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Dietary Supplement Fact Sheet:

# Carnitine

Health Professional **Other Resources**



## Carnitine: What is it?

Carnitine, derived from an amino acid, is found in nearly all cells of the body. Its name is derived from the Latin *carnus* or flesh, as the compound was isolated from meat. Carnitine is the generic term for a number of compounds that include L-carnitine, acetyl-L-carnitine, and propionyl-L-carnitine [1-2].

Carnitine plays a critical role in energy production. It transports long-chain fatty acids into the mitochondria so they can be oxidized ("burned") to produce energy. It also transports the toxic compounds generated out of this cellular organelle to prevent their accumulation. Given these key functions, carnitine is concentrated in tissues like skeletal and cardiac muscle that utilize fatty acids as a dietary fuel [1-2].

The body makes sufficient carnitine to meet the needs of most people. For genetic or medical reasons, some individuals (such as preterm infants), cannot make enough, so for them carnitine is a conditionally essential nutrient [1].

## What are recommended intakes for carnitine?

Healthy children and adults do not need to consume carnitine from food or supplements, as the liver and kidneys produce sufficient amounts from the amino acids lysine and methionine to meet daily needs [1-3]. The Food and Nutrition Board (FNB) of the National Academy of Sciences reviewed studies on the functions of carnitine in 1989 and concluded it was not an essential nutrient [3]. The FNB has not established Dietary Reference Intakes (DRIs)—including a recommended dietary allowance (RDA)—for carnitine [4].

## What foods provide carnitine?

Animal products like meat, fish, poultry, and milk are the best sources. In general, the redder the meat, the higher its carnitine content. Dairy products contain carnitine primarily in the whey fraction [1,3,5]. The carnitine content of several foods is listed in Table 1.

**Table 1: Selected food sources of carnitine [1]**

Food	Milligrams (mg)
Beef steak, cooked, 4 ounces	56-162
Ground beef, cooked, 4 ounces	87-99
Milk, whole, 1 cup	8
Codfish, cooked, 4 ounces	4-7
Chicken breast, cooked, 4 ounces	3-5
Ice cream, ½ cup	3
Cheese, cheddar, 2 ounces	2
Whole-wheat bread, 2 slices	0.2
Asparagus, cooked, ½ cup	0.1

Carnitine occurs in two forms, known as D and L, that are mirror images (isomers) of each other. Only L-carnitine is active in the body and is the form found in food [1,6].

## Absorption and metabolism of carnitine

Adults eating mixed diets that include red meat and other animal products obtain about 60-180 milligrams of carnitine per day [6]. Vegans get considerably less (about 10-12 milligrams) since they avoid animal-derived foods. Most (54-86%) dietary carnitine is absorbed in the small intestine and enters the bloodstream [1,6].

The kidneys efficiently conserve carnitine, so even carnitine-poor diets have little impact on the body's total carnitine content [1,5]. Rather than being metabolized, excess carnitine is excreted in the urine as needed via the kidneys to maintain stable blood concentrations.

## When can a carnitine deficiency occur?

Two types of carnitine deficiency states exist. Primary carnitine deficiency is a genetic disorder of the cellular carnitine-transporter system that usually manifests itself by five years of age with symptoms of cardiomyopathy, skeletal-muscle weakness, and hypoglycemia. Secondary carnitine deficiencies may occur due to certain disorders (such as chronic renal failure) or under particular conditions (e.g., use of certain antibiotics) that reduce carnitine absorption or increase its excretion [1,5]. There is scientific agreement on carnitine's value as a prescription product for treating such deficiencies [2].

## What are some current issues and controversies about carnitine?

Carnitine has been studied extensively because it is important to energy production and is a well-tolerated and generally safe therapeutic agent [7]. Researchers prefer to use acetyl-L-carnitine in research studies because it is better absorbed from the small intestine than L-carnitine and more efficiently crosses the blood-brain barrier (i.e., gets into brain tissue) [8].

### ***Athletic performance***

Some athletes take carnitine to improve performance. However, twenty years of research finds no consistent evidence that carnitine supplements can improve exercise or physical performance in healthy subjects—at doses ranging from 2-6 grams/day administered for 1 to 28 days [9-11]. (The total body content of carnitine is about 20 grams in a man weighing 155 pounds, almost all of it in the skeletal muscle [11].) For example, carnitine supplements do not appear to increase the body's use of oxygen or improve metabolic status when exercising, nor do they necessarily increase the amount of carnitine in muscle [10].

### ***Aging***

A decline in mitochondrial function is thought to contribute to the aging process. Carnitine may be involved because its concentration in tissues declines with age and thereby reduces the integrity of the mitochondrial membrane [12]. Research in aged rats found supplementation with high doses of acetyl-L-carnitine and alpha-lipoic acid (an antioxidant) to reduce mitochondrial decay [13-15]. The animals also moved about more and improved their performance on memory-requiring tasks. At present there are no equivalent studies of this kind in humans. However, a meta-analysis of double-blind, placebo-controlled studies suggests that supplements of acetyl-L-carnitine may improve mental function and reduce deterioration in older adults with mild cognitive impairment and Alzheimer's disease [16]. In these studies, subjects took 1.5-3.0 grams/day of acetyl-L-carnitine for 3-12 months.

### ***Cardiovascular and peripheral-arterial disease***

Several studies have examined supplemental carnitine in the management of cardiac ischemia (restriction of blood flow to the heart) and peripheral arterial disease (of which the most important symptom is poor circulation in the legs, known as intermittent claudication) [17-18]. Because levels of carnitine are low in the failing heart muscle, supplemental amounts might be beneficial to the organ by counteracting the toxic effects of free fatty acids and improving carbohydrate metabolism [17]. In short-term studies, carnitine has demonstrated anti-ischemic properties when given orally and by injection. A double-blind, placebo-controlled, multicenter clinical trial in Italy with patients who had suffered a first heart attack found that supplemental carnitine (given intravenously for five days, then 6 grams/day orally for one year) reduced heart failure and overall mortality [19]. The results were not conclusive but promising enough to justify a larger study whose results have not yet been reported [17,20].

Claudication results from an inadequate supply of oxygen-rich blood to the legs and leads to an accumulation of acetylcarnitine in muscle due to its incomplete utilization. Patients with peripheral arterial disease who develop claudication have significant impairments in exercise performance and find it difficult to walk even short distances at a slow speed [18]. Two published randomized, controlled trials raise the possibility that carnitine may improve the performance of skeletal muscles in the leg. In one European multicenter clinical trial, subjects with moderate to severe claudication who were supplemented with L-carnitine (in the form of propionyl-L-carnitine at 2 grams/day for 12 months) significantly improved their maximal walking distance and perceived quality of life as compared to subjects receiving the placebo [21]. A similar multicenter trial in the United States and Russia found the same daily dose and form of carnitine administered for 6 months in patients with disabling claudication to significantly improve walking distance and speed, reduce bodily pain, enhance physical function, and improve perceived health state as compared to controls [22].

### ***Cancer***

Fatigue resulting from chemotherapy, radiation treatment, and poor nutritional status is common in cancer patients [23]. They may also be deficient in carnitine [23]. In one study, treatment with carnitine supplements (4 grams/day for one week) ameliorated fatigue in most chemotherapy-treated subjects and restored normal blood levels of carnitine [24]. In another trial, terminal cancer patients supplemented with carnitine (doses ranged from 250 milligrams to 3 grams/day) experienced less fatigue and improved mood and quality of sleep [23]. In both studies, most subjects were carnitine deficient before taking the supplements.

### ***Type 2 diabetes***

Insulin resistance, which plays an important role in the development of type 2 diabetes, may be associated with a defect in fatty-acid oxidation in muscle [25]. This raises the question as to whether mitochondrial dysfunction might be a factor in the development of the disease. Increased storage of fat in lean tissues has become a marker for insulin resistance [25]. Early research suggests that supplementation with L-carnitine intravenously may improve insulin sensitivity in diabetics by decreasing fat levels in muscle and may lower glucose levels in the blood

by more promptly increasing its oxidation in cells [25-27]. A recent analysis of two multicenter clinical trials of subjects with either type 1 or type 2 diabetes found that treatment with acetyl-L-carnitine (3 grams/day orally) for one year provided significant relief of nerve pain and improved vibration perception in those with diabetic neuropathy. The treatment was most effective in subjects with type 2 diabetes of short duration [28].

### **HIV and AIDS**

The human immunodeficiency virus (HIV) causes a decline in the number of lymphocytes (one type of white blood cell), resulting in acquired immunodeficiency syndrome (AIDS). HIV-infected individuals often accumulate fat in some areas of the body and lose fat in others and develop high levels of blood fats (hyperlipidemia) and insulin resistance, which together constitute the lipodystrophy syndrome. This syndrome may represent mitochondrial toxicity brought about by the HIV infection and the antiretroviral drugs used to treat it, and can induce a carnitine deficiency that limits mitochondrial fat metabolism [29]. The molecular mechanisms by which this occurs are poorly understood. Preliminary research provides conflicting findings [30] but suggests that supplementation with carnitine both intravenously and orally (at doses of 2-6 grams/day for weeks or months) in HIV-infected individuals may slow the death of lymphocytes (which in turn may slow HIV progression) [31-32], reduce neuropathy [33-35], and favorably affect blood lipid levels [36-38].

### **End-stage renal disease and hemodialysis**

Carnitine homeostasis (balance within the body) among individuals with renal diseases can be substantially impaired by several factors, particularly reduced synthesis and increased elimination of the compound by the kidneys as well as reduced intake from food due to poor appetite and consumption of fewer animal products [39]. Many patients with end-stage renal disease, particularly those on hemodialysis, become carnitine insufficient. Carnitine blood levels and muscle stores are low, which may contribute to anemia, muscle weakness, fatigue, altered levels of blood fats, and heart disorders. Numerous studies suggest that high doses of supplemental carnitine (often injected) in patients on maintenance hemodialysis can correct some or all of these symptoms, though most involve small numbers of patients and are not double-blinded trials. A recent meta-analysis of these studies concludes that carnitine supplements may aid anemia management but not blood-lipid profiles, and that their effects on exercise capacity or heart stability are inconclusive [40].

### **Male infertility**

The carnitine content of seminal fluid is directly related to sperm count and motility [41-42], suggesting that the compound might be of value in treating male infertility. Several studies indicate that carnitine supplementation (2-3 grams/day for 3-4 months) may improve sperm quality [43-45], and one randomized, double-blind crossover trial found that 2 grams/day of carnitine taken for 2 months by 100 infertile men increased the concentration and both total and forward motility of their sperm [46]. The reported benefits may relate to increased mitochondrial fatty-acid oxidation (providing more energy for sperm) and reduced cell death in the testes [47]. However, a recent randomized controlled trial with 21 infertile men found that 3 grams/day of carnitine taken for 24 weeks produced no significant increases in sperm motility or total motile sperm counts as compared to placebo [48]. Larger and more carefully designed studies are needed to evaluate carnitine's potential value as an infertility therapy.

## **Are there health risks from too much carnitine?**

At doses of approximately 3 grams/day, carnitine supplements may cause nausea, vomiting, abdominal cramps, diarrhea, and a "fishy" body odor [1-2]. More rare side effects include muscle weakness in uremic patients and seizures in those with seizure disorders.

## **Carnitine and medication interactions**

Carnitine interacts with pivalate-conjugated antibiotics such as pivampicillin that are used in the long-term prevention of urinary-tract infections [49]. Chronic administration of these antibiotics increases the excretion of pivaloyl-carnitine, which can lead to carnitine depletion. However, while tissue carnitine levels may become low enough to limit fatty acid oxidation, no cases of illness due to deficiency have been described [1,6]. Blood concentrations of carnitine may be reduced in children treated for convulsions with phenobarbital, valproic acid, phenytoin, or carbamazepine, but no clinical consequences have been shown [50-51].

## **Supplemental sources of carnitine**

L-carnitine, acetyl-L-carnitine, and propionyl-L-carnitine are available over-the-counter as dietary supplements. Carnitine is often promoted as an aid for weight loss, to improve exercise performance, and to enhance a sense of well-being [2]. It is also a drug approved by the Food and Drug Administration to treat primary and certain secondary carnitine-deficiency syndromes.

## **Carnitine intakes and healthful diets**

Most people obtain sufficient carnitine because of the body's natural production of the substance as well as from their diets. The *Dietary Guidelines for Americans* describes a healthy diet as one that:

- emphasizes a variety of fruits, vegetables, whole grains, and fat-free or low-fat milk and milk products;
- includes lean meats, poultry, fish, beans, eggs, and nuts;
- is low in saturated fats, *trans* fats, cholesterol, salt (sodium), and added sugars; and
- stays within your daily calorie needs.

For more information about building a healthful diet, refer to the *Dietary Guidelines for Americans* (<http://www.healthierus.gov/dietaryguidelines/index.html>) and the U.S. Department of Agriculture's food guidance system (*MyPyramid*; <http://www.mypyramid.gov>).

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