

Coenzyme Q10

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Guest Editors

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Coenzyme Q10, or CoQ10, is a naturally occurring, lipid-soluble antioxidant and an essential electron carrier involved in the mitochondrial respiratory chain. In mitochondria, CoQ10 functions as a coenzyme that assists in the oxidative phosphorylation of nutrients, leading to production of cellular adenosine triphosphate (ATP), or energy.[1–4] It is endogenously synthesized by mammals and plants and is found in virtually all aerobic cells.[5]

The best food sources of CoQ10 are meat and poultry, and the typical US diet provides approximately 5 to 10 mg of CoQ10 per day. The highest levels of dietary CoQ10 are found in red meat products, particularly organ meats (liver and heart), from which this compound was first isolated.[6] After absorption, CoQ10 is circulated to the liver and incorporated into very-low-density lipoproteins.[2]

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In the body, more than 90% of CoQ10 is converted to its active form, called CoQH2-10 or ubiquinol. Ubiquinol has strong antioxidant properties. Although humans are capable of producing adequate amounts of CoQ10, certain medications, such as statins, beta-blockers, antidepressants, and antipsychotics, may decrease the body's natural production of this compound. Conditions that cause oxidative stress, such as liver disease, have been noted to decrease the ratio of ubiquinol to CoQ10, and tissue levels of CoQ10 have also been found to decline with age.[4] Serum concentrations of CoQ10 have been shown to increase after consumption of supplemental CoQ10 and after meals containing CoQ10. It is absorbed well, although rather slowly; peak plasma levels occur 5 to 10 hours after ingestion.[2] Serum levels of CoQ10 have been used to determine the amount of ingested CoQ10 needed to raise endogenous levels of CoQ10. Research suggests that a range of 150 to 300 mg of dietary CoQ10 may be needed to achieve physiologic effects.[7,8]



HOW IS COQ10 CURRENTLY USED?

While CoQ10 has been used for several decades as a dietary supplement for general health maintenance, the benefits of its administration have been most extensively evaluated in a variety of cardiovascular and neurodegenerative conditions. In patients with congestive heart failure, CoQ10 supplementation in addition to conventional medical therapy may improve quality of life, New York Heart Association classification, and congestive symptoms including dyspnea and edema.[9–13] Similar benefits were seen in a study of patients with hypertrophic cardiomyopathy.[14]

Rosenfeldt et al, in a meta-analysis of 12 published clinical trials, reported that CoQ10 administration decreases systolic and diastolic blood pressure.[15]

These cardiovascular changes may be a result of effects of CoQ10 on vascular endothelium, including improvements in the activity of superoxide dismutase, an enzyme thought to protect the vasculature against oxidant-induced damage.[16,17] Equivocal results have been described following efforts to prevent myalgias and myopathy in patients receiving HMG-CoA reductase inhibitors—the “statin” drugs—with CoQ10 supplementation.[18–21]

Some data suggest high-dose CoQ10 administration may slow functional decline in patients with early Parkinson’s disease.[22] Unfortunately, 300 mg CoQ10 twice daily did not improve total functional capacity in 347 patients with early Huntington’s disease.[23] CoQ10 supplementation has been shown to be effective in the uncommon primary CoQ10 deficiency syndromes associated with specific genetic defects in the CoQ10 biosynthesis pathway.[24–26] Placebo-controlled, double-blind, randomized trials have demonstrated efficacy of CoQ10 in men with idiopathic infertility.[27,28] Supplementation led to increased seminal plasma and sperm motility, but it is not clear if these changes lead to increased rates of pregnancy.

In light of its role in mitochondrial energy generation, CoQ10 supplementation has been evaluated in a variety of patient populations with fatigue. It has clearly been demonstrated to improve the symptoms of weakness and fatigue in the rare patient with inherited defects in CoQ10 biosynthesis.[24,25] As described, CoQ10 may have beneficial effects on dyspnea and exercise tolerance—cardiac fatigue—in patients with congestive heart failure and/or cardiomyopathy.[11,29,30] However, conflicting data exist regarding the effect of CoQ10 on fatigue in a normal population. Cooke et al described a trend towards an increased time to exhaustion following 2 weeks of CoQ10 intake.[31] A number of other placebo-controlled studies have failed to demonstrate an improvement in physical functioning in similar trained and untrained populations.[32–36]

WHAT IS THE EVIDENCE RELATED TO COQ10 AND CANCER?

During cancer treatment, many patients experience flavor aversions, particularly to meat, and may not be able to consume adequate amounts of dietary CoQ10. In addition, antineoplastic therapy may have a direct impact on CoQ10 synthesis.

Unfortunately, clinical and epidemiologic investiga-

tions of CoQ10 in cancer are limited and the few studies that have been reported have involved small numbers of participants. Importantly, the incidence of CoQ10 deficiency has been found to be significantly higher in cancer patients than in healthy controls.[8] CoQ10 deficiency has also been reported in women diagnosed with breast cancer. In a study conducted in 200 women hospitalized for breast cancer surgery, a CoQ10 deficiency was noted in patients with both malignant and nonmalignant breast lesions.[37] In contrast, CoQ10 deficiency at baseline was not observed in a prospective, placebo-controlled trial of CoQ10 administration in women with breast cancer and self-reported fatigue who were receiving adjuvant chemotherapy.[38] Additionally, Folkers et al reported reductions of total CoQ10 levels in patients with myeloma.[8] The importance of potential CoQ10 deficiencies in these patients is unclear, however.

Of some concern is the finding reported from the largest epidemiologic evaluation of CoQ10, in which investigators described a positive association between higher prediagnostic levels of CoQ10 and breast cancer risk in postmenopausal women.[39] In contrast, Rusciani et al reported an association between low CoQ10 levels and metastasis and progression of melanoma, while Palan et al reported an inverse association between cervical intraepithelial neoplasia and cervical cancer with circulating levels of CoQ10.[40,41]

A number of trials have evaluated the ability of CoQ10 supplementation to ameliorate or prevent cardiotoxicity in patients receiving anthracycline chemotherapy. Iarussi et al reported a protective effect for CoQ10 on left ventricular global function during anthracycline therapy in a prospective, randomized, controlled trial in 20 children.[42]

Okuma et al described no changes in QRS voltage or QTc duration in a heterogeneous group of 39 patients receiving CoQ10 along with doxorubicin-containing chemotherapy, whereas decreased QRS voltage and lengthened QTc duration was seen in a 41-patient control group.[43]

Until recently, no published data existed on the effects of CoQ10 on fatigue in patients with cancer. As a result, we performed a prospective, randomized, double-blind, placebo controlled study of Co-Q10 in women with breast cancer and self-reported fatigue while receiving adjuvant chemotherapy.[38] Between 2004 and 2009, a total of 236 women were enrolled.

Online Information About CoQ10

- **International Coenzyme Q10 Association** > *A nonprofit group formed in 1997 to promote research and educational activities related to coenzyme Q10*—<http://www.icqa.org/ICQA/home.html>
- **Linus Pauling Institute Micronutrient Information Center** > **CoQ10**—<http://lpi.oregonstate.edu/infocenter/othernuts/coq10/>
- **Mayo Clinic** > **monograph on CoQ10**—http://www.mayoclinic.com/health/coenzyme-q10/NS_patient-coenzymeq10/METHOD=print
- **Memorial Sloan-Kettering Cancer Center** > **About Herbs, Botanicals, and Other Products** > **CoQ10**—<http://www.mskcc.org/mskcc/html/69186.cfm>
- **Drugs.com** > **CoQ10 information**—<http://www.drugs.com/mtm/coenzyme-q10.html>
- **University of Maryland Medical Center** > **Coenzyme Q10 overview**—<http://www.umm.edu/altmed/articles/coenzyme-q10-000295.htm>
- **Natural Medicines Comprehensive Database** > **Coenzyme Q10**—<http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=9&Product=coenzyme+q10&btnSearch.x=15&btnSearch.y=3>

Treatment arms were well balanced with respect to age, performance status, ethnicity, and planned chemotherapy. At 24 weeks, there were no significant differences between the CoQ10 and placebo arms on the POMS-Fatigue, FACIT-Fatigue, or FACT-Breast subscales despite sustained increases in serum CoQ10 levels in treated patients. No serious adverse events were noted. Therefore, these data provide no support for an effect of CoQ10 supplementation on fatigue in newly diagnosed breast cancer patients.

WHAT ARE THE POTENTIAL RISKS?

Data from preclinical and clinical studies indicate that dietary supplementation with CoQ10 is safe, well tolerated, and free of any significant toxicities.[44] A large number of patients with cardiovascular disorders, including hypertension, heart failure, and hyperlipidemia have been treated with 100 to 300 mg per day of CoQ10 for up to 6 years without experiencing significant adverse events.[11,45] A meta-analysis of 12 studies and 362 patients with hypertension treated

with 30 to 225 mg per day of CoQ10 for up to 56 weeks failed to identify significant drug-related toxicities.[15]

The safety of escalated doses of CoQ10 was evaluated in a randomized, double-blind, placebo-controlled trial in early Parkinson's disease. A total of 80 patients received 300 to 1,200 mg per day of CoQ10 for up to 16 months, and there was no difference in the incidence of adverse events between the placebo and treatment arms.[22]

In a randomized, placebo-controlled trial of 300 mg of CoQ10 twice daily for 30 months in patients with early Huntington's disease, CoQ10 was generally well tolerated; a small increase in stomach upset was observed in the treated patients.[23] CoQ10 dosages of up to 3,000 mg per day for 8 months have also been well

tolerated in small numbers of patients with Parkinson's disease and amyotrophic lateral sclerosis.[46,47]

Treated patients in all of these trials had a low incidence of primarily gastrointestinal symptoms including nausea, vomiting, diarrhea, and abdominal discomfort. These symptoms do not appear to be dose-related and occurred at identical frequencies in both groups of patients treated in placebo-controlled trials.[11,22,23,48]

In light of its demonstrated hypotensive effects, CoQ10 could further decrease the blood pressure of patients on antihypertensive medications. In the meta-analysis previously described, CoQ10 supplementation decreased systolic and diastolic pressures by 17 mmHg and 10 mmHg, respectively.[23]

Limited anecdotal data suggest CoQ10 could reduce the anticoagulation effects of warfarin. It is hypothesized that the structural similarity of CoQ10 to Vitamin K might produce procoagulant effects.[49–51] Regular monitoring of the INR (International Normalized Ratio) should be considered in patients taking CoQ10 supplements while on warfarin anticoagulation therapy.

WHAT'S THE BOTTOM-LINE MESSAGE?

Over the past three decades, the safety of CoQ10 has been convincingly demonstrated over a wide range of doses and schedules and in patients with a variety of medical conditions. There is evidence to support a role for CoQ10 supplementation as an adjunct in patients with congestive heart failure and hypertension, and there are some data that suggest a benefit of high doses in patients with Parkinson's disease. The rare patient with a genetic defect in CoQ10 biosynthesis will also clearly benefit from exogenous CoQ10 administration. There are minimal data to support a beneficial effect of CoQ10 supplementation in patients with cancer, except for limited observations in patients receiving anthracycline-containing chemotherapy. ■

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Integrative Medicine Conference Calendar

FALL 2011 – SPRING 2012

- **4th European Congress for Integrative Medicine (EDIM) 2011: The Future of Comprehensive Patient Care**
> October 7–8, 2011, Berlin, Germany
> For more information, visit: <http://www.ecim-congress.org/>
- **Consortium of Academic Health Centers for Integrative Medicine: One-Day Research Symposium in Integrative Medicine and Health**
> October 26, 2011, Los Angeles, California
> For more information, visit: <http://www.imconsortium.org/researchday/index.htm>
- **Society for Integrative Oncology—8th International Conference
Innovating Integrative Oncology: Honoring the Patient, Personalizing the Science**
> November 10–12, 2011, Cleveland, Ohio
> For more information, visit: <http://www.integrativeonc.org/8th-annual-sio-conference>
- **American Association for Cancer Research (AACR) Annual Meeting**
> March 31–April 4, 2012, Chicago, Illinois
> For more information, visit: <http://www.aacr.org/home/scientists/meetings-workshops/aacr-annual-meeting-2012.aspx>
- **9th Annual Health and Nutrition Conference (presented by Arizona Center for Integrative Medicine)**
> April 15–18, 2012, Boston, Massachusetts
> For more information, visit: <http://www.nutritionandhealthconf.org/>
- **7th Annual Joint American Homeopathic Conference 2012**
> April 20–22, 2012, Reston, Virginia
> For more information, visit: <http://www.homeopathic.org/content/conference-2012>
- **Integrative Medicine and Health—International Research Conference**
> May 15–18, 2012, Portland, Oregon
> For more information, visit: www.imconsortium-conference.org/