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The Exercise Paradox: Why Staying Fit Increases Your Need for Antioxidants

Most people know that physical activity is good for health. However, in one of the ironies of biology, regular and strenuous exercise can increase formation of dangerous free radicals. These rogue molecules damage cell membranes, proteins, and deoxyribonucleic acid (DNA)—the material that forms your genes. The long-terms consequences may be faster aging and an increased risk of cancer.

The solution, according to a top antioxidant researcher, is not to become an exercise-avoiding couch potato. It's to make sure you take your antioxidants, including vitamins E and C and coenzyme Q10.

Lester Packer, PhD, of the University of California, Berkeley, has conducted extensive research on how exercise stimulates production of free radicals and how antioxidants minimize their damage. He reviewed his findings and those of other researchers in a recent article in the *Journal of Sports Sciences*.

Normally, "there is a delicate balance between oxidants [free radicals] and antioxidants in biological systems," Packer wrote. Both are essential for converting food into energy. Yet exercise, like disease, can tip the balance toward excessive free radical production.

Most free radicals—molecules missing an electron are produced when cells burn glucose and fats for energy. This energy is carried by electrons, which are largely contained within chemical reactions and by antioxidants, such as vitamins E and C. However, during exercise, oxygen consumption can increase 10-20 times, with electrons leaking beyond the energy-producing chemical reactions. When they do, they can overwhelm the body's antioxidant defenses and lead to large numbers of free radicals injuring nearby cells.

Other free radicals are produced during a process known as ischemia-reperfusion. Ischemia describes the narrowing of blood vessels, which redirects oxygen-rich blood away from many organs and tissues and to muscles. When a person stops exercising, normal blood flow resumes and tissues become reoxygenated. This reoxygenation of oxygen-deprived tissues generates still more free radicals.

Animal and human studies have found that exerciseinduced free radicals dramatically increase the oxidation of cell proteins. In particular, the oxidation of DNA can have serious long-term effects, and might speed the aging process and increase the risk of cancer.

However, a number of researchers, including Packer, have found that vitamin E supplements can prevent exercise-induced free radical damage to cells, including the breakage of DNA strands.

While Packer doubts that antioxidant supplements can increase exercise performance, they do appear to reduce exercise-induced fatigue. In one animal study, a diet deficient in vitamin E reduced endurance. Restoring vitamin E might correct the situation, giving the appearance of increased endurance.

"There is some evidence that bolstering cellular antioxidant status may increase muscle resistance to fatigue," Packer wrote. In one study, pretreatment with N-acetylcysteine, an antioxidant that boosts levels of glutathione, a major cellular antioxidant, increased physical output in animals by 15 percent.

In a separate study of exercisers, researchers found that a combination of antioxidants slowed the oxidation of low-density lipoprotein (LDL) cholesterol, considered a risk factor for coronary heart disease.

Tommi J. Vasankari, PhD, of the University of Turku, Finland, gave a small group of endurance athletes either a placebo or an antioxidant supplement containing 294 mg of vitamin E, 1,000 mg of vitamin C, and 60 mg of coenzyme CoQ10 daily daily for four weeks.

The supplements increased LDL's antioxidant capacity by 30-40 percent, both before and after exercise.

References: Packer L, "Oxidants, antioxidant nutrients and the athlete," *J Sports Sciences*, 1997;15:353-63; Vasankari TJ, Kujala UM, Vasankari TM, et al., "Increased serum and low-density-lipoprotein antioxidant potential after antioxidant supplementation in endurance athletes," *Am J Clin Nutr*, 1997;65:1052-6.

The Role of Scurvy in Rheumatism

Although scurvy is generally considered a "disease of the past," it still occurs and can cause rheumatic symptoms, such as rheumatoid arthritis. That's the intriguing observation of Jean Léone, MD, of the Robert Debré Teaching Hospital, Reims, France.

In a recent issue of *Revue Du Rhumatisme*, Léone Continues on next page described two patients, 44-year-old and 49-year-old men, with rheumatism as the presenting symptom of scurvy.

Scurvy results from a severe deficiency of vitamin C and is usually characterized by bleeding gums and other types of abnormal bleeding. "Rheumatic manifestations can occur as a result of bleeding into the muscles and / or joints, as in our two patients," Léone wrote.

In a literature review cited by Léone, rheumatic symptoms were present in 21 of 26 scurvy cases. Fatigue and joint and muscle pain are early symptoms, whereas bleeding into the muscles and joints of the legs are symptoms of advanced scurvy. Scurvy can also result in weak bones and fractures.

The bleeding characteristic of scurvy is caused by weak capillary walls, which leak blood into tissues. Vitamin C is essential for the production of collagen, which strengthens blood vessel walls and other tissues.

Léone's patients recovered after treatment with 1,000 mg of intravenous vitamin daily for 10 days and taking oral supplements.

An unanswered question: how many cases of rheumatism are caused or exacerbated by levels of vitamin C that are low, but not low enough to result in scurvy?

Reference: Léone J, Delhinger V, Maes D, et al., *Revue Du Rhumatisme* (English edition), 1997; 64:428-431.

Broccoli Sprouts Contain Potent Anticancer Compound

Broccoli sprouts contain extremely high levels of a key anticancer substance known to be present in the vegetable's flowers, and the sprouts also taste better than the mature vegetable.

The anticancer substance, sulforaphane, is part of a family of beneficial compounds called isothiocyanates, found in broccoli, cauliflower, and Brussel sprouts. Sulforaphane speeds up activity of the liver's "phase 2 enzymes," which help detoxify and remove toxic substances from the body.

In experiments, Paul Talalay, PhD, of the Johns Hopkins University School of Medicine, Baltimore, found that broccoli sprouts harvested after just three days of growth contained 10-100 times more sulforaphane than did mature broccoli and cauliflower.

As part of his experiments, Talalay fed laboratory rats different forms of sulforaphane and exposed them to a chemical known to cause breast cancer. The number of animals developing tumors, the number of tumors per animal, and the size of tumors were significantly lower among animals getting the broccoli extract, compared with animals that did not receive it.

Reference: Fahey JW, Zhang Y, Talalay P, "Broccoli sprouts: an exceptionally rich source of inducers that protect against chemical carcinogens," *Proc Natl Acad Sci USA*, 1997;94:10367-72.

Fish Oil Supplements May Lower the Risk of Breast Cancer

Taking fish oil capsules for just three months can improve the fatty acid composition of breast tissue and might lower the risk of new or recurrent breast cancers.

Animal and cell-culture experiments have shown that the omega-6 fatty acids from corn and safflower oils promote the growth of breast cancer cells, whereas the omega-3 fatty acids from fish oils can inhibit the growth of such cancers.

Researchers studied 25 women who had breast cancer but were in remission. The women were asked to eat low-fat diets with lots of soy foods and vegetables and to take 4,000 mg of omega-3 fatty acids (fish oil capsules) for three months.

During the course of the experiment, blood levels of the omega-3 fatty acids increased by three times, according to John A. Glaspy, MD, of the University of California, Los Angeles. Levels of the omega-3 fatty acids increased in breast tissue, and the ratio of omega-3 to omega-6 fatty acids also improved significantly.

"It has been shown that fatty acid composition of breast tissue fatty acids, including tumors, depends in part on fatty acid availability, which is influenced by dietary fatty acids," wrote Glaspy. "Thus, dietary intervention could provide an effective means to alter the fatty acid availability in tumor tissue and thereby possibly affect tumor growth."

Reference: Bagga D, Capone S, Wang H-J, et al., "Dietary modulation of omega-3/omega-6 polyunsatured fatty acid ratios in patients with breast cancer," *J Natl Cancer Inst*, 1997;89:1123-31.

Soy, Fiber Linked to Lower Risk of Endometrial Cancer

Diets high in soy foods and fiber may lower the risk of endometrial cancer, according to a study of several ethnic groups in Hawaii.

Marc T. Goodman, PhD, of the University of Hawaii, Honolulu, compared the diets of 332 women diagnosed with endometrial cancer and those of 511 healthy women. Women who consumed the largest amount of soybeans and other legumes were 54 percent less likely to develop endometrial cancer. High consumption of whole grains, vegetables, fruits, and seaweeds were also strongly associated with a reduced risk of endometrial cancer, according to Goodman. Women who ate relatively few of these foods had a higher risk of developing endometrial cancer.

Endometrial cancer is a malignancy of the lining of the uterus, called the endometrium. About 35,000 Americans are diagnosed with the disease each year.

Women who had been pregnant were also much less

likely to develop endometrial cancer. Conversely, users of "unopposed" estrogen-replacement therapy (i.e., estrogen without progesterone) were 2.6 times more likely than nonusers to develop endometrial cancer. The risk of cancer "increased sharply" with more than three years of estrogen-replacement therapy.

Goodman attributed many of the benefits of soy and other plant foods to naturally occurring estrogen-like compounds, called phytoestrogens. These substances seem to protect against the cancer-stimulating effect of hormonal estrogen.

Reference: Goodman MT, Wilkens LR, Hankin JH, et al., "Association of soy and fiber consumption with the risk of endometrial cancer," *Am J Epidemiology*, 1997;146:294-306.

Applying Capsaicin Cream Eases Pain After Surgery

A study at the Mayo Clinic has found that capsaicin creams can reduce post-surgical pain in patients.

Doctors studied 99 patients who had undergone surgery for the removal of cancerous tumors. About half of the patients were given a 0.075 percent capsaicin cream to rub on the site of nerve pain, while others were given a placebo cream, for eight weeks. After this time, the capsaicin and placebo creams were reversed.

When the patients were asked to rate the two creams, three out of every four patients said the capsaicin cream was more effective in relieving pain. A total of 12 percent of patients reported "complete pain relief." On average, capsaicin accounted for about a 53 percent reduction in pain, whereas the placebo accounted for only a 17 percent reduction, according to Charles L. Loprinzi, MD, of the Mayo Clinic.

Capsaicin, the pungent ingredient in hot peppers, lowers levels of substance P, a neurotransmitter responsible for the sensation of pain. Other studies have reported that capsaicin cream helps relieve pain associated with rheumatoid arthritis and osteoarthritis. The cream is most effective when applied several times daily. Its initial burning sensation generally stops with regular use.

Reference: Ellison N, Loprinzi CL, Kugler J, et al., "Phase III placebo-controlled trial of capsaicin cream in the management of surgical neuropathic pain in cancer patients," *J Clin Oncol*, 1997;15:2974-80.

Alpha-Lipoic Acid Safely Lowers Blood Sugar Levels

Alpha-lipoic acid, found in foods (such as spinach) and made by the body, can lower and stabilize blood sugar levels.

Although alpha-lipoic acid has been years for years in Germany to treat nerve pain in diabetics, it was only recently discovered to be an antioxidant. Recent human studies have found that it can lower glucose levels in diabetics about 20-30 percent.

In a study using laboratory rats, Nava Bashan, PhD, of Ben-Gurion University, Israel, found that alpha-lipoic acid lowered fasting glucose levels by 46 percent and post-meal glucose levels by 22 percent. Glucose uptake was comparable to that of nondiabetic animals.

Reference: Khamaisi M, Potashnik R, Tirosh A, et al., "Lipoic acid reduces glycemia and increases muscle GLUT4 content in streptozotocin-diabetic rats," *Metabolism*, 1997;46:763-8.

A Higher RDA for Vitamin E?

There are compelling reasons to increase the Recommended Dietary Allowance (RDA) for vitamin E, contend a team of researchers from Hoffman-La Roche Inc.

The current RDA ranges from 10-15 IU daily, depending on a person's age and sex. However, numerous studies have reported that higher supplemental doses, on average between 100-400 IU, can significantly reduce the risk of coronary heart disease, improve immunity, and increase resistance to some types of cancer.

"Of equal importance, there is a solid body of literature that demonstrates that these and much higher vitamin E intakes are safe," Peter Weber, MD, PhD, wrote in the journal *Nutrition*. He concluded that intakes of vitamin E "significantly higher than current recommended levels...could be of benefit to human health."

Reference: Weber P, Bendich A, Maclin LJ, "Vitamin E and human health: rationale for determining recommended intake levels," *Nutrition*, 1997;13:450-60.

Greater Use of Supplements Would Lower Hospital Costs

Hospital charges in the United States could be reduced by \$20 billion annually if large numbers of people took vitamin and mineral supplements. That's the finding of a joint study conducted by Pracon, a hospital-outcomes research firm, and Roche Vitamins, a manufacturer of vitamin products.

Preventable illnesses may account for 70 percent of U.S. health care costs. Adrianne Bendich, PhD, and her collaborators analyzed annual hospital charges for three types of illnesses: birth defects, low-weight premature births, and coronary heart disease. They also reviewed published data on how vitamin supplements could reduce the risk of these conditions.

The researchers calculated that hospital charges for these three conditions could be reduced by 40, 60, and 38 percent respectively. The specific types of supplements Continued on bottom of next page

Quick Reviews of Recent Research

• Vitamin E might protect against breast cancer

Researchers exposed laboratory rats to N-methyl-Nnitrosourea (NMU), a compound that can cause breast cancer. Some of the rats also received vitamin E. Seven (87.5 percent) of the eight NMU-exposed rats developed breast cancer. In contrast, all eight vitamin E-treated rats developed some tissue fibrosis but no cancerous tumors.

Omer B, et al., J Natl Cancer Inst, 1997;89:972-3.

• Ginkgo improves cardiovascular function

Using laboratory rats, researchers analyzed how *Ginkgo biloba* extracts protect against cardiac ischemia. Myocardial function was notably improved after 15 days of consuming the extracts. Based on their analysis, the researchers concluded that Ginkgo prevented the formation of free radicals instead of scavenging them.

Pietri S, J Molecular and Cell Cardiology,1997; 29:733-42.

• Ozone boosts free radicals, depletes vitamin E

Ozone, a major component of smog, generates large numbers of free radicals. The skin is the organ most directly exposed to ozone; and the skin's outermost layer of skin, the stratum corneum, is particularly sensitive to ozone. Exposure to ozone increased concentrations of malondialdehyde, a marker of free radical activity. Ozone also depleted vitamin E levels in the stratum corneum. The greater the exposure to ozone, the more malondialdehyde that was produced and the more vitamin E that was destroyed.

Thiele JJ, et al., J Investigative Dermatology, 1997;108:757-7.

• Diabetics have lower antioxidant levels

Researchers compared an analytical method for measuring a person's total ability to neutralize free radicals to a mathematical model based on blood levels of several antioxidants. Both methods offered reliable measurements of diabetic patients' ability to quench free radicals, and both methods found diabetics to suffer more oxidative stress than healthy subjects. Although the mathematical model was not as precise as the

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were folic acid to prevent birth defects, zinc-containing multivitamins to prevent low-weight premature births, and vitamin E to lower the risk of heart disease among people over age 50.

The cost of these vitamins would be substantially less than the cost of hospital care. They would likely reduce the risk of other diseases as well.

Reference: Bendich A, Mallick R, Leader S, "Potential health economic benefits of vitamin supplementation," *Western J Medicine*, 1997;166:306-312.

analytical method, the researchers and physicians concluded that it was sufficient for routine assessment of oxidative stress in diabetics.

Ceriello A, et al., Diabetes Care, 1997;20:194-7.

• Beta-carotene enhances natural killer cells

In a study using laboratory mice, researchers compared the effects of beta-carotene and estrone, the principal estrogenic hormone produced by women, on natural killer (NK) cells. NK cells from mice given beta-carotene were 65 percent more effective than NK cells from controls in destroying cancer cells. In contrast, NK cells from mice given estrone were less effective than NK cells from controls. The results reflect the findings of other studies showing that beta-carotene enhances immunity against cancer cells, whereas estrogen increases susceptibility to cancer.

Fernandes-Carlos T, et al., Anticancer Research, 1997;17:2523-8.

• Research supports protective role of carotenoids

Researchers identified high levels of two carotenoids, lutein and zeaxanthin, in 58 pairs of human retinas and one monkey retina. They found forms of these nutrients identical to those found in fruits and vegetables. They also identified oxidized forms of lutein and zeaxanthin, suggesting that they had absorbed free radicals that could have damaged the eyes.

Khachik F, et al., Invest Ophthalmol Vis Sci, 1997;38:1802-1811.

• Diet can improve eye protection

Thirteen people were asked to eat daily servings of spinach and corn, or corn alone. These foods are rich in lutein and zeaxanthin, nutrients that form the macular pigment in the eye. Adding these foods increased their consumption of lutein and zeaxanthin by 6.7 percent. Most of the subjects had increases in the density of their macular pigment, which should reduce the risk of macular degeneration.

Hammond BR, et al., Invest Ophthalmol Vis Sci, 1997;38:1795-1801.

