## Ubiquinol Explained

Since the ubiquinol form has two additional hydrogens, it results in the conversion of two ketone groups into hydroxyl groups on the active portion of the molecule. This causes an increase in the polarity of the $CoQ_{10}$ molecule and may be a significant factor behind the observed enhanced bioavailability of ubiquinol. Orally, ubiquinol exhibits greater bioavailability than ubiquinone: one study showed subjects ingesting 150 mg per day ubiquinol supplementation displayed peak values within 28 days of 3.84 mcg/ml of plasma. Additionally, research in an animal model investigating the neuroprotective effects of both forms of CoQ10 showed greater blood levels and improved efficacy by ubiquinol in comparison to ubiquinone.

*Table:* $CoQ_{10}$ levels in selected foods

| *Food* | *Coenzyme $Q_{10}$ concentration [mg/kg]* |
|---|---|
| *Meat* | |
| - beef | |
| -- heart | 113 |
| -- liver | 39-50 |
| -- muscle | 26-40 |
| - pork | |
| -- heart | 11.8-128.2 |
| -- liver | 22.7-54.0 |
| -- muscle | 13.8-45.0 |
| - chicken | |
| -- heart | 116.2-132.2 |
| *Fish* | |
| - sardine | 5-64 |
| - mackerel | |
| -- red flesh | 43-67 |

| | |
|---|---|
| -- white flesh | 11-16 |
| - salmon | 4-8 |
| - tuna | 5 |
| | |
| *Oils* | |
| - soybean | 54-280 |
| - olive | 4-160 |
| - grapeseed | 64-73 |
| - sunflower | 4-15 |
| - rice bran | / |
| - coconut | / |
| | |
| *Nuts* | |
| - peanuts | 27 |
| - walnuts | 19 |
| - sesame seeds | 18-23 |
| - pistachio nuts | 20 |
| - hazelnuts | 17 |
| - almond | 5-14 |
| | |
| *Vegetables* | |
| - parsley | 8-26 |
| - broccoli | 6-9 |
| - cauliflower | 2-7 |
| - spinach | up to 10 |
| - grape | 6-7 |
| - Chinese cabbage | 2-5 |
| | |

| *Fruit* | |
|---|---|
| - avocado | 10 |
| - blackcurrant | 3 |
| - strawberry | 1 |
| - orange | 1-2 |
| - grapefruit | 1 |
| - apple | 1 |

Meat and fish are the richest source of dietary $CoQ_{10}$ and levels over 50 mg/kg can be found in beef, pork and chicken heart and chicken liver. Dairy products are much poorer sources of $CoQ_{10}$ compared to animal tissues. Vegetable oils are also quite rich in $CoQ_{10}$. Within vegetables, parsley, and perilla are the richest $CoQ_{10}$ sources, but significant differences in their $CoQ_{10}$ levels can be found in the literature. Broccoli, grape, and cauliflower are modest sources of $CoQ_{10}$. Most fruit and berries represent a poor to very poor source of $CoQ_{10}$, with the exception of avocado, with a relatively high $CoQ_{10}$ content

*Effect of heat and processing*

Cooking by frying reduces $CoQ_{10}$ content by 14-32%.

Coenzyme q10 is an important nutrition. It is also known as coq10. This substance is there in all our cells. This is vital for our energy metabolism. Considering these facts, we will be curious to know what food has coenzyme q10 in it. We should not limit to single nutrition but a holistic approach is the best option.

*The Energy cycle*

Unless all the 100 trillion cells in our body are provided with the energy, we will not lead a healthy life. We will have one disease or the other.

The food we eat is converted into energy after undergoing many phases. In one such phase, the food it synthesized as adenosine triphosphate (ATP), an energy store house. This is one of the important compartments in our cells. To produce this ATP, coq10 is essential.

While our general health will be affected in case of low level of coq10, particularly we should know that the deficiency will have great impact for our heart. As we all know, heart is the most dynamic organ in our body which requires lot of energy. That is why the coq10 is kept more in the heart than any other place.

Since this is important to convert food into energy, its role to ensure sugar level in the blood is crucial. The deficiency of coq10 will cause increased sugar in the blood leading to diabetes.

It is a good antioxidant by itself apart from enabling vitamin E to help scavenge free radicals. Obviously this shows the importance of this nutrition for good immune system and to prevent cancer.

Now, let us come to the important aspect of what food has coenzyme q10 in it. The coq10 richest food is sardine and mackerel followed by reindeer muscle meat, pork and beef heart, liver etc. Other than these, it is also available in varying degrees in other meat, poultry and fish products. Though this is not rich in many vegetables, vegetarians should eat more of broccoli, spinach, soy products, peanuts etc., to improve the coq10 level.

The best form of taking the coq10 rich food is by boiling instead of frying or firing. This is because, such heating wipes out the coq10. Also, the meat while boiling should not be overcooked. Else, the level will be depleted.

Milled, canned, frozen and preserved foods will have very minimal level of coq10 when compared to fresh and unprocessed items.

The coq10 is a fat soluble substance. Generally, to get the maximum benefit, it is taken along with olive or soy bean oil or any other fat substance.

Coq10 is naturally synthesized in our liver. While the food above prescribed will definitely improve the level of coq10, in many cases we may not be able to get required dose. The daily dosage of this nutrition varies according to health conditions of a person.

A normal person should have 30 to 60 mg. Cancer patients are prescribed to take 200 to 600 mg per day. Cardiac related problems should be addressed with a dosage of 360 mg per day. 200 mg per day is ideal for diabetes patients. One should also keep in mind the dosage per time should not exceed 180 mg.

*Function*

Coenzyme $Q_{10}$ is soluble in lipids (fats) and is found in virtually all cell membranes, as well as lipoproteins. The ability of the benzoquinone head group of coenzyme $Q_{10}$ to accept and donate electrons is a critical feature in its biochemical functions. Coenzyme $Q_{10}$ can exist in three oxidation states:

1) fully reduced ubiquinol form ($CoQ_{10}H_2$),

2) radical semiquinone intermediate ($CoQ_{10}H\cdot$),

3) fully oxidized ubiquinone form ($CoQ_{10}$).

*Mitochondrial ATP synthesis*

The conversion of energy from carbohydrates and fats to adenosine triphosphate (ATP), the form of energy used by cells, requires the presence of coenzyme Q in the inner mitochondrial membrane. As part of the mitochondrial electron transport chain, coenzyme Q accepts electrons from reducing equivalents generated during fatty acid and glucose metabolism and then transfers them to electron acceptors. At the same time, coenzyme Q transfers protons outside

the inner mitochondrial membrane, creating a proton gradient across that membrane. The energy released when the protons flow back into the mitochondrial interior is used to form ATP.

*Lysosomal function*

Lysosomes are organelles within cells that are specialized for the digestion of cellular debris. The digestive enzymes within lysosomes function optimally at an acid pH, meaning they require a permanent supply of protons. The lysosomal membranes that separate those digestive enzymes from the rest of the cell contain relatively high concentrations of coenzyme $Q_{10}$. Recent research suggests that coenzyme $Q_{10}$ plays an important role in the transport of protons across lysosomal membranes to maintain the optimal pH.

*Antioxidant functions*

In its reduced form, $CoQ_{10}H_2$ is an effective fat-soluble antioxidant. The presence of a significant amount of $CoQ_{10}H_2$ in cell membranes, along with enzymes that are capable of reducing oxidized $CoQ_{10}$ back to $CoQ_{10}H_2$, supports the idea that $CoQ_{10}H_2$ is an important cellular antioxidant. $CoQ_{10}H_2$ has been found to inhibit lipid peroxidation when cell membranes and low-density lipoproteins (LDL) are exposed to oxidizing conditions outside the body (ex vivo). When LDL is oxidized ex vivo, $CoQ_{10}H_2$ is the first antioxidant consumed. Moreover, the formation of oxidized lipids and the consumption of □-tocopherol (□-TOH, biologically the most active form of vitamin E) are suppressed while $CoQ_{10}H_2$ is present. In isolated mitochondria, coenzyme $Q_{10}$ can protect membrane proteins and DNA from the oxidative damage that accompanies lipid peroxidation. In addition to neutralizing free radicals directly, $CoQ_{10}H_2$ is capable of regenerating □-TOH from its one-electron oxidation product, □-tocopheroxyl radical (□-TO·).

*Nutrient Interactions*

*Vitamin E*

Alpha (□)-tocopherol (vitamin E) and coenzyme $Q_{10}$ are the principal fat-soluble antioxidants in membranes and lipoproteins. When □-TOH neutralizes a free radical, such as a lipid peroxyl radical (LOO·), it becomes oxidized itself, forming □-TO·, which can promote the oxidation of lipoproteins under certain conditions in the test tube. When the reduced form of coenzyme $Q_{10}$ ($CoQ_{10}H_2$) reacts with □-TO·, □-TOH is regenerated and the semiquinone radical ($CoQ_{10}H$·) is formed. It is possible for $CoQ_{10}H$· to react with oxygen ($O_2$) to produce superoxide anion radical ($O_2$·-), which is a much less oxidizing radical than LOO·. However, $CoQ_{10}H$· can also reduce □-TO· back to □-TOH, resulting in the formation of fully oxidized coenzyme $Q_{10}$ ($CoQ_{10}$), which does not react with $O_2$ to form $O_2$·

*Sources*

*Biosynthesis*

Coenzyme $Q_{10}$ is synthesized in most human tissues. The biosynthesis of coenzyme $Q_{10}$ involves three major steps:

1) Synthesis of the benzoquinone structure from either tyrosine or phenylalanine, two amino acids.

2) Synthesis of the isoprene side chain from acetyl-coenzyme A (CoA) via the mevalonate pathway,

3) The joining or condensation of these two structures. The enzyme hydroxymethylglutaryl (HMG)-CoA reductase plays a critical role in the regulation of coenzyme $Q_{10}$ synthesis as well as the regulation of cholesterol synthesis.

The first step in benzoquinone biosynthesis (the conversion of tyrosine to 4-hydroxyphenylpyruvic acid) requires vitamin $B_6$ in the form of pyridoxal 5'-phosphate. Thus, adequate vitamin $B_6$ nutrition is essential for coenzyme $Q_{10}$ biosynthesis.

*Does oral coenzyme $Q_{10}$ supplementation increase tissue levels?*

Oral supplementation with coenzyme $Q_{10}$ is known to increase blood and lipoprotein concentrations of coenzyme $Q_{10}$ in humans. However, it is not clear whether oral supplementation increases coenzyme $Q_{10}$ concentrations in other tissues of individuals with normal endogenous coenzyme $Q_{10}$ biosynthesis. Oral coenzyme $Q_{10}$ supplementation of young healthy animals has not generally resulted in increased tissue concentrations, other than in the liver, spleen, and blood vessels.

Supplementation of healthy men with 120 mg/d for three weeks did not increase muscle concentrations of coenzyme $Q_{10}$. However, supplementation may increase coenzyme $Q_{10}$ levels in tissues that are deficient. For example, oral supplementation of aged rats increased brain coenzyme $Q_{10}$ concentrations, and a study of 24 older adults supplemented with 300 mg/d of coenzyme $Q_{10}$ or placebo for at least seven days prior to cardiac surgery found that the coenzyme $Q_{10}$ content of atrial tissue was significantly increased in those taking coenzyme $Q_{10}$, especially in those over 70 years of age. Clearly, this is an area of research that requires further investigation.

*Deficiency*

No coenzyme $Q_{10}$ deficiency symptoms have been reported in the general population, so it is generally assumed that normal biosynthesis and a varied diet provides sufficient coenzyme $Q_{10}$ for healthy individuals. It has been estimated that dietary consumption contributes about 25% of plasma coenzyme $Q_{10}$, but there are currently no specific dietary intake recommendations for coenzyme $Q_{10}$ from the Food and Nutrition Board or other agencies. The extent to which dietary consumption contributes to tissue coenzyme $Q_{10}$ levels is not clear.

Genetic defects of coenzyme $Q_{10}$ biosynthesis appear to be rare because only four cases have been reported in the medical literature. Coenzyme $Q_{10}$ levels have been found to decline gradually with age in

a number of different tissues, but it is unclear whether this age-associated decline constitutes a deficiency.

Decreased plasma levels of coenzyme $Q_{10}$ have been observed in individuals with diabetes, cancer, and congestive heart failure. Lipid lowering medications that inhibit the activity of HMG-CoA reductase, a critical enzyme in both cholesterol and coenzyme $Q_{10}$ biosynthesis, decrease plasma coenzyme $Q_{10}$ levels (see HMG-CoA reductase inhibitors (statins) under Drug Interactions), although it remains unclear whether this has clinical or symptomatic implications.

*Disease Prevention*

*Aging*

According to the free radical and mitochondrial theories of aging, oxidative damage of cell structures by reactive oxygen species (ROS) plays an important role in the functional declines that accompany aging. ROS are generated by mitochondria as a byproduct of ATP production. If not neutralized by antioxidants, ROS may damage mitochondria over time, causing them to function less efficiently and to generate more damaging ROS in a self-perpetuating cycle. Coenzyme $Q_{10}$ plays an important role in mitochondrial ATP synthesis and functions as an antioxidant in mitochondrial membranes.

Moreover, tissue levels of coenzyme $Q_{10}$ have been reported to decline with age (21). One of the hallmarks of aging is a decline in energy metabolism in many tissues, especially liver, heart, and skeletal muscle. It has been proposed that age-associated declines in tissue coenzyme $Q_{10}$ levels may play a role in this decline. In recent studies, lifelong dietary supplementation with coenzyme $Q_{10}$ did not increase the life spans of rats or mice; however, one study showed that coenzyme $Q_{10}$ supplementation attenuates the age-related increase in DNA damage. Presently, there is no scientific evidence that

coenzyme $Q_{10}$ supplementation prolongs life or prevents age-related functional declines in humans.

*Cardiovascular disease*

Oxidative modification of low-density lipoproteins (LDL) in arterial walls is thought to represent an early event leading to the development of atherosclerosis. Reduced coenzyme $Q_{10}$ ($CoQ_{10}H_2$) inhibits the oxidation of LDL in the test tube (*in vitro*) and works together with α-TOH to inhibit LDL oxidation by reducing the □-TO· back to □-TOH. In the absence of a co-antioxidant such as $CoQ_{10}H_2$ (or vitamin C), □-TOH can, under certain conditions, promote the oxidation of LDL in *vitro*.

Supplementation with coenzyme $Q_{10}$ increases the concentration of $CoQ_{10}H_2$ in human LDL. Studies in apolipoprotein E-deficient mice, an animal model of atherosclerosis, found that coenzyme $Q_{10}$ supplementation with supra-pharmacological amounts of coenzyme $Q_{10}$ significantly inhibited the formation of atherosclerotic lesions. Interestingly, co-supplementation of these mice with □-TOH and coenzyme $Q_{10}$ was more effective in inhibiting atherosclerosis than supplementation with either □-TOH or coenzyme $Q_{10}$ alone.

Another important step in the development of atherosclerosis is the recruitment of immune cells known as monocytes into the blood vessel walls. This recruitment is dependent in part on monocyte expression of cell adhesion molecules (integrins). Supplementation of ten healthy men and women with 200 mg/d of coenzyme $Q_{10}$ for ten weeks resulted in significant decreases in monocyte expression of integrins, suggesting another potential mechanism for the inhibition of atherosclerosis by coenzyme $Q_{10}$. Although coenzyme $Q_{10}$ supplementation shows promise as an inhibitor of LDL oxidation and atherosclerosis, more research is needed to determine whether coenzyme $Q_{10}$ supplementation can inhibit the development of atherosclerosis in humans.

*Disease Treatment*

*Mitochondrial encephaloymopathies*

Mitochondrial encephaloymopathies represent a diverse group of genetic disorders resulting from numerous inherited abnormalities in the function of the mitochondrial electron transport chain. Coenzyme $Q_{10}$ supplementation has resulted in clinical and metabolic improvement in some patients with various types of mitochondrial encephaloymopathies. Neuromuscular and widespread tissue coenzyme $Q_{10}$ deficiencies have been found in a very small subpopulation of individuals with mitochondrial encephaloymopathies. In those rare individuals with genetic defects in coenzyme $Q_{10}$ biosynthesis, coenzyme $Q_{10}$ supplementation has resulted in substantial improvement.

*Cardiovascular diseases*

*Congestive heart failure*

Impairment of the heart's ability to pump enough blood for all of the body's needs is known as congestive heart failure. In coronary artery disease, accumulation of atherosclerotic plaque in the coronary arteries may prevent parts of the heart muscle from getting adequate blood supply, ultimately resulting in cardiac damage and impaired pumping ability. Myocardial infarction (MI) may also damage the heart muscle, leading to heart failure. Because physical exercise increases the demand on the weakened heart, measures of exercise tolerance are frequently used to monitor the severity of heart failure. Echocardiography is also used to determine the left ventricular ejection fraction; an objective measure of the heart's pumping ability. The finding that myocardial coenzyme $Q_{10}$ levels were lower in patients with more severe versus milder heart failure led to several clinical trials of coenzyme $Q_{10}$ supplementation in heart failure patients. A number of small intervention trials that administered supplemental coenzyme $Q_{10}$ (100-200 mg/d of coenzyme $Q_{10}$ for one to three months) to congestive heart failure patients, in conjunction with conventional medical therapy, have demonstrated improvements

in some cardiac function measures. However, other researchers have found that supplementing the diet with 100-200 mg/d of enzyme $Q_{10}$, along with conventional medical therapy, did not significantly improve left ventricular ejection fraction or exercise performance in heart failure patients. Although there is some evidence that coenzyme $Q_{10}$ supplementation may be of benefit, large well-designed intervention trials are needed to determine whether coenzyme $Q_{10}$ supplementation has value as an adjunct to conventional medical therapy in the treatment of congestive heart failure. One such large trial is presently being conducted.

*Myocardial infarction and cardiac surgery*

The heart muscle may become oxygen-deprived (ischemic) as the result of myocardial infarction (MI) or during cardiac surgery. Increased generation of ROS when the heart muscle's oxygen supply is restored (reperfusion) is thought to be an important contributor to myocardial damage occurring during ischemia-reperfusion. Pretreatment of animals with coenzyme $Q_{10}$ has been found to decrease myocardial damage due to ischemia-reperfusion. Another potential source of ischemia-reperfusion injury is aortic clamping during some types of cardiac surgery, such as coronary artery bypass graft (CABG) surgery. Three out of four placebo-controlled trials found that coenzyme $Q_{10}$ pretreatment (60-300 mg/d for 7-14 days prior to surgery) provided some benefit in short-term outcome measures after CABG surgery. In the placebo-controlled trial that did not find preoperative coenzyme $Q_{10}$ supplementation to be of benefit, patients were treated with 600 mg of coenzyme $Q_{10}$ 12 hours prior to surgery, suggesting that preoperative coenzyme $Q_{10}$ treatment may need to commence at least one week prior to CABG surgery in order to realize any benefit. Although the results are promising, these trials have included relatively few people and have only examined outcomes shortly after CABG surgery.

*Angina pectoris*

Myocardial ischemia may also lead to chest pain known as angina pectoris. People with angina pectoris often experience symptoms when the demand for oxygen exceeds the capacity of the coronary circulation to deliver it to the heart muscle, e.g., during exercise. Five small placebo-controlled studies have examined the effects of oral coenzyme $Q_{10}$ supplementation (60-600 mg/d) in addition to conventional medical therapy in patients with chronic stable angina. In most of the studies, coenzyme $Q_{10}$ supplementation improved exercise tolerance and reduced or delayed electrocardiographic changes associated with myocardial ischemia compared to placebo. However, only two of the studies found significant decreases in symptom frequency and nitroglycerin consumption with coenzyme $Q_{10}$ supplementation. Presently, there is only limited evidence suggesting that coenzyme $Q_{10}$ supplementation would be a useful adjunct to conventional angina therapy.

*Hypertension*

The results of several small, uncontrolled studies in humans suggest that coenzyme $Q_{10}$ supplementation could be beneficial in the treatment of hypertension. More recently, two short-term placebo-controlled trials found that coenzyme $Q_{10}$ supplementation resulted in moderate blood pressure decreases in hypertensive individuals. The addition of 120 mg/d of coenzyme $Q_{10}$ to conventional medical therapy for eight weeks in patients with hypertension and coronary artery disease decreased systolic blood pressure by an average of 12 mm Hg and diastolic blood pressure by an average of 6 mm Hg, in comparison to a placebo containing B-complex vitamins. In patients with isolated systolic hypertension, supplementation with both coenzyme $Q_{10}$ (120 mg/d) and vitamin E (300 IU/d) for 12 weeks resulted in an average decrease of 17 mm Hg in systolic blood pressure compared with 300 IU/day of vitamin E (300 IU/d) alone. However, further research is needed to determine whether coenzyme $Q_{10}$ supplementation can provide significant long-term benefit in the treatment of hypertension.

*Vascular endothelial function (blood vessel dilation)*

Normal function of the inner lining of blood vessels, known as the vascular endothelium, plays an important role in preventing cardiovascular diseases. Atherosclerosis is associated with impairment of vascular endothelial function, thereby compromising the ability of blood vessels to relax. Endothelium-dependent blood vessel relaxation (vasodilation) is impaired in individuals with elevated serum cholesterol levels as well as in patients with coronary artery disease or diabetes. More recently, a prospective, randomized cross-over study of 25 men with endothelial dysfunction found that coenzyme $Q_{10}$ supplementation (150 mg/d) significantly improved endothelial function, similar to that of a lipid-lowering medication.

Maternally inherited diabetes mellitus and deafness (MIDD) is the result of a mutation in mitochondrial DNA, which is inherited exclusively from one's mother. Although mitochondrial diabetes accounts for less than 1% of all diabetes, there is some evidence that long-term coenzyme $Q_{10}$ supplementation (150 mg/d) may improve insulin secretion and prevent progressive hearing loss in these patients.

*Neurodegenerative diseases*

*Parkinson's disease*

Parkinson's disease is a degenerative neurological disorder characterized by tremors, muscular rigidity, and slow movements. It is estimated to affect approximately 1% of people over the age of 65. Although the causes of Parkinson's disease are not all known, decreased activity of complex I of the mitochondrial electron transport chain and increased oxidative stress in a part of the brain called the substantia nigra are thought to play a role. Coenzyme $Q_{10}$ is the electron acceptor for complex I as well as an antioxidant, and decreased ratios of reduced oxidized coenzyme $Q_{10}$ have been found in platelets of individuals with Parkinson's disease. A 16-month randomized placebo-controlled trial evaluated the safety and efficacy

of 300, 600, or 1200 mg/d of coenzyme $Q_{10}$ in 80 people with early Parkinson's disease. Coenzyme $Q_{10}$ supplementation was well tolerated at all doses and was associated with slower deterioration of function in Parkinson's disease patients compared to placebo. However, the difference was statistically significant only in the group taking 1200 mg/d. More recently, a small placebo-controlled trial showed that oral administration of 360 mg/d of coenzyme $Q_{10}$ for four weeks moderately benefited Parkinson's disease patients. Although these preliminary findings are promising, they need to be confirmed in larger clinical trials before recommending the use of coenzyme $Q_{10}$ in early Parkinson's disease.

*Huntington's disease*

Huntington's disease is an inherited neurodegenerative disorder characterized by selective degeneration of nerve cells known as striatal spiny neurons. Symptoms, such as movement disorders and impaired cognitive function, typically develop in the fourth decade of life and progressively deteriorate over time. Animal models indicate that impaired mitochondrial function and glutamate-mediated neurotoxicity may play roles in the pathology of Huntington's disease. Coenzyme $Q_{10}$ supplementation has been found to decrease brain lesion size in animal models of Huntington's disease and to decrease brain lactate levels in Huntington's disease patients. Feeding a combination of coenzyme $Q_{10}$ (0.2% of diet) and remacemide (0.007% of diet) to transgenic mice that express the Huntington's disease protein (HD-N171-82Q mice) resulted in improved motor performance and/or survival. Remacemide is an antagonist of the neuronal receptor that is activated by glutamate.

It was recently shown that the R6/2 mouse model of Huntington's disease exhibits a progressive decline in behavioral and neurological symptoms similar to that of the human condition. Thus, R6/2 mice may be an ideal model to investigate potential therapies for Huntington's disease. Studies employing these mice have shown that dietary supplementation with coenzyme $Q_{10}$ (0.2% of diet) improves

motor performance, body weight loss, and overall survival; coenzyme $Q_{10}$ supplementation was also associated with reductions in the various hallmarks of Huntington's disease, i.e., brain atrophy, ventricular enlargement, and striatal neuronal atrophy. Interestingly, co-administration of coenzyme $Q_{10}$ with either remacemide or the antibiotic minocycline resulted in even greater improvements in most measured parameters.

*Friedreich's ataxia*

Friedreich's ataxia (FRDA) is an inherited, autosomal recessive neurodegenerative disease caused by mutations in the gene that encodes frataxin, a mitochondrial protein of unknown function. Decreased expression of frataxin is associated with accumulation of iron within the mitochondria, thereby resulting in increased oxidative stress, imbalances in iron-sulfur containing proteins including mitochondrial aconitase, and reduced activities of the mitochondrial respiratory chain.

Clinically, FRDA is a progressive disease characterized by limb ataxia and CNS abnormalities that result from sensory nerve degeneration. In addition, FRDA patients may present with symptoms of hypertrophic cardiomyopathy and diabetes.

A pilot study administering coenzyme $Q_{10}$ (200 mg/d) and vitamin E (2100 IU/d) to ten FDRA patients found that energy metabolism of cardiac and skeletal muscle was improved after only three months of therapy. Follow-up assessments at 47 months indicated that cardiac and skeletal muscle improvements were maintained, and that FRDA patients showed significant increases in fractional shortening, a measure of cardiac function. Moreover, the therapy was effective at preventing the progressive decline of neurological function. Although the results of this pilot study are promising, large-scale randomized clinical trials are necessary to determine whether coenzyme $Q_{10}$, in conjunction with vitamin E, has therapeutic benefit in FRDA.

*Cancer*

Interest in coenzyme $Q_{10}$ as a potential therapeutic agent in cancer was stimulated by an observational study that found that individuals with lung, pancreas, and especially breast cancer were more likely to have low plasma coenzyme $Q_{10}$ levels than healthy controls. Although a few case reports and an uncontrolled trial suggest that coenzyme $Q_{10}$ supplementation may be beneficial as an adjunct to conventional therapy for breast cancer, the lack of controlled clinical trials makes it impossible to determine the effects, if any, of coenzyme $Q_{10}$ supplementation in cancer patients.

*Athletic performance*

Although coenzyme $Q_{10}$ supplementation has improved exercise tolerance in some individuals with mitochondrial encephaloymopathies, there is little evidence that it improves athletic performance in healthy individuals. At least seven placebo-controlled trials have examined the effects of 100-150 mg/d of coenzyme $Q_{10}$ supplementation for three to eight weeks on physical performance in trained and untrained men. Most found no significant differences between groups taking coenzyme $Q_{10}$ and groups taking placebos with respect to measures of aerobic exercise performance, such as maximal oxygen consumption ($VO_2$ max) and exercise time to exhaustion. One study found the maximal cycling workload to be slightly (4%) increased after eight weeks of coenzyme $Q_{10}$ supplementation compared to placebo, although measures of aerobic power were not increased. Two studies actually found significantly greater improvement in measures of anaerobic and aerobic exercise performance after supplementation with a placebo compared to coenzyme $Q_{10}$. Studies on the effect of supplementation on physical performance in women are lacking, but there is little reason to suspect a gender difference in the response to coenzyme $Q_{10}$ supplementation.

*Safety*

*Toxicity*

There have been no reports of significant adverse side effects of oral coenzyme $Q_{10}$ supplementation at doses as high as 1200 mg/d for up to 16 months and 600 mg/d for up to 30 months. In fact, 1200 mg/d has recently been identified as the observed safe level (OSL) for coenzyme $Q_{10}$. Some people have experienced gastrointestinal symptoms, such as nausea, diarrhea, appetite suppression, heartburn, and abdominal discomfort. These adverse effects may be minimized if daily doses higher than 100 mg are divided into two or three daily doses. Because controlled safety studies in pregnant and lactating women are not available, the use of coenzyme $Q_{10}$ supplements by pregnant or breastfeeding women should be avoided.

*Drug Interactions*

*Warfarin*

Concomitant use of warfarin (Coumadin) and coenzyme $Q_{10}$ supplements has been reported to decrease the anticoagulant effect of warfarin in at least four cases. An individual on warfarin should not begin taking coenzyme $Q_{10}$ supplements without consulting the health care provider that is managing his or her anticoagulant therapy. If warfarin and coenzyme $Q_{10}$ are to be used concomitantly, blood tests to assess clotting time (prothrombin time; PT/INR) should be monitored frequently, especially in the first two weeks.

*HMG-CoA reductase inhibitors (statins)*

HMG-CoA reductase is an enzyme that plays a critical role in the regulation of cholesterol synthesis as well as coenzyme $Q_{10}$ synthesis, although it is now recognized that there are additional rate-limiting steps in the biosynthesis of cholesterol and coenzyme $Q_{10}$. HMG-CoA reductase inhibitors, also known as statins, are widely used cholesterol-lowering medications that may also decrease the endogenous synthesis of coenzyme $Q_{10}$. Therapeutic use of statins, including simvastatin (Zocor), pravastatin (Pravachol), lovastatin (Mevacor, Altocor), and atorvastatin (Lipitor), has been shown to decrease blood plasma or serum levels of coenzyme $Q_{10}$. However, it

has been recently suggested that blood coenzyme $Q_{10}$ concentrations should be reported only after normalizing to total lipid or cholesterol levels because coenzyme $Q_{10}$ circulates with lipoproteins and levels of coenzyme $Q_{10}$ are highly dependent upon levels of circulating lipids. Given the lipid-lowering effects of statins, it is therefore unclear whether these drugs actually decrease coenzyme $Q_{10}$ levels independent of a reduction in circulating lipids. Also, very few studies have examined coenzyme $Q_{10}$ content in target organs; thus, it is not clear whether statin therapy affects coenzyme $Q_{10}$ concentrations in the body's tissues. At present, more research is needed to determine whether coenzyme $Q_{10}$ supplementation might be beneficial for those taking HMG-CoA reductase inhibitors.