

Sanford Medical Center

Aunt Cathy's Guide to Nutrition:

By Request:

**A SHORT CARNITINE
DISCUSSION THAT
MIGHT BE HELPFUL**



Aunt Cathy

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The role of supplemental carnitine in conditions characterized by excessive obesity, hunger, lethargy, hypotonia, and poor exercise endurance

Carnitine is a substance normally made in the liver and kidney, and it is also available in meats. It consists of a molecule of methionine and a molecule of lysine — two essential amino acids. It plays a critical role in the ability to burn fat for fuel because it is part of the enzyme system "**carnitine palmitoyl transferase**" which transfers fat molecules into the mitochondria to produce ATP. Because muscle (including and especially heart muscle) is very dependent on fat fuels for aerobic energy production, anything that compromises carnitine's operation can result in a variety of problems. For example, for people with **inborn errors** of mitochondria metabolism, providing additional carnitine can help to prevent extremely serious consequences. An example is the not uncommon beta-oxidation disorder MCADD (Medium-Chain AcylCoA Dehydrogenase Deficiency.)

Some drugs impair the production of carnitine so that one is more dependent on an exogenous source than normal. Valproic acid is an example of this, and relative carnitine insufficiency can often be a big contributor to the lethargy and certain other side effects reported with the use of this medication. Additionally, inadequate carnitine also compromises the efficacy of the valproic acid itself, resulting in break-through seizures and increased risk of liver toxicity. **With this medication, carnitine supplementation appears to decrease liver toxicity significantly.** Valproic acid is the seizure medication most studied in relation to carnitine, but other seizure medications appear to affect carnitine requirements as well. Certainly if the child is symptomatic a trial on carnitine is very reasonable.

People on ketogenic diets for seizure control also need extra carnitine because they are burning fat as almost their only fuel - - they need much more carnitine than they could be relied upon to make on their own. Additionally, many people on these special diets do continue to need seizure medications, which may further increase the need for an outside source of carnitine.

People with **various liver and kidney conditions** are sometimes supplemented with carnitine because production can be compromised. We also use it with **premature infants** on TPN in the NICU because their ability to produce carnitine is compromised by the immaturity of the liver and kidney.

Carnitine-related problems contribute to difficulty burning fat for fuel resulting in symptoms that may include:

- 1. excessive fat storage**
- 2. low muscle tone**
- 3. excessive appetite due to failure to make the needed amount of ATP (usable energy) from food consumed**
- 4. very poor tolerance of aerobic activity and endurance-type of exercise**
- 5. abnormally high sense of fatigue or excessive sleeping**
- 6. muscle pain with exertion**
- 7. cardiomyopathy**
- 8. episodes of dangerously low blood sugars that can result in brain damage, or even death ... sometimes labeled a SIDS event.**
- 9. unusual difficulty with control of blood sugar in people with insulin-dependent diabetes ... we should be especially suspicious of carnitine inadequacy among those with blood sugar volatility who are carefully following their nutrition plans and medications.**

These are among the symptoms that have been corrected by carnitine supplementation in at least 25 people (not counting premies) that I have worked with personally who turned out to have had unrecognized metabolic abnormalities. [This also does not count the patients for whom we automatically initiated carnitine therapy in anticipation of need, thereby preventing the problems described.] If someone way out here in Fargo, ND has found that many patients with what turned out to be (previously unrecognized) carnitine-related health problems, **the likelihood is good that there are lots of folks out there whose carnitine problems are simply not being looked for and therefore not recognized.**

There are clearly many people who have some of the symptoms described above for whom carnitine adequacy/inadequacy is completely unrelated. To determine if carnitine is a problem, **a trial on carnitine** will often result in noticeable changes within few weeks ...

sometimes days. If it is not a factor, supplemental carnitine could be discontinued after a trial of about a couple months. We would normally continue the trial at least that long before writing it off because some conditions result in a degree of carnitine depletion so pervasive that it takes a while to get enough cells operating well enough to see a benefit. [Please see the note on the last page regarding special carnitine issues to consider for people who are candidates for bariatric surgery.]

Carnitine used as described is very safe. The only problem with the stuff is that it is pricey. Insurance will usually cover it (ordered as "Carnitor, or the generic equivalent,") but the amount of coverage varies. For this reason, we do not do this kind of trial casually. However, as I mentioned earlier, **the metabolic abnormalities in symptomatic patients that I have seen who benefitted markedly from carnitine supplementation were undetected at the time the trial was initiated.** As you know, what we often think is extremely rare can sometimes be fairly common but just rarely recognized. The **only way to know for sure is a trial on carnitine.** I much prefer a **prescription form of carnitine for the trial**, as some OTC carnitine products may not provide the amount of carnitine on the label. [I do not want to miss a potential effect because the product used in the trial provided the wrong amount. People can use OTC carnitine after the trial if they wish, but insurance will usually not pay for that form.]

Blood levels can reflect inadequacy when they are low or if the total:free carnitine ratio is disturbed. **However, the blood level apparently does not necessarily reflect the muscle tissue level, including the level available to the heart muscle.** So if a person is symptomatic but labs are normal, one would still do the trial and watch for changes in symptoms. In other words, there is probably little reason to get labs except for curiosity or research. Certainly, when labs do indicate deficiency, we would supplement. But when labs do not reflect a deficiency state, we would still do a trial of supplemental carnitine in a symptomatic patient. So, the labs are really not of great use in this situation. As the health effects of carnitine inadequacy (for whatever reason) are not benign, my prejudice is to do a rule-out trial with symptomatic patients.

So, that is the story in a nutshell. **If you decide to do a trial**, the usual trial in adults is about 1 gram three times a day (i.e. 3000 mg/day.) The pills are in a 330 mg size, so 3000 mg can be adequately approximated by three pills 3 times a day. The pills are spread out (any way that is comfy for the patient) to avoid an osmotic diarrhea that can result from giving the whole lot of tiny particles all at once. The pediatric dose (PDR info) is 50-100 mg/kg/day divided into 3 doses, with a 3000 mg/day the usual upper level. The therapeutic/maintenance amount may be much less than this, but the higher end of the usual range is often best in a test situation, since the person may be starting out with a significant deficiency. If we under-shoot with a low dose, there may not be enough carnitine to see changes during the trial period. I don't want to miss something if it is there.

I have had some **very large patients** whose symptoms (hypotonia, excessive hunger, lethargy, excessive weight gain and poor endurance, etc.) have responded very well, but an amount above the theoretical 3000 mg "top" was sometimes needed to bring the positive changes about. One very heavy and fatigued adolescent responded beautifully but he required 6000 mg/day to bring about the changes we were looking for. [Happy aside: He is now normal weight and going to college.] As is usually the case, when one is very far outside the "normal" range for body weight, a standard per/kg intake level may no longer directly apply.

A number of patients with “**familial hypotonia of unknown etiology**” have responded amazingly well to this therapeutic intervention even though as yet no one has identified their actual metabolic problem. All we know is that something about their genetic pattern causes problems, some of which may be ameliorated by providing supplemental carnitine.

This picture (hypotonia, excessive hunger, lethargy, excessive weight gain and poor endurance) is intriguingly like some of the typical symptoms observed in **Prader-Willi Syndrome**. The #15 chromosome is missing all or part of a leg, but exactly what disturbance in metabolism results from the deletion is not well understood, nor is it the same in all people with PWS. However, as these individuals suffer greatly from their condition, it is reasonable to do a trial as described above. It will either help or it won't in any individual, but I do have four patients with PWS for whom supplementation appears to significantly help control the symptoms, making their lives and those of their families much better.

The children also have more energy to learn and to engage in play. They also learn better because they are not as obsessed with accessing food. Prader-Willi Syndrome is currently treated with growth hormone in some children, so one cannot ascribe all of any observed benefit to carnitine in children treated with both. However, **it is reasonable to do both**, as the efficacy of growth hormone treatment could certainly be compromised if energy metabolism was limited by a relative problem with carnitine adequacy. Certainly a trial would be in order if the symptoms described above continue to be observed after growth hormone therapy has been initiated.

When a patient demonstrates that supplemental carnitine is helpful, **the level that seems to be effective needs to progress with growth** (i.e. mg/kg body weight). I have seen some situations in which a child out-grew his prescription because this aspect of his care was not being monitored and the treatment became less effective the more he grew. With math-competent parents (and the doctor's permission, of course) I teach the parents how to increase the dosage as the child attains certain weights. Other families call me each month with the baby's weight and I calculate the level for them,

When initiating treatment, the carnitine dose is generous in an attempt to correct a possible inadequacy ... that is, the bucket may be empty so we need to fill it up as part of our test. However, once the bucket is appropriately full, the therapeutic level is no longer needed and a maintenance level should be identified. This will be quite individual. As a marker for having reached the point of having a “full bucket” I tell parents that an indication of this will be that the child may “start to smell a bit like a little fish” (reflecting getting rid of unneeded carnitine.) One mother called me and left this message: “At last! We have achieved fishiness!” At that point we back off and set about to find the maintenance level for that particular child.

Other conditions can be characterized by the same symptoms (lethargy, weight gain, hypotonia, etc.) Some of my patients with **Down Syndrome** or **Phenylketonuria** have struggled with the same set of energy-related problems, and in several cases, the carnitine supplementation has helped tremendously. It has been life-altering. For others, the carnitine was not shown to alter the situation at all. The only way to know which person with these symptoms will respond to carnitine supplementation is to do a trial.

There are many other applications of supplemental carnitine being studied in addition to the scenario discussed above. These include (among others): hypertriglyceridemia, mitochondrial diseases, retinal health and macular degeneration, cardiovascular disease, metabolic syndrome, diabetes, renal disease, parkinsonism, chemotherapy adjunct to minimize neurologic damage and fatigue, various chronic conditions characterized by fatigue, prevention of liver toxicity due to use of certain medications, age-related cognitive impairment and osteoporosis. (See my Diabetes hand-out, Eye Health hand-out and Prenatal Nutrition hand-out for more information about those specific carnitine issues.)

SOME THOUGHTS ABOUT BARIATRIC SURGERY IN INDIVIDUALS WHO HAVE A CARNITINE-RELATED WEIGHT PROBLEM

I think it would be very reasonable to do a trial on generous carnitine in severely obese individuals prior to moving to bariatric surgery.

One reason is that people who do respond to carnitine can likely avoid the costs, pain and complication risks of bariatric surgery. Carnitine use does not interfere with an individual's ability to absorb micronutrients the way the surgery does, which avoids the documented problems of clinically significant vitamin and mineral deficiencies like copper, vitamin B12, thiamin (vitamin B1) and many others months or years after surgery. These three nutrients are mentioned specifically because neurologic injury (sometimes irreversible injury) from deficiency is documented in spite of generous oral intake in some bariatric surgery patients.

Long term follow-up of these micronutrient issues is absent in many bariatric surgery programs, and often the only outcome of professional interest has been whether or not weight loss occurred, and whether there were improvements in dyslipidemias or diabetes management. Failure to establish long-term nutrient adequacy is particularly problematic because many women of childbearing age do become pregnant after bariatric surgery. That increases risk of birth defects and other types of poor pregnancy outcome. And now some places have begun to do bariatric surgery on pediatric patients. They do lose weight post-surgically ... but they are likely to lose much more than weight unless overall nutrition is carefully monitored.

One other reason for doing a trial on carnitine before moving on to surgery is that if patients do have a carnitine-related weight problem they will continue to have it. The surgery does not correct the problem. That means they will continue to be unable to burn fat efficiently, and they will continue to experience significant hunger that may drive them to overeat in spite of surgery. This may be a factor especially in the number of individuals who regain their weight after surgery or who undergo a second bariatric surgery. Therefore, a trial on carnitine would help to identify the people who might fail to do well in terms of maintaining weight loss after surgery unless carnitine supplementation was a continued part of their regimen. **For those bariatric surgery patients who do need supplemental carnitine, continuing to provide it can play a role in successfully keeping the weight off.**

Carnitine: Content of Foods and Quick Fact Sheet

Foods providing about 100 mg of carnitine

Beef steak	100 g	95 mg
Ground beef	100 g	94 mg

Foods providing 10-30 mg of carnitine

Pork	100 g	28 mg
Bacon	100 g	23 mg
<u>Tempeh</u>	100 g	20 mg
Promote	100 ml	12 mg

Foods providing 1 to 6 mg of carnitine

Cod fish	100 g	5.6 mg
Chicken breast	100 g	3.9 mg
American cheese	100 g	3.7 mg
Ice cream	100 ml	3.7 mg
Whole milk	100 ml	3.3 mg
Avocado	one medium	2.0 mg
PediaSure	100 ml	1.7 mg
Cottage cheese	100 g	1.1 mg

Foods providing less than 1 mg of carnitine

Whole-wheat bread	100 g	0.36 mg
Asparagus	100 g	0.20 mg
White bread	100 g	0.15 mg
Macaroni	100 g	0.13 mg

Foods providing less than 1/10th of a mg of carnitine

Peanut butter	100 g	0.08 mg
Rice (cooked)	100 g	0.04 mg
Eggs	100 g	0.01 mg
Orange juice	100 ml	0.002 mg
Ensure	100 ml	0 mg

Typical intake from food:

Generally, **20 to 200 mg are ingested** per day by those on an **omnivorous** diet, while a strict **vegetarian** diet may provide **only 1 mg/day**. The word carnitine comes from the Latin word for meat but the amount varies with type of meat.

Also note the high variability in carnitine in commercial “complete nutrition” products.

Production:

In animals, **carnitine is biosynthesized** primarily in the liver and kidneys from the amino acids lysine or methionine. Vitamin C (ascorbic acid) is essential to the synthesis of carnitine.

Requirements:

During **growth, pregnancy or wound healing** requirements for carnitine can exceed its natural production. That is, it is **conditionally essential** during periods of anabolism, and also in a variety of other metabolic conditions.

People with liver or kidney problems may have difficulty producing it. Renal patients may also be eating a low meat diet, which can result in a diet low in pre-formed carnitine. It is also lost in dialysate, so needs of dialyzed patients are greater than they would otherwise be.

The **seizure medication valproic acid** impairs production of carnitine, but needs it to work. Inadequate carnitine reduces **effectiveness** and increases potential for **liver toxicity** of the drug, and it accounts for some of the **reported side effects** such as lethargy and weight gain.

Beneficial Applications:

Supplemental carnitine has a role in low muscle tone, managing diabetes, exercise tolerance, macular degeneration, obesity, heart failure, cancer-related and HIV-related fatigue, male infertility, ischemia / reperfusion brain injury, peripheral neuropathies, dementia, depression and cognitive impairment associated with various conditions.