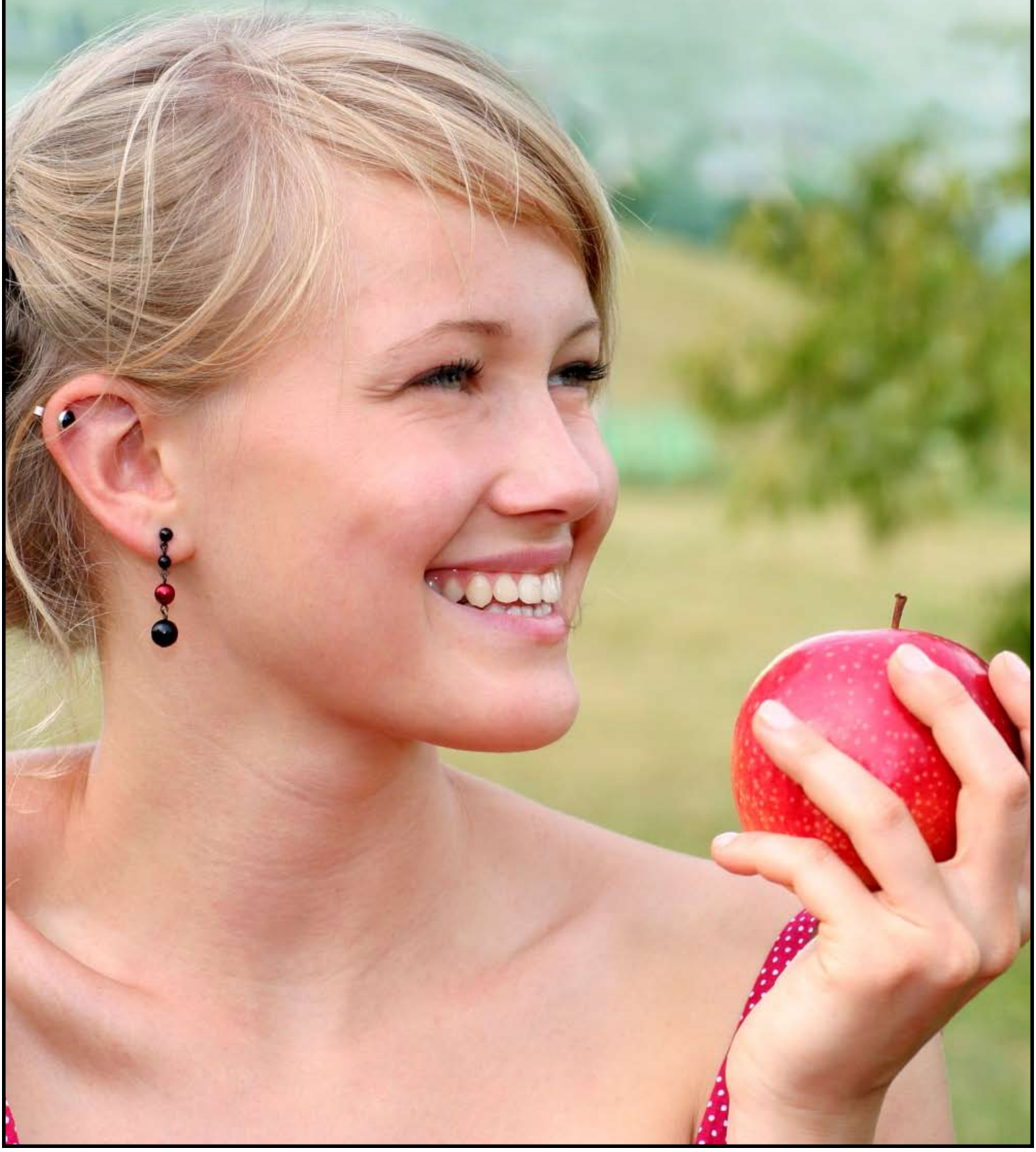
FAT-SOLUBLE VITAMINS℠

Fat-Soluble Vitamins Guide



How Vitamins Work Together

We know that fat-soluble vitamins are essential, but do we understand how they work together? Many clinicians encourage women to take vitamin D along with calcium to protect against osteoporosis, but without vitamin K, the calcium is not as effective. Additionally, low levels of vitamin K can lead to calcification in the arteries instead of the bone. Concurrent arterial calcification and osteoporosis has been called the "calcification paradox" and research finds it may be common in postmenopausal women.[1,2] Besides vitamin D and K, vitamin A is needed for bone remodeling, and supplementation with vitamin E has been shown to improve bone calcium content. Antioxidant intake has also been associated with reduced risk of osteoporotic hip fracture and plays an equally important role in atherogenesis. Vitamin E, beta-carotene, and Coenzyme Q10 (CoQ10) all act as antioxidants.

Vitamin A (Retinol)

Vitamin A has specific maintenance roles that include vision, bone growth, skin, and mucosal integrity.

Deficiencies of vitamin A result from inadequate diets, excessive alcohol intake, gastrointestinal conditions with diarrhea or fat malabsorption, as well as insufficient protein, energy and zinc intake leading to inadequate retinol binding synthesis.[3,4,5] Low serum retinol levels indicate depleted liver stores of vitamin A. Inadequate vitamin A levels are associated with increased respiratory infections, skin conditions, and infertility. Acute, chronic and teratogenic syndromes of vitamin A toxicity have been associated with very high doses. Danger of such toxic responses is especially high during early pregnancy.

Vitamin A		
Selected Foods	**Common Measure**	**IU**
Carrot juice	1 cup	45133
Pumpkin, canned,	1 cup	38129
Carrots, cooked	1 cup	26571
Sweet potato, cooked	1 potato	24554
Spinach, frozen,	1 cup	22916
Beef, variety meats, liver,	3 oz	22175
Sweet potato, canned,	1 cup	20357
Collards, frozen,	1 cup	19538
Kale, frozen,	1 cup	19115
Carrots, raw	1 cup	18377

RDA: 3000 IU (men), 2300 IU (women); Repletion Dose: 5000-25000 IU

Vitamin A in animal foods comes in the form of preformed retinoids. Vitamin A from plants comes from provitamin A or carotenoids.

Beta-Carotene

Carotenoids are the plant sources of vitamin A.

The most well studied carotenoid is beta-carotene. The absorption of beta-carotene and its conversion to vitamin A varies among individuals. Beta-carotene is converted into vitamin A in the liver. Of all the carotenoids, beta-carotene is converted into retinol most efficiently.[6] It also has antioxidant and other roles independent of vitamin A. Body pools of the two compounds are maintained independently so that, unless vitamin A levels are initially low, increased intake of beta-carotene may not affect higher levels of vitamin A.[7] A single beta-carotene is converted to 2 molecules of vitamin A, as seen in figure 1.

Blood concentrations of carotenoids are the best biological markers of fruit and vegetable consumption. A large body of epidemiological evidence suggests that higher blood concentrations of β-carotene and other carotenoids obtained from foods are associated with lower risk of several chronic diseases, such as...

Beta-Carotene		
Selected Foods	**Common Measure**	**(µg)**
Carrot juice	1 cup	21955
Pumpkin, canned	1 cup	17003
Sweet potato, cooked	1 cup	16803
Spinach, frozen	1 cup	13750

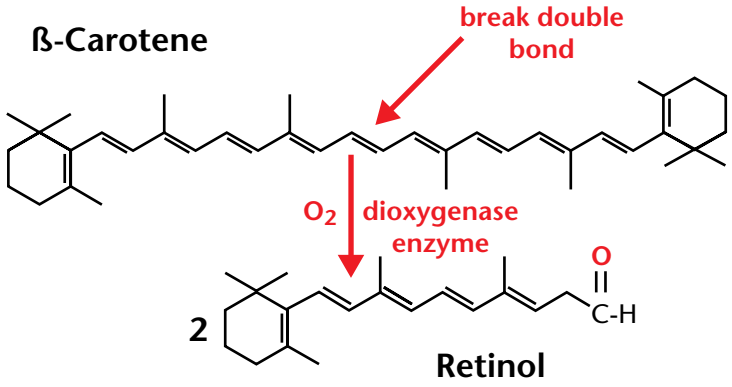
Carrots	1 cup	11971
Kale	1 cup	11470
Turnip greens	1 cup	10593
Vegetables, mixed	1 cup	9242
Pie, pumpkin	1 slice	7366
Beet greens	1 cup	6610
Carrot raw	1 carrot	72

1 µg beta-carotene = .5 µg RAE = 1.67 IU; 1 µg retinol = 1.0 µg RAE = 3.33 IU

Vitamin A and Beta-Carotene Laboratory Pattern

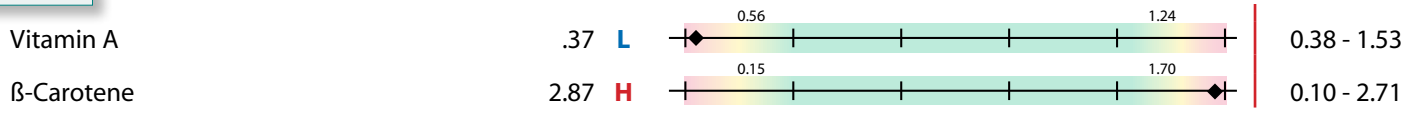
The conversion of beta-carotene (provitamin A) to vitamin A (retinol) is accelerated by thyroxin and is increased in hyperthyroidism. People with low thyroid function may have a slowed conversion of beta-carotene to vitamin A, and thus have a profile as shown in figure 2, with an elevated beta-carotene and low vitamin A. In such a situation it may be warranted to consider a patients thyroid function, which can also be influenced by tyrosine and iodine levels.[8,9]

Figure 1



Because vitamin A is a fat-soluble vitamin, GI conditions affecting the absorption of fats such as cystic fibrosis, pancreatic insufficiency, IBD, or small-bowel surgery may decrease the vitamin A absorption. Patients with low vitamin A levels may have an increased risk of respiratory infections or infertility issues.[10] If a patient has low vitamin A levels, a check of fatty acid levels is advised.

Figure 2



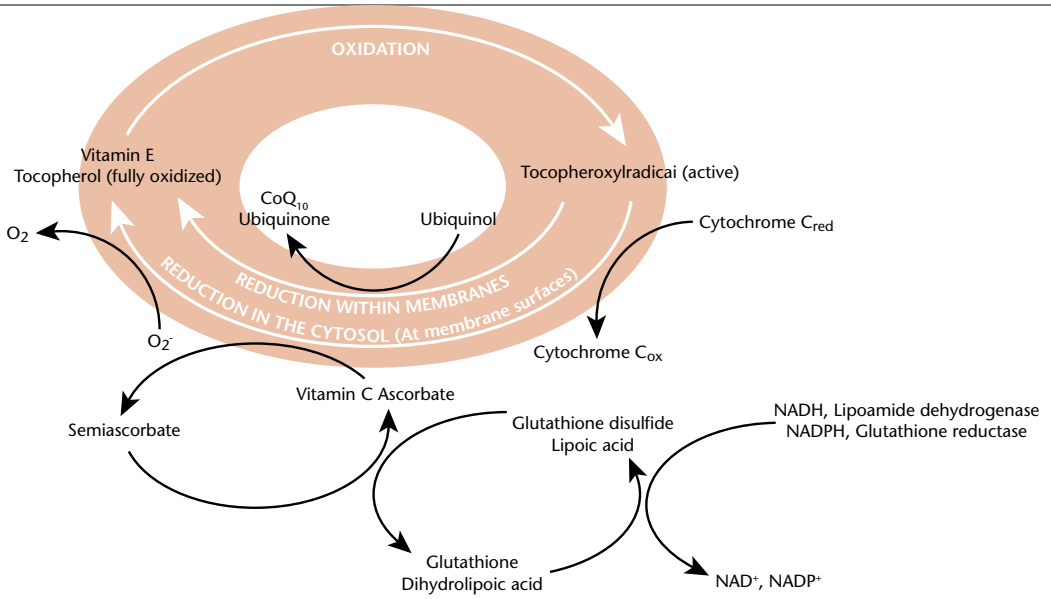
Vitamin E

Vitamin E is a fat-soluble vitamin that has antioxidant properties.

Vitamin E functions as a chain-breaking antioxidant that prevents the propagation of lipid peroxidation (figure 3). Alpha-tocopherol and CoQ_{10} are the primary fat-soluble antioxidants in cell membranes and lipoproteins. Vitamin E protects polyunsaturated fatty acids (PUFAs) within membrane phospholipids and in plasma lipoproteins.[11] Peroxyl radicals ($ROO^{\bullet}$) react with vitamin E one thousand times more rapidly than they do with PUFA.[11]

Vitamin E is transported in plasma in lipoproteins and serves as the most important membrane protective antioxidant and free radical scavenger in the body. Experimental vitamin E deficiency is difficult to produce in humans because of the intricate system of checks and balances in the antioxidant cascade. Although symptoms of mild to moderate vitamin E deficiency are subtle, many clinical effects are well documented. In general, lipid peroxidation markers are elevated during vitamin E depletion and their levels can be normalized upon vitamin E repletion. However, these markers are not necessarily specific to vitamin E, since changes in intake of other antioxidants can also change the levels of these markers. Since patients with hypertriglyceridemia have elevated levels of lipoproteins, vitamin E concentrations also tend to rise, leading to overestimation of vitamin E total body status.

Figure 3



Vitamin E enrichment of endothelial cells downregulates the expression of intercellular cell adhesion molecule (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), thereby decreasing the adhesion of blood cell components to the endothelium. Vitamin E also upregulates the expression of cytosolic phospholipase A_2 and cyclooxygenase-1. The enhanced expression of these two rate-limiting enzymes in the arachidonic acid cascade explains the observation that vitamin E, in a dose-dependent fashion, enhanced the release of prostacyclin, a potent vasodilator and inhibitor of platelet aggregation in humans.[12,13]

Vitamin E absorption from the intestinal lumen is dependent upon biliary and pancreatic secretions, micelle formation, uptake into enterocytes, and chylomicron secretion. Defects at any step lead to impaired absorption. The synthetic form is labeled "D, L", and the natural form is labeled "D". The synthetic form is only half as active.

Vitamin E			
Selected Foods	**Common Measure**	**Alpha-tocopherol (mg)**	**Gamma-tocopherol (mg)**
Olive oil	1 tablespoon	1.9	0.1
Soybean oil	1 tablespoon	1.2	10.8
Corn oil	1 tablespoon	1.9	8.2
Canola oil	1 tablespoon	2.4	4.2
Safflower oil	1 tablespoon	4.6	0.1
Sunflower oil	1 tablespoon	5.6	0.7
Almonds	1 ounce	7.3	0.3
Hazelnuts	1 ounce	4.3	0
Peanuts	1 ounce	2.4	2.4
Spinach	½ cup, raw chopped	1.8	0
Carrots	½ cup, raw chopped	0.4	0

RDA: 22.5 IU; Repletion Dose: 200-1600 IU; UL: 1500 IU; 1 mg alpha-tocopherol = 1.49 IU

Vitamin E Laboratory Pattern

Figure 4

Approximately 70% of dietary vitamin E intake in the U.S. is gamma-tocopherol. This is largely due to the high intake of soybean and other vegetable oils. Alpha-tocopherol supplementation results in significantly lower circulating gamma-tocopherol levels. Figure 4 shows someone who may have a diet with low gamma-tocopherol but is heavily supplementing with alpha-tocopherol.

Vitamin D

Vitamin D is known for regulating calcium and phosphorus levels in the blood.

The two primary forms of vitamin D, or calciferols, are cholecalciferol and ergocalciferol. Vitamin D_3 is formed from the conversion of 7-dehydroxycholesterol to 25-hydroxyvitamin D_3 via UV radiation from the sun. The kidneys are instructed by PTH to produce 1,25-hydroxyvitamin D_3 from circulating 25-hyroxyvitamin D_3 levels. Ergocalciferol is commercially prepared and is added to foods or made into supplements. Vitamin D_2 is absorbed by the gut and follows a similar pathway to vitamin D_3. 1,25-dihydroxyvitamin D_3 up regulates the production of calcium binding protein (CBP) or osteocalcin and is responsible for increasing calcium and phosphorus in the blood via intestinal absorption, bone resorption, and renal tubular absorption in the kidney. Low vitamin D levels have been linked to increased risk of hip fractures, depression, cardiovascular disease, cancer, and all-cause mortality.

Research has found a surprisingly high prevalance of vitamin D insufficiency in adults and children. The researchers at Harvard School of Public Health, Department of Nutrition estimated the optimal 25-hydroxyvitamin D level in relation to multiple health outcomes to be 36-40 ng/mL (90-100 nmol/L) though many clinicians aim for 50 ng/mL.[14]

Vitamin D		
Selected Foods	**Common Measure**	**(IU)**
Pink salmon, canned	3 ounces	530
Sardines, canned	3 ounces	231
Mackerel, canned	3 ounces	213
Cod liver oil	1 tablespoon	1360
Cow's milk, fortified with vitamin D	8 ounces	98

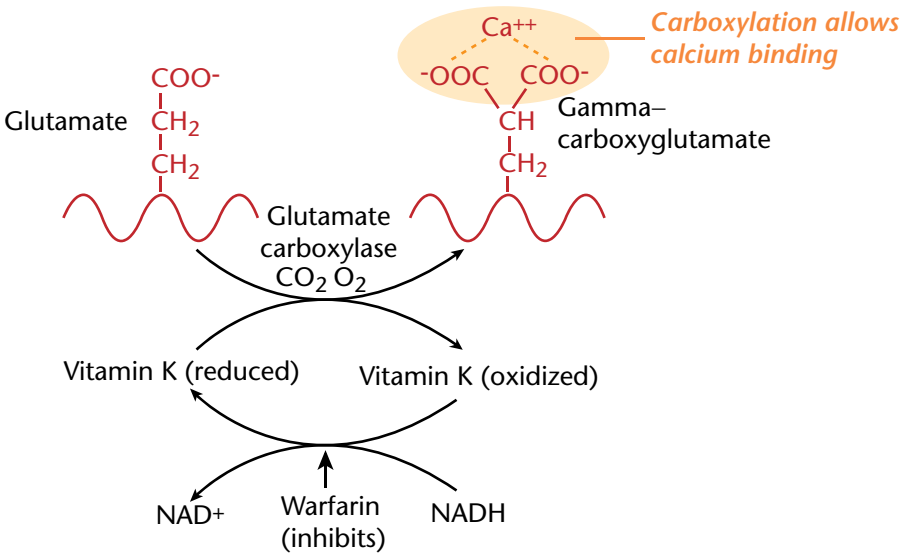
RDA: 400 IU/d; Repletion Dose: 700-10000 IU; UL: 2000 IU/d; 1 µ = 40 IU

Vitamin K

Vitamin K's primary function is the modification of specific proteins.

Vitamin K functions as a cofactor in the carboxylation (the addition of COO^-) of calcium binding proteins (figure 5), such as blood coagulation factors (in the liver), osteocalcin (in bone) and matrix Gla-proteins (in cartilage and vessel walls). The carboxylation of these proteins results in the deposition of ionic calcium.

Figure 5



Phylloquinone (Vitamin K_1) Concentration of Common Foods	
Food Item	**(µg)**
Collards, 1/2 cup	440
Spinach	380

Salad greens	315
Broccoli	180
Brussels sprouts	177
Cabbage	145
Bib lettuce	122
Beef, 3.5 oz	104
Eggs, whole	25

RDA: 120 µg/d (men), 90 µg/d (women); Repletion Dose: 100-1000 µg.d; UL: none set

Menaquinone (Vitamin K_2) is synthesized by bacteria in the large intestine.

Vitamin K status is especially important in the elderly and those with gastrointestinal conditions because of the inadequate dietary intake and absorptive difficulties, frequently complicated by drug therapies, specifically blood thinners. Vitamin K has been shown to be a valuable diagnostic as well as therapeutic parameter in osteoporosis. Higher vitamin K status has been associated with lower fracture rates in large epidemiologic studies.[15] Low vitamin K levels have also been associated with increased cardiovascular disease.[16] Osteocalcin (OC) is a vitamin K-dependent Ca^{2+}-binding protein and a product almost exclusively of mature, active osteoblasts. OC must be carboxylated to function. Proper carboxylation is also regulated by several factors including vitamin A, vitamin D, and calcium.[15] Vitamin K deficiencies can lead to an impairment in the carboxylation of OC, resulting in an increase in undercarboxylated OC (ucOC), in blood and urine where it can be measured. Vitamin K supplementation has been shown to decrease the level of circulating ucOC. Current RDA recommendations for vitamin K are based on coagulation saturation and may not be adequate for carboxylation of OC or other proteins.[17,18]

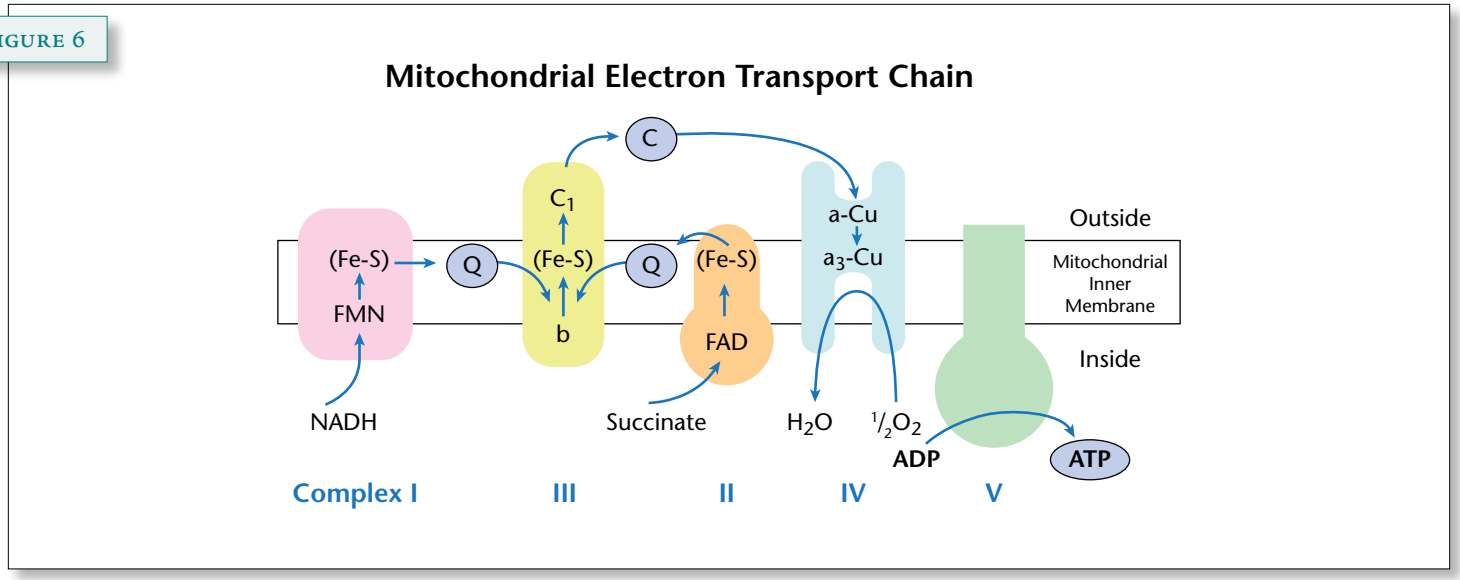
Very little vitamin K is stored by the body; only enough to supply the body's needs for a few days. No adverse effect has been reported for individuals supplementing or consuming higher amounts of vitamin K. Vitamin K from diet is often limited. Symptoms of vitamin K deficiency include easy brisability, epistaxis, gastrointestinal bleeding, menorrhagia and hameturia.

Coenzyme Q_{10} (CoQ_{10})

CoQ_{10} is needed for basic cell functions in energy production.

CoQ_{10}'s primary function is to shuttle electrons through the electron transport chain (ETC) in the mitochondrial inner membrane. This pathway is also referred to as the oxidative phosphorylation part of the central energy pathway. The electrons are received directly from succinate, or indirectly from several other substrates such as pyruvate, acyl-CoA, and alpha-ketoglutarate in the form of NADH. CoQ_{10} moves from one electron carrier complex to the next, ultimately delivering electrons, one at a time, in a never-ending cycle of oxidation and reduction (Figure 6). While the electrons are delivered one at a time, they leave in pairs to form ATP and H_20. If CoQ_{10} availability is not adequate the electrons will not be able to travel in pairs and single electrons will take another, less desirable, pathway that can lead to the generation of superoxide radicals. Optimal functioning of this pathway is critical for the fundamental energy generation that powers all cell functions. CoQ_{10} is also an antioxidant. Therapeutic approaches targeting mitochondrial disfunction and oxidative damage using CoQ_{10} hold great promise.[19]

Figure 6



CoQ_{10} synthesis is dependent on the availability of hydroxymethylglutarate (HMG), if HMG is low it will slow the rate of CoQ_{10} synthesis. Statin drugs block the conversion of HMG to cholesterol and to CoQ_{10}. A functional impairment at the level of mitochondrial CoQ_{10} electron transfer can also lead to elevations of succinate, malate, fumarate, and pyruvate, which are the energy pathway intermediates. The direct transfer of electrons from succinate in the electron transport system is slowed when the electron shuttle action of CoQ_{10} is inadequate to meet the demands. CoQ10 has been found to inhibit LDL-oxidation and atherosclerosis in research studies, the effect was increased with co-supplementation of vitamin E. [20,21]

Coenzyme Q_{10}		
Selected Foods	**Common Measure**	**(mg)**
Beef, fried	3 ounces	2.6
Herring, marinated	3 ounces	2.3
Soybean oil	1 tablespoon	1.3
Canola oil	1 tablespoon	1.0
Rainbow trout, steamed	3 ounces	0.9
Peanuts, roasted	1 ounce	0.8
Sesame seeds, roasted	1 ounce	0.7
Pistachio nuts, roasted	1 ounce	0.6
Broccoli, boiled	1/2 cup, chopped	0.5
Cauliflower, boiled	1/2 cup, chopped	0.4

RDA: none set; Repletion Dose: 30-300 mg/d (larger doses have been used for seerious conditions)

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