 2002;76:1345-1350]



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**Homocysteine and blood pressure in the third National Health and Nutrition Examination Survey, 1988-1994.**

[Lim U, et al. Am J Epidemiol 2002;156:1105-1113]

**Calcium and weight: clinical studies [Review].**

[Heaney RP, et al. J Am Coll Nutr 2002;21:152S-155S]

**Diet and risk of coronary heart disease and type 2 diabetes.[Review]**

[Mann JI. et al. Lancet 2002;360:783-789]

**Does it make a difference how and when you take your calcium? The acute effects of calcium on calcium and bone metabolism.**

[Karkkainen M, et al. Am J Clin Nutr 2001;74:335-342]

**Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk.**

[Fung TT, et al. Am J Clin Nutr 2001;73:61-67]

**Neural tube defects in relation to use of folic acid antagonists during pregnancy.**

[Hernandez-Diaz S, et al. Am J Epidemiol 2001;153:961-968]

**Determinants of plasma total homocysteine concentration in the Framingham offspring cohort.**

[Jacques PF, et al. Am J Clin Nutr 2001;73:613-621]

**Dietary potassium intake and risk of stroke in US men and women. National health and Nutrition Examination Survey I. Epidemiologic follow-up study.**

[Bazzano LA, et al. Stroke 2001;32:1473-1480]

**Lifestyle factors and plasma homocysteine concentrations in a general population sample.**

[De Bree A, et al. Am J Epidemiol 2001;154:150-154]

**Antioxidant vitamin status and carotid atherosclerosis in the elderly.**

[Gale GR, et al. Am J Clin Nutr 2001;74:402-408]

**Relative bioavailability of  $\beta$ -carotene from supplement sources.**

[Fuller CJ, et al. Nutrition Research 2001;21:1209-1215]