Coenzyme Q10 (CoQ10) – *Ubiquinone & Ubiquinol*

Common Indications:

- Energy production & Mitochondrial support
- Cardiovascular health: Hypertension, congestive heart failure
- Myopathies
- Chronic fatigue syndrome - Fibromyalgia
- Oxidative stress
- Diabetes mellitus
- Musculoskeletal weakness/pain
- Neurological issues
- Periodontal disease
- Migraine headache
- Sports Performance

General Comments:

Coenzyme Q10 is an endogenous enzyme cofactor produced from tyrosine made in every cell of the body but involves a 17 step process that includes a number of trace minerals. Consequently any physiologic stress on the body can have an adverse impact and lead to suboptimal levels. It is found in small quantities in whole foods such as meats and vegetables and is better absorbed with a fatty meal. As a fat soluble antioxidant it is key to cellular respiration and protects the mitochondria from excessive oxidative stress. It plays a critical role in the electron transport chain and production of ATP within the mitochondria.

Signs of a deficiency include symptoms of fatigue, muscle aches and pains, muscular dystrophy, chronic gum disease, cardiovascular compromise, neurologic issues such as Parkinson's, diabetes, thyroid disorders, diminished exercise capacity and even cancer states. Deficiency may result from impaired synthesis due to nutritional deficiencies, advancing age or medication.

Drug induced deficiency can be caused by any the following medication (alphabetical order):

- Beta blockers[7]: acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, nadolol, sotalol, timolol
- Biguanides: metformin
- Clonidine
- Fibrates[6]: Gemfibrozil, Fenofibrate

- Haloperidol
- Hydralazine
- Methyldopa
- Phenothiazines: chlorpromazine, fluphenazine, mesoridazine, perphenazine, prochlorperazine, promazine, promethazine, thioridazine, trifluoperazine
- Statins[2-5] : atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, simvastatin
- Sulfonylureas: acetohexamide, glyburide, tolazamide
- Thiazide diuretics: benzthiazide, chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, indapamide, metolazone, polythiazide, quinethazone, trichlormethiazide
- Tricyclic antidepressants: amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine nortriptyline, protriptyline, trimipramine

Benefits & Mechanism of Action:

Energy production (ATP) within the mitochondria of the cell is dependent on coenzyme Q10 and therefore key to all organ systems performance.[8] It buffers free radicals produced during oxidative phosphorylation[9] Supports ATP synthesis as an electron and proton carrier and stabilizes cell membranes[10] , particularly the mitochondrial membranes.

Endothelial function

- CoQ10 supplementation (150-300 mg/daily) for 4-12 weeks associated with significant improvement in flow-mediated dilation of brachial artery[11]
- Prevents oxidative stress and subsequent endothelial dysfunction induced by angiotensin II[12] and oxidized LDL receptor[13], and protects activity of superoxide dismutate and catalase[14]

Cardiovascular diseases

- CoQ10 supplementation improved cardiac function and reduced medication requirements in patients with cardiovascular disorders[15]
- CoQ10 has potential to reduce risk of CVD by maintaining optimal cellular and mitochondrial function in cardiomyocytes and improvement in endothelial function which all may translate to 10-25% reduction in CV risk[11]
- CoQ10 (150 mg daily) reduces IL-6 by 14%, reduces lipid peroxidation and increases endogenous antioxidant activity in CHD patients[16,17]
- Congestive heart failure (CHF): Oxidative stress, mitochondrial dysfunction and energy starvation are believed to play important roles in etiology of CHF[18]Some evidence shows decreased myocardial function is associated with decreased CoQ10 myocardial tissue concentrations and plasma CoQ10 concentration is independent predictor of mortality in patients with CHF[19]
    - Clinical studies

- Body of evidence supports using CoQ10 in mild heart failure before the development of irreversible myocyte loss and fibrosis[20]
- Meta-analysis in 2012 showed that compared to placebo, CoQ10 increased EF from -3.0% to 17.8% and led to a slight improvement (-0.30) in NYHA heart failure classification[19]
- Preliminary results have shown that receiving CoQ10 (2 mg/kg/day) significantly reduces all-cause mortality in CHF patients at 2 years[21]

Hypertension

- A 2007 meta-analysis showed that those taking CoQ10 decreased systolic BP by 16.6 mmHg and decreased diastolic BP by 8.2 mmHg after treatment, with no change in placebo groups[22] May be due to decrease in total peripheral resistance as antagonist of vascular superoxide[23]
  - Suggested MOAs: increased antioxidant activity reducing free radical damage to endothelial lining and increasing nitric oxide bioavailability[24], increased superoxide dismutase-1 which scavenges superoxide anion[25], reduced aldosterone secretion[26]

Cardiac Surgery

- Improves postoperative cardiac function and reduces structural damage after cardiac surgery with presurgery administration of CoQ10. Likely due to improved preservation of mitochondrial ATP-generation after ischemia and repurfusion[27]
- CoQ10 can reduce reperfusion injury after coronary artery bypass surgery, reduce surgical complications, accelerate recovery times and, possibly, shorten hospital stays when given 1-2 weeks prior to surgery[28–34]
- Continuing to administer CoQ10 for 30 days after surgery hastened recovery course to 3-5 days without complications compared to 15-30 days for control group[30,31]
- Especially significant for older patients with less homeostatic reserve and more sensitive to aerobic and physical stress

Hypercholesterolemia

- 2 studies have show cholesterol lowering effects of CoQ10 (100-200mg/day)[35,36]
- May protect LDL cholesterol from oxidation[37]

Statin drug use

- Inhibition of HMG-CoA reductase also adversely affects intrinsic biosynthesis of CoQ10[3,4,38] Statins reduce plasma/serum CoQ10 levels 16-54%[39] Possibly because of lower LDL levels and inhibition of CoQ10 synthesis[40]
- Perhaps statin-induced CoQ10 deficiency (and subsequent mitochondrial energy depletion) is involved in pathogenesis of statin myopathy and possibly impaired cardiac function with longstanding use
- Reduced muscle CoQ10 levels may be associated with impaired cardiac function and theoretical increased risk of myopathy/physical fatigue[4,41,42] (Folkers et al 1990, Silver et al 2004, Paiva et al 2005) although further investigation is needed

- Statin-induced myalgia. A 2012 study examining effect of CoQ10 supplementation (Q max 30 mg twice daily) in 28 statin-associated myopathy patients showed increased serum CoQ10 levels (194%) and reduced muscle pain (54%) and weakness (44%)[43]
    - Other studies have found no difference with CoQ10 supplementation[44], and more placebo controlled studies are currently in the works investigating these effects[45]
- Statin-induced cognitive impairment
    - Brain tissue (like muscle tissue) has high mitochondrial vulnerability and thus more likely to be affected by CoQ10 deficiency[46]
    - A study involving dogs that underwent long-term statin use demonstrated poorer cognition associate with lower parietal cortex CoQ10[47], human trials are warranted.
    - The FDA has issued a warning that statin use may contribute to loss in cognitive function and memory.

  Results are currently inconsistent as to whether CoQ10 supplementation is effective in statin-users, however it's low-risk nature makes a 3-month trial of CoQ10 worth considering patients with statin-associated myalgia, and possibly fatigue, poor concentration and headaches associated with statin use as well[48]

Sports supplement

- CoQ10 is essential for energy metabolism and reducing oxidative stress, however its effect on physical capacity has shown negative results. May be due to insufficient dosing/treatment times, or differences in baseline CoQ10 levels

Chronic obstructive pulmonary disease (COPD)

- COPD patients have increased oxidative stress so the antioxidant capacity of CoQ10 might be beneficial[49] In patients receiving CoQ10 (50 mg), they increased maximum oxygen consumption 13% and maximum expired volume 10% compared to placebo[50]

Cystic Fibrosis

- Malabsorption of fat-soluble antioxidants such as CoQ10 is common in CF
    - Deficiency in these compounds results in increased oxidative stress
    - In a pilot study, CoQ10 in combination with other fat-soluble nutrients and anti-oxidants demonstrated improvement in antioxidant plasma levels associated with reduction in airway inflammation in CF patients[51]

Neuroprotective

- CoQ10 inhibits formation of beta-amyloid protein in vitro (Ono et al 2005) and clinically low levels of CoQ10 are found in cortex of brain of Parkinson's patients[52]
- Protects against neuronal damage produced by ischemia, atherosclerosis and toxic injury

Parkinson's disease

- Pathogenesis points to defect in mitochondrial respiratory chain, oxidative damage and inflammation in the degeneration of nigrostriatal dopaminergic neurons[53–55]
- CoQ10 might exert both neuroprotective and symptomatic effects in PD, data is inconsistent though

Alzheimer's dementia

- Similar pathogenesis to PD with mitochondrial dysfunction and oxidative damage playing a role, but evidence is currently limited to test tube and animal studies

Migraine

- Migraines are known to have an underlying mitochondrial dysfunction component. CoQ10 supplementation (150 mg/day) in 32 patients over 3 months reduced frequency and duration of migraines[56] In double-blind, randomized, placebo-controlled study, CoQ10 (300 mg/day) over 3 months reduced migraines in 47.6% of patients compared to 14.4% for placebo[56]
- CoQ10 also found to reduce frequency, severity and duration of migraines in pediatric patients[57]

Fibromyalgia

- Some have suggested CoQ10 deficiency players a role in the pathophysiology of fibromyalgia[58] as patients have been found to have increased levels of oxidative stress and decreased ATP production[59]
- When treated with CoQ10 (300 mg/day for 12 weeks), fibromyalgia patients decreased their level of oxidative stress to the same level as controls and ATP and catalase increased. Also reduced clinical symptoms and headaches

Male infertility

- Potentially beneficial due to its antioxidant effects and improved mitochondrial activity which influences spermatogenesis and motility. Those with infertility have lower seminal levels of CoQ10 and higher oxidative stress[60]
- CoQ10 supplementation increased seminal CoQ10 levels and antioxidants catalase and superoxide dismutate, and decreased oxidative stress as measure by 8-isoprostane[61]
- This associated with improved sperm parameters[62] and may increase pregnancy rate[63]

Cancer

- Case reports have shown effectiveness of CoQ10 in reducing metastases or elimination of tumors[64,65]

Reducing side effects of tamoxifen

- CoQ10 (100 mg) supplementation in breast cancer patients counteracted effects of tamoxifen on raising triglycerides and increasing angiogenesis[66]

Reducing cardiotoxicity effects of anthracyclines

- Protects mitochondria of heart from anthracycline-induced damage[67]
- Protects against doxorubicin cardiotoxicity[68,69]

Mitochondrial myopathy

- CoQ10 (1200 mg/day) in patients with mitochondrial disease showed 5.5-fold increased CoQ10 levels, reduced post-exercise lactate rise, and increased cycle aerobic capacity[70]

Macular degeneration

- Level of CoQ10 in retina decreases by 40% with age and reduction in antioxidant protection and ATP synthesis may contribute to age-related eye diseases[71]
- In combination with omega-3 fatty acids and acetyl-L-carnitine, CoQ10 may improve mitochondrial dysfunction, improve lipid metabolism and ATP production in regiment epithelium improving photoreceptors turnover and reduced generation of reactive oxygen species[72]

Friedreich's ataxia

- Decreased mitochondrial respiratory chain function, increased oxidative stress and iron accumulation plays role in disease mechanism[73]
- Treatment with CoQ10 (400 mg/day) and vitamin E (2100 IU/day) showed improvement in cardiac and skeletal muscle bioenergetics and heart function in Friedreich's ataxia patients[74]

Tinnitus and hearing loss

- CoQ10 supplement in patients with low plasma CoQ10, may decrease tinnitus expression[75]

Myelodysplastic syndromes

- CoQ10 supplementation may benefit a subset of MDS patients as multiple mutations in mitochondrial DNA found in MDS patients[76]

Huntington's chorea

- CoQ10 (600 mg/day) taken for 30 months produced a slower decline and improvement in secondary measure in patients with early Huntington's chorea[77]

Preeclampsia

- Among women at risk of preeclampsia, receiving CoQ10 (100 mg/twice daily) from week 20 until delivery reduced risk of developing preeclampsia compared to placebo[78]

Diabetes

- Plasma CoQ10 was lower in patients with type 2 diabetes as well as a negative correlation between plasma CoQ10 and HbA1c[79]

- Treatment with CoQ10 (200 mg/day) in patients with T2DM reduced total cholesterol and LDL, and improved glycemic control and HbA1c[36]

Peyronie's disease

- Early treatment with CoQ10 (300 mg/day) for 24 weeks reduced plaque size and penile curvature and improved erectile function[80]

DOSE:

Effective dose depends on the form used. The most absorbable form is in a crystal-free lipid matrix.

Range is 25 to 300 mg daily.

Powdered forms may need to be dosed 4 to 8 fold higher for similar effect.

Food sources

- Most concentrated in meat and fish products, also in boiled broccoli, cauliflower, nuts, spinach and soy. Low levels may be found in all meats and plants.
- Dietary intake approximately 3-5 mg/day[1]

CAUTIONS & SIDE EFFECTS:

- Overall safe and well-tolerated (no known toxicity)
- May cause dizziness, nausea, epicanthic discomfort, anorexia, diarrhea, photophobia, irritability and skin rash occur in less than 1% of patients, often with higher doses
- Possible negative interactions with theophylline, and warfarin (may alter INR)

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