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Combination of Antioxidants and Chemo May Benefit Women with Ovarian Cancer

Ovarian cancer is one of the deadliest of all “female” cancers. More than 26,000 cases are diagnosed each year in the United States, and almost 15,000 women die annually from the disease.

But a combination of chemotherapy drugs and high-potency antioxidants may very well increase survival of women with ovarian cancer. In a preliminary report, Jeanne A. Drisko, MD, and colleagues at the University of Kansas Medical Center, Kansas City, described two successful case histories and also reported that a larger human trial is currently underway at UKMC.

“Because of poor overall survival in advanced ovarian malignancies, patients often turn to alternative therapies despite controversy surrounding their use,” wrote Drisko and her colleagues in the *Journal of the American College of Nutrition*. “Currently, the majority of cancer patients combine some form of complementary and alternative medicine with conventional therapies. Of these therapies, antioxidants, added to chemotherapy, are a frequent choice.”

The first patient, 55 years old, underwent surgery to remove much of a large pelvic cancerous mass that had spread to the intestine, diaphragm, and spleen. She received six cycles of chemotherapy, but also began taking high-potency antioxidant supplements, including vitamin E (1,200 IU), coenzyme Q10 (300 mg), vitamin C (9 grams), beta-carotene and mixed carotenoids (25 mg), and vitamin A (10,000 IU) daily. After the first round of chemotherapy, the patient began receiving vitamin C intravenously, beginning at 15 grams and then increasing to 60 grams twice weekly.

After a year, the patient reduced the vitamin C IVs to once every 10 to 14 days. Now, more than three years after diagnosis, CT and PET scans show no recurrence of cancer. Her blood levels of “cancer antigen 125,” a marker of tumor activity, decreased from 999 at diagnosis to a normal value of 8.8.

The second patient, age 60, underwent surgery to remove a cancer that had spread throughout the

pelvis. Before beginning chemotherapy, she also began taking high-potency antioxidant supplements, including vitamin E (1,200 IU), beta-carotene (25 mg), vitamin C (3 grams), and vitamin A (5,000 IU) daily. After the first round of chemotherapy, the patient was found to have metastasized cancer in the pelvis. She declined further chemotherapy, opting instead for oral antioxidants and twice-weekly 60-gram vitamin C IVs. Her physical exams show no obvious tumors (she has refused further diagnostic imaging), and her most recent CA-125 is 5.0, more than three years after initial diagnosis.

“The use of antioxidants during chemotherapy remains a matter of controversy,” Drisko and her colleagues noted. “The prevailing opinion is that antioxidants may reduce the effectiveness of chemotherapy...[but] animal and in vitro studies have shown that antioxidants inhibit neoplastic cell growth by complex mechanisms...thus, the concept that antioxidants are contraindicated during most chemotherapy regimens is no longer valid...[and] may improve the efficacy of chemotherapy.”

Reference: Drisko JA, Chapman J, Hunter VJ. The use of antioxidants with first-line chemotherapy in two cases of ovarian cancer. *Journal of the American College of Nutrition*, 2003;22:118-123. □

Selenium Helps Gene that Protects Against Some Esophageal Cancers

People with a condition known as “Barrett’s esophagus” may be up to 75 times more likely to develop invasive cancer of the esophagus. But maintaining adequate intake of the essential dietary mineral selenium may sharply reduce that risk.

Barrett’s esophagus, which affects more than 1 million Americans, is a complication of chronic gastroesophageal reflux. The reflux, or heartburn, alters some of the surface cells of the esophagus, leading to an increased risk of cancer. No current treatment lowers the risk of esophageal cancer.

Continues on next page

In a recent study, Rebecca E. Rudolph, MD, of the Fred Hutchinson Cancer Research Center, Seattle, and her colleagues studied the role of two cancer-suppressing genes and selenium levels in 399 patients with Barrett's esophagus.

The researchers found that patients with the higher blood levels of selenium had about half the risk of developing precancerous cell changes in the esophagus. In a detailed genetic analysis, Rudolph and her colleagues found that selenium helped maintain normal functioning of the p53 cancer-suppressing gene, which is damaged or not active in many cancers.

Several years ago, a clinical trial found that supplements of 200 mcg of selenium daily reduced the risk of several common cancers by about half.

Reference: Rudolph RE, Vaughan TL, Kristal AR, et al. Serum selenium levels in relation to markers of neoplastic progression among persons with Barrett's esophagus. *Journal of the National Cancer Institute*, 2003;95:750-757. □

Black Cohosh Reduces Menopausal Symptoms Without Apparent Risks

Recent studies have found that the use of estrogen or estrogen combined with progesterone increases the risk of heart disease, cancer, and Alzheimer's in menopausal women. As a result, many women have sought herbal remedies that might ease hot flashes and other menopause-related symptoms without increasing the risk of disease.

One particular herb, black cohosh (*Cimicifuga racemosa*), has often been recommended for easing hot flushes, and its benefits have been confirmed by numerous studies. In a recent study, Wolfgang Wuttke, MD, of the University of Göttingen, Germany, found that the herb worked just as well as conjugated estrogens (manufactured from the urine of pregnant horses), the most common type of estrogen drug. In addition, black cohosh did not promote the growth of endometrial cells, suggesting that it would not increase the risk of cancer.

Wuttke and his colleagues asked 61 postmenopausal women to take one of the following daily for three months: 40 mg of black cohosh extract, 0.6 mg of conjugated estrogens, or placebos. The subjects recorded 10 different menopause-related symptoms in a daily diary. In addition, Wuttke's team analyzed blood markers of bone health and conducted vaginal ultrasounds to measure endometrial thickness in the subjects.

Black cohosh and estrogen resulted in a similar reduction of symptoms, and both therapies were superior to placebos. Symptoms tracked included hot

flashes, palpitations, sleep difficulties, depression, nervousness, fatigue, decrease in sexual desire, vaginal dryness, increased urination, and rheumatic-like pain in finger joints.

Black cohosh did not increase endometrial thickness, whereas estrogen did. Both black cohosh and estrogen improved blood markers of healthy bone metabolism.

Reference: Wuttke W, Seidlva-Wuttke, Gorkow C. The *Cimicifuga* preparation BNO 1055 vs. conjugated estrogens in a double-blind placebo-controlled study: effects on menopause symptoms and bone markers. *Maturitas*, 2003;44 (Suppl 1):S67-S77. □

Vitamin D: Are We Ignoring the Evidence While Deficiencies Are Commonplace?

Low levels of vitamin D are common in children and adults – and physicians may be overlooking the broad roles of this nutrient in a wide range of diseases. That's the view of Armin Zittermann, PhD, of the University of Bonn, Germany.

In a recent article in the *British Journal of Nutrition*, Zittermann reviewed the evidence showing that vitamin D deficiencies are common in Europe, increasing the risk or severity of many common diseases.

European children and young adults often have low blood levels of vitamin D during winter months, as do elderly subjects throughout the year. People who rarely get outdoors tend to have outright vitamin D deficiencies. (Studies have found similar patterns in the United States.)

The body makes vitamin D when skin is exposed to ultraviolet rays in sunlight, and most of human evolution occurred near the equator, where sunlight was plentiful year round. The body regulates its production of vitamin D, with levels reaching a plateau after about 15-30 minutes of sunlight exposure.

Some vitamin D is converted to calcitriol, a hormone that regulates many different genes. Cells with vitamin D receptors have been found in the intestine, muscle, pancreas, parathyroid, pituitary, immune system, brain, liver, prostate, ovaries, skin, heart – indicating a likely functional role for the vitamin in these tissues.

Extensive research has found that vitamin D is needed for the body's utilization of calcium and can reduce the risk of osteoporosis. In addition, studies have found that a lack of vitamin D may reduce muscle strength and also may be involved in rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, hypertension, diabetes, and some types of cancer (e.g., prostate and colorectal cancer).

“There are no reports of vitamin D intoxication (overdose) in healthy adults after intensive sunlight exposure,” Zittermann wrote.

Reference: Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? *British Journal of Nutrition*, 2003;89:552-572. □

GABA Helps Brain Reduce “Background Noise,” Focus on What’s Important

Gamma-amino butyric acid (GABA) is an amino acid and neurotransmitter that many nutritionally oriented physicians use to calm patients with anxiety.

A new study has found that the addition of GABA improves thinking processes and vision in old monkeys. It appears to work by filtering out stray brain and nerve signals – the equivalent of background noise – while allowing only the most important information to be processed by the brain.

Audie G. Leventhal, PhD, of the University of Utah School of Medicine, Salt Lake City, and Chinese colleagues studied the neurons of both young and old monkeys.

Leventhal noted that as primates age, they experience a loss of visual and brain function. Although the eye deteriorates, so does the part of the brain involved in processing what the eye sees.

“Proper brain function requires that stimuli evoke reliable responses that are easily discernible from background activity,” he wrote in *Science*.

In experiments, a GABA-blocking chemical reduced the visual responsiveness of young and old monkeys watching patterns on a computer screen. When GABA was administered to the older monkeys, they gained improvements in visual responsiveness comparable to those of young monkeys.

Reference: Leventhal AG, Wang Y, Pu M, et al. GABA and its antagonists improved visual cortical function in senescent monkeys. *Science*, 2003;300:812-815. □

Kitchen Herbs Are Potent Source of Dietary Antioxidants

Culinary herbs may be the richest source of dietary antioxidants, according to a study conducted at the University of Oslo and other research centers in Norway and Japan.

The use of herbs may “contribute significantly to the total intake of plant antioxidants, and be an even better source of dietary antioxidants than many other food groups, such as fruits, berries, cereals, and vegetables,” wrote Rune Blomhoff, PhD, and colleagues in the *Journal of Nutrition*.

In a recent analysis of dried culinary herbs, either grown from seed or from commercial vendors,

Blomhoff found a 1,000-time difference in antioxidant concentrations among different species of herbs.

Of the noncommercial herbs tested, oregano had the most antioxidant activity. Other high-antioxidant herbs included sage, peppermint, thyme, lemon balm, clove, allspice, and cinnamon.

Among the commercial herbs tested, clove had almost five times the antioxidant activity of allspice, the next highest. Cinnamon, rosemary, thyme, marjoram, saffron, oregano, and tarragon also had high antioxidant levels.

Perhaps not surprisingly, different sources of the same herb had variations in antioxidants, likely because of growing conditions.

All of the measurements were calculated based on micromoles of antioxidant activity per 100 grams of dry weight of the herbs. Micromoles are based on the molecule weight of a substance and do not easily convert to milligrams or micrograms.

Most of the herbal antioxidants likely consist of phenols and polyphenolic flavonoids.

Reference: Dragland S, Senoo H, Wake K, et al. Several culinary and medicinal herbs are important sources of dietary antioxidants. *Journal of Nutrition*, 2003;133:1286-1290. □

Fish Consumption Reduces Heart Attack Risk in Women with Diabetes

Eating fish on a regular basis can significantly reduce the risk of heart attacks and death for women with diabetes. That’s the finding of a new study by Frank B. Hu, MD, of the Harvard School of Public Health.

Fish, particularly coldwater varieties such as salmon, are rich in omega-3 fatty acids, which are documented for their blood-thinning and antiarrhythmic effects in generally healthy subjects. However, according to Hu, relatively few studies show whether the same benefits extend to people with diabetes, who have an increased risk of cardiovascular disease.

Hu and his colleagues tracked the health of 5,103 female nurses over 16 years. All had been diagnosed with type 2 (adult-onset) diabetes, but were free of cardiovascular disease and cancer at the start of the study.

During the study, 141 women died from cardiovascular disease, and 221 had nonfatal heart attacks. There were 468 deaths from all causes.

Women who consumed fish one to three times per month were 30 percent less likely to suffer a fatal or nonfatal heart attack. But women who consumed fish five or more times per week were 64 percent less

Continues on next page

Quick Reviews of Recent Research

• Low CoQ10 again linked to ataxia

Two years ago, researchers reported that large dosages of coenzyme Q10, a vitamin-like substance, improved the functioning of patients with hereditary ataxia. The condition, an incurable neurological disorder, affects coordination, balance, arm and leg movements, and speech. In this follow-up study, researchers conducted muscle biopsies on 135 patients with cerebellar ataxia. Thirteen patients with childhood-onset ataxia had very low levels of CoQ10. According to the researchers, this confirmed the existence of an ataxic syndrome involving low CoQ10 levels that "may be responsive to CoQ10 supplementation."

Lamperti C, et al. *Neurology*, 2003;60:1206-1208.

• Vitamin E slows oxidation of LDL

The oxidation of low-density lipoprotein (LDL) cholesterol is an early step in the development of coronary artery disease. Oxidized LDL triggers an immune response, leading to inflammation of blood vessels. Researchers asked 16 patients with high blood pressure and 31 with normal blood pressure to take 400 IU of natural vitamin E daily for two months. By the end of the study, patients with hypertension had an 18.5 percent slowing in the rate of their LDL oxidation. Those with normal blood pressure had a 34 percent slowing of LDL oxidation. The researchers wrote, "Vitamin E may therefore act as an inhibitor of atherogenesis."

Brockes C, et al. *British Journal of Biomedical Science*, 2003;60:5-8.

Eating fish reduces heart attack...

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likely to have a heart attack.

Women who consumed larger amounts of omega-3 fats per se, which the researchers calculated based on fish consumption, had a 31 percent lower risk of cardiovascular disease and a 37 percent lower risk of death from all causes.

"These findings suggest that regular fish consumption should be considered as part of a healthy diet for diabetic management," Hu and his colleagues wrote.

The American Heart Association recommends the consumption of at least two fish meals each week to reduce the risk of cardiovascular disease.

Reference: Hu FB, Cho E, Rexrode KM, et al. Fish and long-chain n-3 fatty acid intake and risk of coronary heart disease and total mortality in diabetic women. *Circulation*, 2003;107:1852-1857. □

• Antioxidants block sun damage to skin

Tyrosine kinase is a molecule involved in turning on a number of harmful cellular processes. Ultraviolet radiation in sunlight can boost the activity of tyrosine kinase, and some antioxidants are known to counteract it. In a study with human volunteers, researchers found that topical application of two antioxidants, N-acetylcysteine and genistein, inhibited the activity of tyrosine kinase in skin cells exposed to ultraviolet radiation. Neither antioxidant served as a sunscreen, but they did block early changes that would have led to accelerated "photoaging" of skin cells.

Kang S, et al. *Journal of Investigative Dermatology*, 2003;120:835-841.

• Vitamin E succinate may have anti-cancer benefits

In an extensive review of cell and rodent studies, researchers described the evidence supporting the anti-cancer properties of natural d-alpha tocopheryl succinate, one of the forms of vitamin E sold as supplements. Other types of vitamin E do not share this property. Cell studies suggest that vitamin E succinate can inhibit the growth of breast, prostate, and colon cancer, often by prompting the cells to self-destruct. Research also shows that vitamin E succinate can enhance the therapeutic effects of radiation and chemotherapy while protecting normal cells. The researchers wrote that vitamin E succinate "can be used as an adjunct to standard and experimental cancer therapies in order to improve their efficacy."

Prasad KN, et al. *Journal of the American College of Nutrition*, 2003;22:108-117.

• Quercetin might protect against cancer

Quercetin, an antioxidant flavonoid found in apples and onions, inhibits angiogenesis, the growth of new blood vessels in tumors. Quercetin is also known for its anti-inflammatory properties.

Tan WF, et al. *European Journal of Pharmacology*, 2003;459:255-262.

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Post Office Box 30246 • Tucson AZ 85751-0246 USA

Editor and Publisher: **Jack Challem**

Copy Editor: **Mary E. Larsen**

Medical and Scientific Advisors:

Richard P. Huemer, MD Lancaster, California

Ralph K. Campbell, MD Polson, Montana • **Peter Langsjoen, MD** Tyler, Texas

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