

LE Magazine August 1999

## MEDICAL UPDATES

### Studies from throughout the world that can help you live longer

[Click here to access the complete Medical Update Archives.](#)

[Click here to access the Complete Scientific Abstracts Online.](#)

## August 1999 Table Of Contents

1. **Damage to DNA is factor in cancer**
2. **Adenosine improves patients with chronic heart failure**
3. **N-acetylcysteine (NAC) inhibits DL oxidation**
4. **Dietary chitosan inhibits hypercholesterolemia and atherogenesis**
5. **Antioxidant status in asymptomatic hypercholesterolemic men**
6. **Curcumin inhibits nitric oxide synthase gene expression**
7. **PUFAs induce tumor cell death**
8. **Brussels sprouts prevent oxidative DNA damage**
9. **Caffeine and exercise**
10. **Cancer gene therapy**
11. **Adenosine protects against neuronal loss**
12. **Vitamin E concentrations fluctuate during the menstrual cycle**
13. **Melatonin inhibits cell proliferation**
14. **Effects of piracetam on the performance of rats**
15. **Inhibitory effects of curcumin on tumor development**
16. **Prevention of progression of prostate cancer**
17. **Vitamin C improves function of arteries**
18. **DHA protects small intestine**

### 1. **Damage to DNA is factor in cancer**

Full source: *Acta Biochimica Polonica*, 1998, Vol 45, Iss 2, pp 561-572

Free radicals can cause extensive DNA modifications. Some of the DNA base damage has been found to possess premutagenic properties and, if not repaired, can contribute to cancer growth. Elevated amounts of modified DNA bases have been found in cancerous and precancerous tissues as compared with normal tissues. Most of the drugs used in anticancer therapy are paradoxically responsible for causing secondary malignancies and some of them may generate free radicals. This study shows that exposure of cancer patients to therapeutic doses of ionizing radiation and anticancer drugs causes base modifications in genomic DNA of immune system cells. Some of this damage could lead to mutations in critical genes and ultimately to secondary cancers such as leukemias. Therefore free radical damage to DNA may lead to genetic instability, and metastatic potential of tumor cells.

### 2. **Adenosine improves patients with chronic heart failure**

Full source: *American Heart Journal*, 1998, Vol 136, Iss 1, pp 37-42

This study assessed the effects of adenosine accumulation of the blood circulation in patients with chronic heart failure. Adenosine has been shown to reduce pulmonary vascular resistance and to increase cardiac index in normal subjects and in patients with pulmonary hypertension or end-stage biventricular heart failure. Endogenous adenosine accumulation induced by ultra-low-dose dipyridamole infusion acutely improved the blood circulation profile, decreasing pulmonary and systemic vascular resistance and increasing cardiac index in patients with severe chronic heart failure.

### 3. **N-acetylcysteine (NAC) inhibits LDL oxidation**

Full source: *Atherosclerosis*, 1998, Vol 138, Iss 2, pp 319-327

We investigated the ability of NAC to inhibit LDL oxidation. NAC inhibited in vitro LDL oxidation induced by copper sulfate, 2,2'-azobis(2-amidinopropane) dihydrochloride, and UV light, and protected LDL against depletion of antioxidant vitamins. Glutathione was similarly effective against copper-mediated LDL oxidation. Sequential additions of NAC slowed down LDL oxidation more effectively than the initial addition of the same total dose. NAC reduced antibody formation during the oxidation of native LDL by oxidized LDL. NAC's effectiveness as an inhibitor of LDL oxidation is dependent on the timing sequence of the oxidation reaction, sequential additions of NAC, and the presence of previously oxidized LDL.

### 4. **Dietary chitosan inhibits hypercholesterolemia and atherogenesis**

Full source: *Atherosclerosis*, 1998, Vol 138, Iss 2, pp 329-334

Chitosan, the deacetylated form of chitin, is extracted from the shells of crustaceans. The strong positive charge carried by the chitosan molecule causes it to bind negatively charged substrates such as lipids. Orally administered chitosan binds fat in the intestine, blocking absorption, and has been shown to lower blood cholesterol in animals and humans. As a result it has been proposed that dietary supplementation with chitosan may inhibit the formation of atherosclerotic plaque. This hypothesis was tested on mice bred to develop atherosclerosis without surgical intervention, therefore providing an ideal model in which to study the effects of dietary chitosan on both blood cholesterol and atherosclerosis. Animals were fed for 20 weeks on a diet containing 5% chitosan or on a control diet. Blood cholesterol levels were significantly lower in the chitosan fed animals throughout the study, and at 20 weeks were 64% less than in the animals not receiving the chitosan. When the area of aortic plaque in the two groups was compared, a highly significant inhibition of atherogenesis, in both the whole aorta and the aortic arch, was observed in the chitosan fed animals-42% and 50%, respectively. Body growth was significantly greater in the chitosan fed animals. This study is the first to show a direct correlation between lowering of serum cholesterol with chitosan and inhibition of atherogenesis, and suggests that the chitosan could be used to inhibit the development of atherosclerosis in individuals with hypercholesterolaemia.

### 5. **Antioxidant status in asymptomatic hypercholesterolemic men**

Full source: *Atherosclerosis*, 1998, Vol 138, Iss 2, pp 375-381

An imbalance between antioxidant and oxidant-generating systems leading to an oxidative stress has been proposed in the disease of atherosclerosis. This study investigated the antioxidant status in 60 asymptomatic hypercholesterolemic (HC) men compared with 48 normocholesterolemic (NC) men. Hypercholesterolemic subjects had a significantly lower red blood (RBC) cell vitamin E content in spite of their normal total blood and HDL vitamin E concentrations. Activities of endogenous antioxidant superoxide dismutase and glutathione peroxidase were not significantly different between groups. The resistance of RBCs to an oxidative stress by the extent of RBC destruction induced by a water-soluble compound was significantly decreased in HC men compared with NC subjects. These results demonstrate an altered antioxidant status of RBC in asymptomatic HC men associated with an increased RBC susceptibility to an oxidative stress. The measure of the vitamin E content in RBC might be the most sensitive parameter for evidencing early oxidative stress.

### 6. **Curcumin inhibits nitric oxide synthase gene expression**

Full source: *Biochemical Pharmacology*, 1998, Vol 55, Iss 12, pp 1955-1962

Curcumin is a naturally occurring, dietary polyphenolic phytochemical that has been shown to inhibit cancer among other things. With respect to inflammation, it inhibits the activation of free radical activated transcription factors, and reduces the production of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF), interleukin-1 and interleukin-8). Upon inflammation, an enzyme is induced (nitric oxide synthase) that catalyzes the production of nitric oxide (NO), a molecule that may lead to carcinogenesis. In this study in mouse immune cells curcumin reduced the production of nitric oxide in a concentration-dependent manner. Furthermore, curcumin reduced nitric oxide expression in the livers of mice by 50-70%. Investigators were able to obtain potency at nanomoles per gram of body weight, even though it is believed that curcumin needs to be given at dosages that are unattainable through diet to produce an in vivo effect. Inhibition was not observed in mice that were fed ad lib., suggesting that food intake may interfere with the absorption of curcumin.

## 7. PUFAs induce tumor cell death

Full source: *Biochemistry and Molecular Biology International*, 1998, Vol 45, Iss 2, pp 331-336

The effects of polyunsaturated fatty acids (PUFAs) on the induction of apoptosis were studied over a 24 hour period in human larynx tumour cells. While oleic and linoleic acids had little effect on the apoptosis (cell death), the polyunsaturated fatty acids alpha-linolenic, gamma-linolenic, arachidonic, eicosapentaenoic and docosahexaenoic acids all induced apoptosis, beginning at similar to 6 hours after fatty acid exposure. By 24 hours after exposure, the apoptosis had reached as much as 19% in the presence of docosahexaenoic or alpha-linolenic acid. The inhibition of the enzyme mitochondrial carnitine palmitoyltransferase I (CPT I) and subsequent fatty acid oxidation by polyunsaturated fatty acids leads to a significant increase in apoptosis, which also suggests that CPT I may be involved in the processes of programmed cell death in human tumour cells.

## 8. Brussels sprouts prevent oxidative DNA damage

Full source: *Free Radical Research*, 1998, Vol 28, Iss 3, pp 323-333

The cancer preventive effects of cruciferous vegetables could be related to protection from mutagenic oxidative DNA damage. In this study, excess oxidative DNA damage was induced by 2-nitropropane (2-NP 100 mg/kg). Four days oral administration of 3 grams of cooked Brussels sprouts homogenate reduced oxidative DNA damage by 31%. However, raw sprouts, beans and endive, isolated indolyl glucosinolates and breakdown products had no significant effect. An aqueous extract of cooked Brussels sprouts (corresponding to 6.7 g vegetable per day for 4 days) decreased the spontaneous 8-oxodG excretion (a measure of oxidative damage) from 92 to 52 pmol per 24 hours. After administration, the 8-oxodG excretion was increased to 132 pmol/24 hours whereas pretreatment with the sprouts extract reduced this to 102 pmol/24 hours. The spontaneous level of 8-oxodG in nuclear DNA from liver and bone marrow was not significantly affected by the sprouts extract whereas the level decreased by 27% in the kidney. In the liver the 8-oxodG levels increased in nuclear DNA 8.7 and 3.8 times 6 and 24 hours after dose, respectively. The sprouts extract reduced this increase by 57% at 6 hours whereas there was no significant effect at 24 h. In the kidneys the 8-oxodG levels increased 2.2 and 1.2 times 6 and 24 hours after dose, respectively. Pretreatment with the sprouts extract abolished these increases. Similarly, in the bone marrow the extract protected completely against a 4.9-fold induced increase in the 8-oxodG level. These findings demonstrate that cooked Brussels sprouts contain bioactive substance(s) with a potential for reducing the physiological as well as oxidative stress induced oxidative DNA damage in rats. This could explain the suggested cancer preventive effect of cruciferous vegetables.

## 9. Caffeine and exercise

Full source: *Journal of Applied Physiology*, 1998, Vol 85, Iss 1, pp 154-159

This study examined the acute effects of caffeine on the cardiovascular system during dynamic leg exercise. Ten trained, caffeine-naive cyclists (7 women and 3 men) were studied at rest and during bicycle ergometry before and after the ingestion of 6 mg/kg caffeine or 6 mg/kg fructose (placebo) with 250 ml of water. Measurement of mean arterial pressure (MAP), forearm blood flow (FBF), heart rate, skin temperature, and rectal temperature and calculation of forearm vascular conductance (FVC) were made at baseline and at 20-min intervals. Before exercise, caffeine increased both systolic blood pressure (17%) and MAP (11%). During dynamic exercise, caffeine slowed the increase in FBF (53%) and FVC (50). Systolic blood pressure and MAP were higher during exercise plus caffeine; however, these increases were secondary to the effects of caffeine on resting blood pressure. No significant differences were observed in heart rate, skin temperature, or

rectal temperature. These findings indicate that caffeine can alter the cardiovascular response to dynamic exercise in a manner that may modify regional blood flow and conductance.

#### 10. **Cancer gene therapy**

Full source: *Journal of Clinical Oncology*, 1998, Vol 16, Iss 7, pp 2548-2556

Molecular genetics has spawned an impressive outpouring of insights into the biology of abnormal tissue growth and the host-tumor relationship. This deeper understanding of cancer pathogenesis presents an opportunity to develop therapeutic agents with improved selectivity for cancer cells. One promising approach involves gene therapy, which is the introduction of genetic material into a patient's tissues with the intent to achieve therapeutic benefit. A number of gene transfer systems have been designed that enable the generic modification of target cells, with varying strengths and limitations. Several strategies to exploit gene transfer as a tool to target specific molecular defects intrinsic to cancer cells, enhance tumor chemosensitivity, and augment tumor immunogenicity are under intensive investigation. A number of these approaches have entered initial clinical testing and already provide intriguing new information about the biology of cancer in patients. The full article highlights the critical issues and controversies that underscore preclinical experiments in cancer gene therapy, discuss some of the preliminary findings from the first wave of clinical trials, and speculate about the prospects that cancer gene therapy will change the way that cancer medicine is practiced.

#### 11. **Adenosine protects against neuronal loss**

Full source: *Journal of Neurotrauma*, 1998, Vol 15, Iss 7, pp 473-483

Intraspinal injection of the nonspecific inhibitor of nitric oxide synthase N-nitro-L-arginine methyl ester (L-NAME) results in a dose-dependent loss of neurons in the rat spinal cord. This effect is thought to result from a reduction in basal levels of nitric oxide (NO), thereby producing an ischemic reaction secondary to vasoconstriction and reduced spinal cord blood flow (SCBF). An important component of this ischemic reaction is the release of excitatory amino acids and the initiation of an excitotoxic cascade. In the present study, microinjections of adenosine were made in the spinal cord to evaluate the neuroprotective effects. Injections of L-NAME produced a unilateral loss of spinal neurons, a local inflammatory response. Adenosine significantly reduced the area of L-NAME-induced neuronal loss, and a synergistic effect was observed when ineffective doses of these adenosine agonists were co-injected with L-NAME. The results have shown that adenosine provides significant neuro protection against induced neuronal loss, presumably by inhibiting ischemia induced release of excitatory amino acids. Finally, the results provide support for the continued investigation of specific adenosine agonists as therapeutic agents directed against the ischemic and excitotoxic components of spinal injury.

#### 12. **Vitamin E concentrations fluctuate during the menstrual cycle**

Full source: *Journal of Nutrition*, 1998, Vol 128, Iss 7, pp 1150-1155

Because premenopausal women experience cyclic fluctuations of plasma carotenoids and their lipoprotein carriers, it was hypothesized that plasma vitamin E fluctuates by phase of the menstrual cycle. Twelve free-living women, with a confirmed ovulatory cycle, were given a controlled diet for two consecutive menstrual cycles. Blood was drawn during the menses, early follicular, late follicular and luteal phases to simultaneously measure serum hormones, plasma lipoproteins and vitamin E, and vitamin E distribution in the lipoprotein fractions. Blood vitamin E concentrations were significantly lower during menses than during the luteal phase by similar to 12% in each controlled diet cycle. Adjustment for serum cholesterol and triglyceride concentrations did not alter these findings. The distributions of vitamin E in lipoprotein cholesterol fractions were not significantly different by menstrual phase. From 61 to 62% of vitamin E was concentrated in the LDL fraction, with another 9-14% in HDL2, 17-22% in HDL3 and the remaining 6-8% in VLDL + LDL. There were no significant differences in lipoprotein cholesterol fractions by menstrual phase, except for a significant increase in HDL2 cholesterol from the early follicular to the late follicular phase. Fluctuations of vitamin E concentrations by phase of the menstrual cycle should be taken into consideration in future research concerning premenopausal women and the risk of chronic disease.

#### 13. **Melatonin inhibits cell proliferation**

Melatonin has been shown to prevent induced apoptosis in undifferentiated and neuronal cells. This neurohormone is also able to prevent the decrease in the mRNA for antioxidant enzymes. Although the antioxidant capability of melatonin seems to be clearly implicated in its anti-apoptotic activity, literature suggests that its antiproliferative property could also be involved in its prevention of apoptosis. This study demonstrates that melatonin is able to inhibit cell proliferation in undifferentiated cells, decreasing cell number and the total amount of DNA, and the mRNA for the histone H4, which are known to increase during DNA synthesis. Melatonin does not decrease the number of cells in nonproliferating cells, indicating that it does not cause cell death. Also this study shows that other inhibitors of cell proliferation, as well as other antioxidants, are able to mimic the anti-apoptotic effect of melatonin. This is interpreted to mean that melatonin acts by both mechanisms to inhibit artificially induced apoptosis, and the findings support the hypothesis of a relationship between oxidative stress and regulation of the cell cycle.

#### 14. **Effects of piracetam on the performance of rats**

Full source: *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 1998, Vol 22, Iss 1, pp 211-228

The influence of acute and chronic treatment with piracetam on spatial working memory of rats was examined. Injections of scopolamine (a hypnotic and sedative) significantly reduced the percentage of correct responses. The impairment of correct choices was reversed after chronic treatment with piracetam (250 mg/kg). Scopolamine also induced an increase of repetitive errors (a measure of perseverance), and the chronic treatment with piracetam caused full reversal of this increase. These results represent the first observation of a piracetam induced reversal of scopolamine impairments in a working memory test. In normal animals not treated with scopolamine, acute injection of piracetam had no effect compared to saline injected controls, but chronic treatment with piracetam significantly enhanced working memory performance. The resulting data suggest that piracetam has distinct effects on working memory depending on the mode of treatment (acute versus chronic).

#### 15. **Inhibitory effects of curcumin on tumor development**

Full source: *Journal of Cellular Biochemistry*, 1997, Suppl. 27, pp 26-34

In this study, curcumin, the naturally occurring yellow pigment in turmeric and curry, inhibited tumor development during both initiation and post-initiation periods in experimental animals. Topical application of curcumin inhibited formation of DNA adducts in the skin. It also inhibited induced increases in the percent of skin cells in synthetic (S) phase of the cell cycle. In addition, curcumin has been shown to reduce the following: skin inflammation, skin DNA synthesis, ornithine decarboxylase (ODC) mRNA level, ODC activity, hyperplasia (increase in number of cells in a tissue or organ), formation of c-Fos, and c-Jun proteins, hydrogen peroxide, and the oxidized DNA base 5-hydroxymethyl-2'-deoxyuridine (HmdU). Curcumin is a strong inhibitor of arachidonic acid-induced edema (excess of watery fluid) of mouse ears and skin cyclooxygenase (a platelet enzyme that converts arachidonate acid and H<sub>2</sub>O<sub>2</sub> to endoperoxides and thromboxane prostaglandins) and lipoxygenase (oxidizes unsaturated fatty acids) activities. Topical application of curcumin inhibits chemical induced tumor initiation and tumor promotion in mouse skin. Dietary curcumin (commercial grade) inhibits chemical-induced forestomach cancer, duodenal cancer, and colon cancer.

#### 16. **Prevention of progression of prostate cancer**

Full source: *Cancer*, 1998, Vol 82, Iss 3, pp 531-537

This study determined whether latent rat prostate carcinoma can be prevented as a result of the prophylactic effects of a 5-alpha reductase inhibitor (e.g., finasteride) and a pure anti-androgen (e.g., casodex). (An anti-androgen inhibits effects of androgenic hormones that stimulate male characteristics, e.g. testosterone). Rats were administered a carcinogen (DMAB) for the first 20 weeks and testosterone propionate throughout the 60-week study. Finasteride and casodex were administered orally during the last 40 weeks of the study. The incidence of visible prostate carcinoma was 51% in the positive control group, 40% in the finasteride 5 mg/kg group, 16.7% in the finasteride 15 mg/kg group, 20% in the casodex 15 mg/kg group, 14.3% in the casodex 30 mg/kg group, and 0% in the casodex 60 mg/kg group. Finasteride and casodex significantly inhibited of macroscopic (visible) rat prostate carcinogenesis, although both drugs showed insufficient

prevention of carcinogenesis at the microscopic level. These findings indicate that, in clinical medicine as well, such drugs may also be able to prevent the progression of latent prostate carcinoma to life-threatening disease.

#### 17. **Vitamin C improves function of arteries**

Full source: *Circulation*, 1998, Vol 97, Iss 4, pp 363-368

Chronic heart failure (CHF) is associated with endothelial cell dysfunction. These cells line the cavities of the heart. There is evidence for increased free radical formation in CHF. This raises the possibility that nitric oxide (NO) is inactivated by the free radicals, thereby impairing endothelial function. Nitric oxide causes dilation of the blood vessels and is derived from L-arginine in endothelial cells, macrophages, neutrophils, platelets, etc. It is a gaseous mediator of cell-to-cell communication formed in bone, brain, endothelium, granulocytes, pancreatic cells, and peripheral nerves. The short-lived NO molecule is manufactured by tissues, and plays a role in various processes, primarily by interacting between endothelium and smooth muscle cells. It is involved in dilation of blood vessels and penile erection, and possibly affects immune reactions and memory. Shortage or inactivation of NO may contribute to high blood pressure and formation of atherosclerotic plaque. An excess of NO, which is a free radical, is toxic to brain cells, and NO is also responsible for the often fatal, drop in blood pressure accompanying shock from abdominal or pelvic infection. This study tested the hypothesis that (NO) is inactivated by free radicals, by determining the effect of vitamin C (25 mg/min) on impaired dilation in patients with CHF. It consisted of 15 patients with CHF and 8 healthy volunteers. An excitotoxic amino acid was used to inhibit endothelial synthesis of nitric oxide. The result was that vitamin C restored impaired endothelium in patients with heart failure after both intra-arterial administration (13.2% vs. 8.2%) and oral therapy (11.9% vs. 8.2%) for 4 weeks. The portion of the dilation mediated by nitric oxide (which was inhibited by the excitotoxic amino acid) was increased after acute as well as after chronic treatment (CHF baseline: 4.2%, acute: 9.1%; chronic: 7.3%; normal subjects: 8.9%). Thus, vitamin C improved arterial dilation in patients with CHF as the result of increased availability of nitric oxide. This supports the concept that endothelial cell dysfunction in patients with CHF is, at least in part, due to accelerated degradation of nitric oxide by free radicals.

#### 18. **DHA protects small intestine**

Full source: *Life Sciences*, 1998, Vol 62, Iss 15, pp 1333-1338

Oral administration of methotrexate (MTX) to mice causes the damage of the small intestine. The permeability of a typically poorly absorbable compound (FITC-dextran) through the small intestine increased in the MTX-treated mice. However, oral administration of DHA (docosahexaenoic acid) ethyl ester protected the small intestine from the increase in the small intestinal permeability induced by the MTX treatment. The MTX treatment also decreased retinol concentration in the blood of mice and the coadministration of DHA maintained its concentration to the level of mice untreated with MTX. The present study showed that DHA protected the small intestine of mice from the MTX-induced damage.

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.