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Coenzyme Q10: More Evidence of Its Benefits in Breast and Other Cancers

A recent report on the use of Coenzyme Q10 (CoQ10) in breast cancer patients suggests that the ideal therapeutic dose of the nutrient might be as high as 390 mg daily. In the paper, Knud Lockwood, MD, of Copenhagen, Denmark, also describes the successful treatment of three patients, including one whose cancer spread to her liver.

Lockwood's article in *Biochemical and Biophysical Research Communications* (July 6, 1995;212:172-177) is the third medical journal description of CoQ10 in the treatment of cancer. The other articles were by Lockwood (*Biochemical and Biophysical Research Communications*, March 30, 1994;199:1504-8) and Karl Folkers, PhD, (*Biochemical and Biophysical Research Communications*, April 15, 1993;192:241-5).

The latest paper recounts that the potential value of CoQ10 in cancer was documented back in 1961, when CoQ10 deficiencies were found in cancer patients. The first use of CoQ10 in the treatment of cancer was in the late 1970s and was described in Folkers' 1993 paper.

The cases histories describe the following three patients:

• A 49-year-old woman had a breast removed in 1990, but the tumor recurred a year later in the chest wall. Most but not all of the metastases were removed surgically, and the woman received x-ray therapy. In January 1992, Lockwood began giving her 90 mg CoQ10 daily. In December, the dose was increased to 390 mg daily. Six months later, a diagnostic chest x-ray showed no fluid build up in the chest, and in March 1995, the woman was free of cancer.

• A 75-year-old woman had a lumpectomy followed by a mastectomy in 1992. She received 90 mg CoQ10 daily, which was subsequently increased to 390 mg daily. In February 1995, an examination found no signs of tumor or metastases, and the patient was judged in excellent condition.

• A 44-year-old woman had a mastectomy in September 1992. An exam in April 1994 found numerous metastases of the breast cancer in her liver. She was given 30 mg of the drug tamoxifen and 390 mg of CoQ10 daily. Periodic diagnostic echo scans of the liver were taken, and in March 1995 a scan found no trace of the liver metastases. "The patient is in excellent condition in April, 1995, and no signs of metastases have been found elsewhere," Lockwood wrote.

The regression of liver metastases was significant because, as Lockwood observed, they "can be regarded as a prelude to imminent death."

In interpreting these results and those of other breast cancer patients, Lockwood described his initial lower dose of 90 mg daily as "ineffective." Doses of 390 mg had much greater benefits.

"Although in the past, the ethical treatment of breast cancer was based upon mastectomy, x-ray treatment, and anti-cancer drugs, this overall treatment rarely, if ever, caused highly significant regressions of the primary tumor and metastases in the liver," wrote Lockwood. The effect of CoQ10 was attributed to stimulating the immune system rather than by functioning as an anti-tumor drug. □

CoQ10 May Also Be of Value in Muscular Dystrophy

Researchers have known for three decades that a peculiar type of hereditary exercise intolerance and extreme fatigue is caused by defects in cellular energy production. Because CoQ10 is essential for cellular energy, supplements of the nutrient have sometimes been used to compensate for these inborn defects.

The benefits of CoQ10, however, may extend to some other types of "energy deficiency" diseases, including muscular dystrophies and neurogenic atrophies. These muscular dystrophies are often associated with heart diseases, particularly cardiomyopathy. CoQ10 has been well documented for its beneficial role in cardiomyopathy.

Karl Folkers, PhD, of the University of Texas, Austin, focused on some of these disorders in a recent article in *Biochimica et Biophysica Acta* (May 24, 1995;1271:281-6). He described two double-blind studies in which he used CoQ10 and a placebo to treat people with muscular dystrophies and nervous system atrophies. He began his paper with an anecdote describing a lawyer who developed muscular dystrophy and was told by his neurologist to mentally prepare himself for being confined to a wheelchair within two years.

The man began taking CoQ10 supplements. "His neurologist remarked that if this patient could be kept

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out of a wheelchair for five years, we should take an even greater interest in CoQ10 to treat muscular dystrophy," Folkers wrote. "After not five, but six years, he not only was not in a wheelchair, but he would swim, bowl, and play golf frequently, and conducted a vigorous business life in his legal profession."

The finding was significant since there was not—and is not today—any kind of drug therapy specifically for muscular dystrophy.

In the first study, Folkers gave 12 patients diagnosed with muscular dystrophy either 100 mg of CoQ10 or a placebo daily for three months. Four of the eight patients taking CoQ10 improved, whereas none of the placebo-treated patients did. When the four placebo patients subsequently received CoQ10, three of them improved.

In the second double-blind study, the eight patients receiving CoQ10 noted dramatic improvement, including greater physical activity and endurance and less fatigue. "Although these physical improvements were subjective, they are apparently valid," Folkers wrote.

He speculated that "in a future trial with a daily dosage of 300 to 400 mg, the improvement in metabolic and physical performance would be even more impressive." □

Vitamins B2 and E May Help Genetic Exercise Intolerance

A variety of defects in cellular metabolism can affect energy production. Depending on the nature of the defect, CoQ10 (previous article) and other nutrients may be helpful.

To that end, a team of Dutch researchers recently reported that either vitamin B2 or vitamin E supplements helped compensate for an inborn error of energy production in several people.

The principal subjects were two girls, ages 11 and 15, a 22-year-old man, and his 24-year-old sister. Each had suffered from "easy fatiguability and exercise intolerance since early childhood," according to an article in *Biochimica et Biophysica Acta* (May 24, 1995, 1271:75-83).

Researchers from Erasmus University and two other medical centers in The Netherlands identified a specific type of energy-production cellular defect in these people. The defect resulted in poor utilization of vitamin B2 and carnitine, the latter a nutrient made from two amino acids, lysine and methionine.

The teenage girl was given 10-100 mg of B2, and the man and woman received 100 mg of the vitamin daily. The youngest girl was given a number of vitamins (biotin, riboflavin, and niacinamide), amino acids, and 2 grams of carnitine daily.

Immediately after receiving the supplements, all four gained greater physical endurance, which was confirmed by exercise testing. Exercise-related nausea and pain also stopped. The 15-year-old girl, who had suffered a stroke-like incident, had no more strokes.

The researchers also described a wheelchair-bound patient whose lack of stamina was attributed to excessive free radical production. He was treated with 1,000 IU of vitamin E daily. "He improved within a short time, and no longer required his wheelchair, except for long distances," the researchers wrote. □

Many Nutrients Enhance Detoxification Enzyme System

The body's cytochrome P450 enzyme system detoxifies drugs, pesticidies, carcinogens and other potentially hazardous chemicals that enter the body. About 40 P450 enzymes have been identified in people, and six of them seem to break down most chemicals and prepare them for excretion. Perhaps the best known P450 enzyme is glutathione-S-transferase.

In a thoughtful article, F. Peter Guengerich, PhD, of the Vanderbilt University School of Medicine, Nashville, reviewed the role of numerous nutrients in enhancing or diminishing the function of the P450 enzymes.

Many of the B vitamins, vitamin A, vitamin E, and many minerals promote the normal activity of the P450 enzymes. One of the most powerful inducers of P450 enzyme activity is diallyl sulfone, which the body makes from diallyl sulfide found in garlic and onions, according to Guengerich's article in the *American Journal of Clinical Nutrition* (March 1995;61:651S-8S).

Isothiocyanates, found in broccoli and cauliflower, appear to prevent some cancers by stimulating production of glutathione-S-transferase.

Nutrients that promote P450 enzyme activity include

- indoles, found in broccoli and cauliflower;
- capsaicin, the pungent component of peppers;
- terpenes, such a limonene, in citrus fruits;
- ellagic acid, a flavonoid found in berries; and
- other flavonoids, which are found widely in fruits and vegetables.

In contrast, long-term high-carbohydrate diets decrease P450 activity, according to Guenerich. □

Quercetin and Allergies

Quercetin, a common flavonoid, may reduce inflammation associated with allergies. In an experiment, Elliott Middelton Jr., MD, of the State University of New York, Buffalo, looked at how quercetin affects adhesion molecules, which begin and continue the inflammatory process.

According to Middleton's article in the *International*

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Archives of Allergy and Immunology (1995;107:435-6) quercetin dampened the activity of adhesion molecules. The effect was dose related. Higher levels of quercetin were more effective than lower doses in dampening the effect of adhesion molecules in vitro.

Although quercetin has at times been identified as a carcinogen, some studies have shown that this nutrient inhibits the growth of many types of cancer. One study found that large doses of quercetin had a dramatic suppressive effect on squamous cell cancers of the head and neck (Castillo MH, *American Journal of Surgery*, Oct. 1989,158:351-5). This nutrient also inhibits reverse transcriptase, the method HIV uses to replicate itself (Spedding G, et al., *Antiviral Research*, 1989;12:99-110).

Pine Bark for AIDS? A Dubious Study

A commercial flavonoid product called Pycnogenol® might boost a depressed immune system, according to a recent study.

Pycnogenol contains proanthocyanidins, a class of flavonoids found widely in the food supply. The product is derived from the bark of a French pine tree.

Ronald R. Watson, PhD, headed a team at the University of Arizona, Tucson, that infected mice with a retrovirus known to cause leukemia and AIDS-like immune depression in mice. The researchers reported that both the retrovirus and alcohol consumption interfered with many aspects of immunity. Pycnogenol supplements restored many aspects of immune function in the mice, including the activity of natural-killer cells, which attack both cancer cells and virus-infected cells. The supplement had little effect on healthy mice, according to an article in *Life Sciences* (1996;58:87-96).

The study may not actually prove much. Watson and his colleagues argued that the mouse and the virus were accepted models for AIDS experiments. However, primates and the simian immunodeficiency virus (SIV) are the preferred models for AIDS.

Pycnogenol, which has been aggressively marketed through health food stores and multi-level marketers, has relatively little direct medical support. Most of the claims made on behalf of Pycnogenol—from curing heart disease to cancer—have been derived from more general research on flavonoids. More than 4,000 flavonoids and 250 proanthocyanidins have been identified, and it's not clear that extrapolations are justified. Proanthocyanidins, in general, are well documented for strengthening blood vessel walls.

Proanthocyanidins also function as antioxidants and free radical scavengers. Free radicals do speed replication of HIV whereas antioxidants, such as vitamin C and glutathione, slow it (Sappey C, et al., *AIDS Research and Human Retroviruses*, 1994;10:1451-1461).

B vitamins: Pretty 'Basic' Stuff

With all the attention given to antioxidants, it's easy to overlook the B vitamins and their fundamental roles in health. For example, deoxyribonucleic acid (DNA), the complex molecule that forms our genetic blueprint, is made from different arrangements of four compounds called bases: adenine, guanine, cytosine, and thymine.

You can't get much more fundamental than that when it comes to life. But can you tell which vitamins are essential for DNA synthesis and replication?

Thymine depends in part on vitamins B3 and B6, guanine and adenine need folic acid, and cytosine must have B3. Impair the body's production of any of these DNA bases, such as by nutritional deficiencies, and the foundation of life starts to disintegrate.

An article in *Medical Hypotheses* (Jennings E, 1995;45:297-303) describes how a deficiency of folic acid alone results in breaks in DNA strands. These breaks likely lead to mutations and cancerous cells. In addition to breaking apart DNA, a deficiency of folic acid also scuttles DNA's attempts to repair the damage.

Evidence supporting the role of folic acid comes from an understanding of DNA, as well as experimental and epidemiological studies showing a strong association between folic acid deficiency and cancers of the rectum and colon and precancerous colon adenomas. In addition, precancerous cervical dysplasia often disappears after folic acid supplementation.

Folic acid supplementation might be useful in cancer prevention. "The requirement for folic acid in DNA synthesis provides a plausible mechanism for a DNA-damaging effect of a low-folic acid diet. Additional epidemiological studies and clinical trials are needed to define the role of folic acid in human carcinogenesis," the author wrote in *Medical Hypotheses*.

Note: Always take vitamin B12 along with folic acid. Both of the vitamins play important roles in DNA synthesis and repair, and the B12 will eliminate the risk of folic acid masking a B12 deficiency.

Beta-carotene and DNA repair

In an experiment, researchers exposed hamsters to a chemical known to cause DNA damage and cancer. Both vitamin A and beta-carotene supplements prevented DNA damage by reducing the number of adducts, chemicals that attach carcinogens to DNA, suggesting a role in DNA repair. However, beta-carotene was two to three times more effective than vitamin A.

Wolterbeek AP, *Cancer Letters*, May 8, 1995;91; 205-14.

Quick Reviews of Recent Research

• Antioxidants and immunity

Antioxidants, including vitamin E, beta-carotene, and glutathione, are essential for normal immunity. However, these nutrients may be more critical in the elderly because immune function, particularly the activity of T cells, decreases with age. This decline is likely the result of lifelong free radical damage.

Meydani SN, et al., *American Journal of Clinical Nutrition*, Dec 1995;62 (suppl):1462S-76S.

• Antioxidants and immune stimulation

A study in China used combinations of micronutrients to assess their effect on disease prevention. Among men, the combined supplementation of beta-carotene, vitamin E, and selenium enhanced the activity of T cells, compared with men who did not receive these supplements.

Zhang YH, et al., *Am J Clin Nutr*, Dec 1995;62 (suppl):1477S-82S.

• Cataracts and antioxidants

Cataracts, the clouding of the lens of the eye, is exacerbated by low levels of antioxidants, including vitamins C and E and beta-carotene. Smoking, which generates free radicals and further depletes antioxidant levels in the body, is strongly associated with cataract formation. In a Chinese study, researchers found that a simple multivitamin supplement reduced the incidence of cataracts by 43 percent.

Taylor A, et al., *Am J Clin Nutri*, Dec 1995;62 (suppl)1439S-47S.

• Nutrients and cervical cancer

Folic acid is already well established for its role in preventing and treating cervical dysplasia, precancerous changes to cervical cells. In a series of pilot studies, researchers also found that precancerous cells disappeared in 43 to 50 percent of patients after they regularly applied topical applications of a special form of retinoic acid (a type of vitamin A). In another study, 30 women consumed 30 mg of beta-carotene daily for six months. Seventy percent of women with mild or moderate dysplasia improved.

Meyskens FL Jr and Manetta A, *Am J Clin Nutr*, Dec 1995;62 (suppl)1417S-19S.

• Fruits, vegetables, and vitamins in cancer prevention

Diets rich in fruits and vegetables reduce the risk of gastrointestinal and respiratory tract cancers. However, fruits and vegetables are less protective against hormone-related cancers of the breast and prostate. "If vitamins C or E are indeed protective against cancer, that protection may derive from their consumption in complex mixtures with other nutrients and with other bioactive compounds as found in the matrix provided by whole foods."

Byers T and Guerrero N, *Am J Clin Nutr*, Dec 1995;62 (suppl);1385S-92S.

• Vitamin E and co-antioxidants

The oxidation of the low-density lipoprotein (LDL) form of cholesterol is considered a major causative factor in coronary heart disease. As an antioxidant, the alpha-tocopherol form of vitamin E protects LDL against oxidative damage. However, the effectiveness of vitamin E may depend on the activity of other antioxidants, called co-antioxidants, that recycle the vitamin. These co-antioxidants include coenzyme Q10 (ubiquinol), the gamma-tocopherol fraction of vitamin E, and the carotenoids lycopene and beta-carotene.

Thomas SR, et al., *Am J Clin Nutr*, Dec 1995;62 (suppl)1357S-64S.

• Beta-carotene and cardiovascular disease

Although beta-carotene is well established as an antioxidant, the nutrient may not always play a primary role in preventing cardiovascular disease. Instead, blood levels of beta-carotene may be a marker of antioxidant consumption in general. Studies have shown that the alpha-tocopherol fraction of vitamin E is the first antioxidant used in preventing LDL oxidation. Next, the gamma-tocopherol fraction is used, followed by lycopene and then beta-carotene. "The active substances in fruit and vegetables may be other carotenoids or among the many hundreds of active ingredients such as phenolic compounds (ie, quercetin) that are present in this group of foods."

Kohlmeier L and Hastings SB, *Am J Clin Nutr*, Dec 1995;62 (suppl) 1370S-6S.

• Vitamin E: more than an antioxidant

Vitamin E has numerous functions besides its role as the major fat-soluble dietary antioxidant. It appears to be involved in gene expression, cell growth, and normal cellular differentiation. The vitamin also appears to inhibit cancerous cellular proliferation. This effect was originally demonstrated with massive amounts of alpha-tocopherol. However, much smaller doses of alpha-tocopheryl succinate, an ester form of the vitamin, seem to be effective as an anti-proliferative agent, at least in vitro.

Traber MG and Packer L, *Am J Clin Nutr*, Dec 1995;62 (suppl):1501S-9S.

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Post Office Box 5505
Aloha, OR 97006-5505 USA

Editor and Publisher: **Jack Challem** Associate Publisher: **Renate Lewin**