

# *Human Nutrition Research Monthly Update*

*Human Nutrition Research Department, Parsippany, NJ*

*Vol 3 No 4 – May 2001*

## **TABLE OF CONTENTS**

### **Antioxidants**

<b>Serum Carotenoids, <math>\alpha</math>-Tocopherol and Mortality Risk Among Dutch Elderly* .....</b>	<b>2</b>
<b>Plasma Vitamin C Levels Correlate with Brain Damage in Patients with Intracranial Hemorrhage or Head Trauma** ....</b>	<b>3</b>

### **Carotenoids**

<b>Case-Control Study of Carotenoid and Vitamin A intake and Ovarian Cancer .....</b>	<b>4</b>
<b>Dietary Tomato Paste Protects against UV Light-Induced Erythema in Humans* .....</b>	<b>5</b>

### **B-Vitamins**

<b>Association of Vitamins B<sub>6</sub>, B<sub>12</sub> and Folate with Lung Cancer Risk in Older Men* .....</b>	<b>6</b>
---	----------

# Serum Carotenoids, $\alpha$ -Tocopherol and Mortality Risk Among Dutch Elderly

---

## Article Title:

**Serum carotenoids,  $\alpha$ -tocopherol and mortality risk in a prospective study among Dutch elderly.**

## Article Commentary:

Several observational studies have associated  $\beta$ -carotene intakes and serum or adipose tissue levels inversely with cancer and cardiovascular disease. Other studies showed that  $\alpha$ -carotene intake was a better predictor for lung cancer than  $\beta$ -carotene and that lycopene from tomato intake or serum levels was inversely associated with prostate cancer and myocardial infarction. In addition, lower serum levels of lutein/zeaxanthin and  $\beta$ -cryptoxanthin were seen in cases with asymptomatic atherosclerosis than in the matched controls. In this current study of Dutch elderly (638 persons) over 7.2 years of follow-up, the authors examined the association between all-cause mortality and serum levels of six carotenoids ( $\beta$ -carotene,  $\alpha$ -carotene, lycopene,  $\beta$ -cryptoxanthin, lutein, zeaxanthin) and  $\alpha$ -tocopherol. They found that the strongest increase in mortality risk was associated with the lowest serum levels of  $\beta$ -cryptoxanthin, lutein, zeaxanthin and the sum of these oxygenated carotenoids. Significant inverse trends ( $p < 0.05$ ) were seen between all-cause mortality and serum levels of total carotenoids, sum of oxygenated carotenoids and  $\beta$ -cryptoxanthin with borderline significance for lutein. No association was seen for  $\alpha$ -tocopherol at the normal physiological range of these subjects. The inverse associations with vitamin E found in other studies are usually due to intake of high-dosed supplements. **(JG Elliott)**

## Article Abstract:

**Background:** Although  $\beta$ -carotene has shown inverse associations with chronic diseases involving free radical damage in observational epidemiological studies less attention has been paid to five other major carotenoids also showing antioxidant activity in vitro.

**Methods:** We studied the associations between 7.2-year mortality and serum levels of six carotenoids, and  $\alpha$ -tocopherol, measured in stored serum, sampled in 1991/1992 during a health survey among 638 independently living elderly subjects aged 65–85 years. Proportional hazards regression was used to estimate hazard ratios of all-cause mortality for the lowest tertiles of serum vitamins with the highest tertiles, adjusting for possible confounding effects.

**Results:** During a follow-up period of 7.2 years 171 elderly died. The adjusted hazard ratios for all-cause mortality for the lowest tertiles of vitamins compared with the highest tertiles were between 1.02 and 1.73. The strongest increase in mortality risk was seen for  $\beta$ -cryptoxanthin (1.52, 95% CI : 1.00, 2.32), lutein

(1.56, 95% CI : 1.05, 2.31) and zeaxanthin (1.32, 95% CI : 0.89, 1.97) and their sum (oxygenated carotenoids: 1.73, 95% CI : 1.12, 2.67). Tests for trend were significant ( $P < 0.05$ ) for all-cause mortality risk and serum levels of total carotenoids, oxygenated carotenoids and  $\beta$ -cryptoxanthin.

**Conclusions:** Our findings suggest that serum levels of individual carotenoids, particularly the oxygenated species are inversely associated with all-cause mortality and should be considered as candidates for further investigations.

**Full Citation:**

**De Waart FG, Schouten EG, Stalenhoef AFH, Kok FJ.** Serum carotenoids,  $\alpha$ -tocopherol and mortality risk in a prospective study among Dutch elderly. *Int J Epidemiol* 2001; 30:136-143.

# Plasma Vitamin C Levels Correlate with Brain Damage in Patients with Intracranial Hemorrhage or Head Trauma

---

## Article Title:

**Plasma vitamin c levels are decreased and correlated with brain damage in patients with intracranial hemorrhage or head trauma.**

## Article Commentary:

Based on a number of studies, increased production of free radicals and reactive oxygen species leading to oxidative stress may play an important role in the disease process of ischemic, hemorrhagic and traumatic brain injury. In humans, hemorrhage is associated with the release of hemoglobin-bound heme iron, which can participate in free radical reactions. In addition, the brain appears to be particularly vulnerable to oxidative lipid damage due to its high content of polyunsaturated fatty acids. In this study, plasma levels of vitamin C, uric acid, vitamin E and ubiquinol-10 were measured in 13 patients with intracranial hemorrhage and in 15 patients with head trauma on the day of the injury and every other day up to one week. The results with the 28 patients were compared to those of 40 healthy controls. Only vitamin C levels were lower in the patients than in the controls ( $p < 0.002$ ). Plasma vitamin C levels were found to be significantly inversely correlated with the severity of the neurological impairment ( $p < 0.02$ ) and with the major diameter of the lesion ( $p < 0.002$ ). The authors discuss prior studies in animals in which treatment with vitamin E and selenium before traumatic brain injury significantly protected the nervous tissue from progressive declines in white matter blood flow and treatment with vitamin C before trauma delayed post trauma spinal cord hydrofusion. Further work is needed to determine the early consequences of vitamin C depletion after brain damage in humans and the potential benefit of vitamin C supplementation in these patients. **(JG Elliott)**

## Article Abstract:

**Background and Purpose:** Free radical hyperproduction may play an important role in brain hemorrhage and ischemia/reperfusion injury. The aims of this study were to assess whether antioxidant depletion occurs after intracranial hemorrhage (ICH) and head trauma (HT) and to evaluate the relation between the diameter of the brain lesion, the degree of the neurological impairment, and any observed antioxidant changes.

**Methods:** We measured plasma levels of vitamin C (ascorbic acid, AA), uric acid (UA), vitamin E ( $\alpha$ -tocopherol), and ubiquinol-10 in 13 patients with ICH and 15 patients with HT on the day of the brain

injury and subsequently every other day up to 1 week. Patients were compared with 40 healthy control subjects.

**Results:** ICH and HT patients had significantly lower plasma levels of AA compared with healthy subjects, in contrast to plasma levels of UA,  $\alpha$ -tocopherol, and ubiquinol-10. AA levels were significantly inversely correlated with the severity of the neurological impairment as assessed by the Glasgow Coma Scale and the National Institutes of Health Stroke Scale. AA levels were also significantly inversely correlated with the major diameter of the lesion. In addition, mean plasma AA levels were lower in jugular compared with peripheral blood samples obtained from 5 patients.

**Conclusions:** These findings suggest that a condition of oxidative stress occurs in patients with head trauma and hemorrhagic stroke of recent onset. The consequences of early vitamin C depletion on brain injury as well as the effects of vitamin C supplementation in ICH and HT patients remain to be addressed in further studies.

**Full Citation:**

**Polidori MC, Mecocci P, Frei B.** Plasma vitamin c levels are decreased and correlated with brain damage in patients with intracranial hemorrhage or head trauma. *Stroke* 2001; 32:898-902.

# Case-Control Study of Carotenoid and Vitamin A intake and Ovarian Cancer

---

## Article Title:

**A population-based case-control study of carotenoid and vitamin A intake and ovarian cancer (United States).**

## Article Commentary:

Ovarian cancer ranks fourth as the most common cause of cancer death among women in the United States. Early detection is difficult and the disease is very invasive. Primary prevention has been the major focus of research since treatment options are limited. In several studies, the risk of ovarian cancer has been modestly lowered with greater intakes of  $\beta$ -carotene, retinol and vitamin A but the results have been inconsistent. In this study of 327 cases of ovarian cancer and 3129 controls from Massachusetts and Wisconsin, data collected by telephone on food consumption 5 years prior to diagnosis were used to quantify consumption of  $\alpha$ -carotene,  $\beta$ -carotene, lutein, zeaxanthin, retinol and total vitamin A. Subjects with the highest intakes of lutein/zeaxanthin had a 40% lower risk of ovarian cancer than those with the lowest intake. Intake of  $\alpha$ -carotene,  $\beta$ -carotene, retinol and total vitamin A was not related to risk. These results confirm and extend previous findings of an inverse association between carotenoids and ovarian cancer risk. **(JG Elliott)**

## Article Abstract:

**Objective:** To evaluate the association between dietary intake of carotenoids and vitamin A and the incidence of ovarian cancer.

**Methods:** We conducted a population-based case-control study of ovarian cancer in Massachusetts and Wisconsin. Incident cases diagnosed between 1991 and 1994 were identified through statewide tumor registries. We selected community controls at random from lists of licensed drivers and Medicare recipients; 327 cases and 3129 controls were included in the analysis. Data were collected by telephone interview, which included an abbreviated food and supplement list to quantify typical consumption of carotenoids (lutein/zeaxanthin, alpha-carotene, beta-carotene), retinol and total vitamin A at 5 years prior to diagnosis in cases, or to a comparable reference date in controls. Results were adjusted for age, state, and other risk factors.

**Results:** Participants with the highest dietary intake of lutein/zeaxanthin ( $>$  or  $=24,000$  microg/week) experienced a 40% lower risk of ovarian cancer (95% CI = 0.36-0.99) compared to those with the lowest

intake. Intake of alpha-carotene, beta-carotene, retinol and total vitamin A was unrelated to risk. Among foods, we observed non-significantly lower risks with high consumption of spinach, carrots, skim/lowfat milk and liver.

**Conclusion:** These results support previous findings suggesting an inverse relationship between carotenoid intake and ovarian cancer risk.

**Full Citation:**

**Berton ER, Hankinson SE, Newcomb PA, Rosner B, Willet WC, Stampfer MJ, Egan KM.** A population-based case-control study of carotenoid and vitamin A intake and ovarian cancer (United States). *Cancer Causes Control* 2001; 12:83-90.

# Dietary Tomato Paste Protects against UV Light-Induced Erythema in Humans

---

## Article Title:

**Dietary tomato paste protects against ultraviolet light-induced erythema in humans.**

## Article Commentary:

It has been reported that photooxidative stress is induced by UV irradiation via light-dependent formation of reactive oxygen species such as singlet oxygen, superoxide radical anion and peroxy radicals. These species are thought to affect light exposed tissues such as the skin and or the eye and produce disorders such as erythema, premature aging of the skin, photodermatosis, skin cancer, cataracts and age-related macular degeneration. The role of lycopene from a diet rich in tomatoes and tomato products in reducing the risk of cancer and cardiovascular disease has been covered in a number of reviews. This new study examines a role for lycopene from tomatoes in protecting against light-induced erythema (redness of the skin due to capillary dilatation). While it has already been shown that high doses of  $\beta$ -carotene protects skin against UV-induced erythema, this role has not been previously investigated for lycopene. In the test group (9 subjects) consuming 40 g tomato paste (~16 mg/day lycopene) along with 10 g of olive oil for 10 weeks, dorsal erythema induced with a solar simulator was 40% lower than in the control group (10 subjects) consuming olive oil only ( $p = 0.02$ ). No significant difference between groups was seen after 4 weeks of treatment. **(JG Elliott)**

## Article Abstract:

Carotenoids are efficient antioxidants capable of scavenging reactive oxygen species generated under conditions of photooxidative stress. It has been shown that supplementation with high doses of beta-carotene protects skin against UV-induced erythema. This study was designed to investigate whether intervention with a natural dietary source rich in lycopene protects against UV-induced erythema in humans. Tomato paste (40 g), providing approximately 16 mg/d of lycopene, was ingested with 10 g of olive oil over a period of 10 wk by 9 volunteers. Controls ( $n = 10$ ) received olive oil only. Erythema was induced by illumination of dorsal skin (scapular region) with a solar simulator at the beginning of the study, after 4 wk and after 10 wk. Intensity of erythema was measured by chromatometry; the  $a$ -value was determined directly before and 24 h after irradiation. Serum carotenoid levels were measured by HPLC. At the beginning of the study, carotenoid levels did not differ between the two groups. Serum levels of lycopene increased in supplemented subjects; the other carotenoids did not change significantly, and no

change in serum carotenoids was observed in the control group. At wk 10, dorsal erythema formation was 40% lower in the group that consumed tomato paste compared with controls ( $P = 0.02$ ; Wilcoxon-Mann-Whitney test). No significant difference between groups was found at wk 4 of treatment. The data demonstrate that it is feasible to achieve protection against UV light-induced erythema by ingestion of a commonly consumed dietary source of lycopene.

**Full Citation:**

**Stahl W, Heinrich U, Wiseman S, Eichler O, Sies H, Tronnier H.** Dietary tomato paste protects against ultraviolet light-induced erythema in humans. *J Nutr* 2001; 131:1449-1451.

# Association of Vitamins B<sub>6</sub>, B<sub>12</sub> and Folate with Lung Cancer Risk in Older Men

---

## Article Title:

Association of the B-vitamins pyridoxal 5'-phosphate (B<sub>6</sub>), B<sub>12</sub>, and folate with lung cancer risk in older men.

## Article Commentary:

Lung cancer is a major public health problem in Western countries. In Finland, approximately 1,500 new lung cancer cases are diagnosed among men each year and in the United States an estimated 172,000 new cases occurred in 1999. This prospective study was performed as a nested case-control study within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC) which was conducted in Finland between 1985 and 1993 involving 29,133 male smokers from 50 to 69 years of age. Serum from 300 lung cancer cases and 300 matched controls was analyzed for vitamins B<sub>12</sub>, B<sub>6</sub> and folate plus homocysteine. No significant associations were seen between serum folate, vitamin B<sub>12</sub> or homocysteine and lung cancer risk but a significantly lower risk of lung cancer occurred in men with higher serum B<sub>6</sub> levels. Male smokers in the highest quintile for vitamin B<sub>6</sub> intake had a 49% lower risk of lung cancer than those in the lowest quintile (p-trend = 0.02). This is the first prospective study to report an association between vitamin B<sub>6</sub> and lung cancer risk. Several possible mechanisms of action are discussed in to the report most of which relate to vitamin B<sub>6</sub>'s role in the transfer of a methyl group to tetrahydrofolate. Thus, lowered levels in the serum may lead to reduced DNA synthesis and impaired DNA repair. Must further work is needed to explore these mechanisms and confirm these observations. (JG Elliott)

## Article Abstract:

A nested case-control study was conducted within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort to test for associations between selected B-vitamins (folate, vitamin B<sub>6</sub>, vitamin B<sub>12</sub> and incident lung cancer. This trial was conducted in Finland between 1985 and 1993. Serum was analyzed for these nutrients and homocysteine among 300 lung cancer cases and matched controls (1:1). Odds ratios and 95% confidence intervals were determined in conditional and unconditional (controlling for the matching factors) logistic regression models, after adjusting for body mass index, years of smoking, and number of cigarettes smoked per day. No significant associations were seen between serum folate, vitamin B<sub>12</sub>, or homocysteine and lung cancer risk. The authors found significantly lower risk of lung cancer among men who had higher serum vitamin B<sub>6</sub> levels. Compared with men with the lowest vitamin

B<sub>6</sub> concentration, men in the fifth quintile had about one half of the risk of lung cancer (odds ratio = 0.51; 95% confidence interval: 0.23, 0.93; p-trend = 0.02). Adjusting for any of the other serum factors (folate, B<sub>12</sub>, and homocysteine) either alone or jointly did not significantly alter these estimates. This is the first report from a prospectively conducted study to suggest a role for vitamin B<sub>6</sub> in lung cancer.

**Full Citation:**

**Hartman TJ, Woodson K, Stolzenberg-Solomon R, Virtamo J, Selhub J, Barrett MJ, Albanes D.** Association of the B-vitamins pyridoxal 5'-phosphate (B<sub>6</sub>), B<sub>12</sub>, and folate with lung cancer risk in older men. *Am J Epidemiol* 2001; 153:688-694.