By Request: A Discussion about Carnitine

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

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Carnitine is a substance we normally make in the liver, kidney and brain. It is also available in small amounts meats. It is a tiny substance made from a molecule of methionine and a molecule of lysine — two essential amino acids that we need to make all of our body's protein.

Carnitine 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 energy as ATP.

This picture of a logging truck illustrates the role of carnitine if you imagine the long trees as long chains of fat. Carnitine "trucks" are needed to get the fat into the saw mill to cut it up in to small enough bits to go into the furnace.

[The sign on the door of the truck says that it is the "**Cart-It-In Trucking Company**" to help remember that a very important function of carnitine is to cart fat (the fuel) into the mitochondria (the furnace) to convert it to energy we can use.]

Muscle (including heart muscle and the diaphragm) is very dependent on fat fuels for aerobic energy production. It is especially necessary for physical activity that involves endurance. When carnitine is inadequate people become less able to do endurance exercise like running or walking for more than a short time. They may show wheezing after endurance exercise because the diaphragm is also a muscle and it can't work right without carnitine carting in some fat fuel to keep going. Low muscle tone and muscle pain are also commonly seen for the same reason.

People with insufficient carnitine often gravitate toward exercise activities that do not require endurance exercise … like pitching a baseball, throwing the shot put, or standing there in the line of scrimmage, playing the position of "large wall" in a football game. By trial and error they find a way to participate in activities in spite of physical limitations.

They typically find other kinds of things to do that require very little endurance activity at all … like working at the computer, reading or watching television. This often results in being labeled a "couch potato" and told that they are fat because of "too much screen time." Keep in mind that although some folks may be very heavy because they are "just lazy," folks who have a carnitine insufficiency problem will often be labeled couch potatoes, but for them being a couch potato is not a choice.

Some folks with inadequate carnitine have **very low muscle tone** and so they not only sit around a lot, they tend to always be leaning against something as well. This is not laziness although it can look that way.

Some people have trouble with balance because of low muscle tone which can lead to falls or other problems. One eight-year-old girl I saw could not ride her bike without training wheels and she found this to be very embarrassing. Additionally, she could not walk up the stairs one foot after another. She stepped up with her left foot, brought up the right foot, rested again and continued until she finally reached the top. This girl also had to hold on to the table with one hand when she ate to prevent tipping over. [You will be happy to learn that she can now ride her bike all over the place, run up the stairs, and eat with both hands if she wants to.]

Correcting carnitine inadequacy can help with **muscle <u>strength</u> and <u>stamina</u>**, and people's choices of activity change and they begin to move around a lot more. One of my little "couch potatoes" comes to mind who is now far too busy riding her bike around the neighborhood to sit and watch TV. The point … and it is a big one … is that for <u>some</u> folks carnitine inadequacy is the reason they are sedentary and heavy, and that being sedentary is not the primary cause of their weight issue. **Correcting inadequacy can greatly improve quality of life.**

As mentioned earlier, inadequacy of carnitine can also cause **muscle pain**, and children in this situation will often complain a lot about it. One ten-year-old who benefitted from carnitine used to whine a lot even when the activity was supposed to be fun. She complained all over Disneyland that her legs hurt and she had a horrible time. The next year she was thinner and had far better endurance and no muscle pain. The family went back to Disneyland and they all had a wonderful time. [Older folks may just attribute pain from carnitine inadequacy to "getting older" …which actually may be the case if inadequate carnitine was not a problem earlier in life. Age-related changes are discussed later.]

Medication that changes carnitine intake requirements:

Some drugs impair the production of carnitine so that one is more dependent on an outside (exogenous) source than normal. The seizure control medication **valproic acid** is an example of this. As an unwelcome side-effect it tells the body to **quit making carnitine**. Relative carnitine insufficiency can often be a big contributor to the lethargy, weight gain and certain other side effects reported with the use of this medication.

Additionally, inadequate carnitine also **compromises the seizure-controlling effectiveness** of the valproic acid drug itself, resulting in break-through seizures and increased risk of liver toxicity. **Carnitine supplementation decreases the liver toxicity of this drug significantly.** We once had a toddler in our pediatric ICU who was "life-flighted" in because of severe liver toxicity. Her home physician had been advised by people here that carnitine should be given with her valproic acid seizure medication, and he simply did not prescribe it.

Immediate IV administration of carnitine saved her life and her liver, but she had already suffered some brain injury due to severe hypoglycemia (low blood sugar.) This was because inadequacy of carnitine meant that she could not burn fat very well at all, and in order to run her body she had to find another source of fuel. As a result, she used up blood sugar that would normally have been spared and used as the primary fuel for her brain.

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 (e.g. lethargy, weight gain, low blood sugar, increased seizures) a trial on carnitine is very reasonable.

Special diets that increase carnitine requirements:

People on extremely low carbohydrate "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. "Fatty liver" … deposits of fat in the liver … and "high triglycerides" in the blood can be caused by many things but one of them is relative carnitine inadequacy

People with certain **inborn errors of metabolism** that effect energy production also need supplemental carnitine. One of the most common examples of this is a condition called **MCADD** (Medium Chain AcylCoA Dehydrogenase Deficiency.) It impairs the person's ability to burn fats of certain sizes and it makes it unsafe to fast. In this kind of condition **carnitine requirements can increase because the parts of fat that cannot be burned have to be removed from the mitochondria.** Failure to move them out can cause a build-up of unusable fat in the mitochondria. That means that they need enough carnitine to haul fat in both directions, and they may be unable to manufacture enough extra carnitine to do that.

Age-related changes in carnitine intake requirements.

People may gradually be able to make less carnitine than they need as they get older. For some it can be a player in the development of "middle age spread" and general weight gain. There is evidence that it can also contribute to the muscle weakness, poor tolerance of exercise and muscle pain that can accompany aging.

Relative carnitine inadequacy also appears to be a factor in the **maintenance of cognitive ability** as we age. Production of any many things our bodies normally made in adequate amounts when we are young can fail to keep up production as we age. Examples of this include estrogen, (and babies!) testosterone, hair, thyroid hormone, and the ability to continue making vitamin D in the skin. Production of carnitine in the brain may also follow this timetable.

Bottom line: Assuring adequacy is a very good idea, and again, I would recommend doing a trial on carnitine for any person who is symptomatic. I have personally seen significant improvement in strength, stamina, pain, quality of life, and cognition in several older adults.

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

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1. **Excessive fat storage**

2. **Low muscle tone ("hypotonia") and muscle weakness.**

3. **Excessive appetite due to failure to make the needed amount of ATP (usable energy) from the 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 … impaired functioning of heart muscle.**

8. **Episodes of dangerously low blood sugars that can result in brain damage, or even death … sometimes labeled a "SIDS" event ("Sudden Infant Death Syndrome.")**

9. **Unusual difficulty with control of blood sugar in people who have insulin-dependent diabetes … we should be especially suspicious of carnitine inadequacy among those with blood sugar volatility <u>in spite of</u> carefully following their nutrition plans and medications.**

10. **Failure to maintain weight loss achieved via medical fasts or bariatric surgery**

These are among the symptoms that have been corrected by carnitine supplementation in at least 30 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 <u>automatically</u> initiated carnitine therapy in anticipation of need, thereby <u>preventing</u> 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 for an individual, a trial of carnitine supplementation will often result in noticeable changes within few weeks … sometimes days.

If carnitine is apparently not a factor for a particular person because no measurable benefit was observed, 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 as unhelpful 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.]

A Trial on Carnitine:

Carnitine used as described is very safe. The only problem with the stuff is that it is pricey. Insurance will sometimes 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 prefer a **prescription form of carnitine for the trial if insurance will cover it.** People can use over-the-counter carnitine but insurance will usually not pay for that form. However, if the prescription form is unavailable for financial reasons, these days there are a number of reputable products that could be used.

I prefer to use a form called **acetyl-L-carnitine (or just acetylcarnitine)** because there is some evidence that that form may have superior absorption … and nothing works well if it is not absorbed but just passes right through. **Carnitine fumerate** is also well utilized but generally more expensive.

Should We Get Labs?

Blood carnitine levels can reflect inadequacy when they are low or if the **"total:free carnitine ratio"** is disturbed. [The total:free ratio is an indication of how many empty trucks are available to haul fat. If one has a normal total amount of trucks, but all the trucks are already in service, the ratio shows whether or not a person has enough empty trucks available to be able to keep up with the workload.]

However, the blood level apparently does not necessarily reflect the muscle tissue level, including the level available to the heart and diaphragm muscles. So even if a person's labs were normal one would still do the trial if a person is symptomatic, and watch for changes in symptoms.

In other words, there is probably little reason to get labs in this situation 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. It also saves the cost of getting an unlikely-to-be-very-useful lab.

Dosage Specifics

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 available in several sizes: 250 mg, 330 mg, 500 mg and 1000 mg sizes. [Math examples: The 3000 mg can be adequately approximated by three 330 mg pills 3 times a day. Happily, some products now are available that provide more per capsule, so the dosage to give 3000 mg/day in that case would be two 500 mg pills 3 times a day, or one 1000 mg pill three times a day.]

It is also available as a liquid by prescription for "Carnitor Liquid" from Sigma Tau Pharmaceuticals. It provides 1 gram of carnitine per 10 mL, which is equal to 100mg carnitine per mL. This can be helpful with young children, for people being fed by tube and for anyone with swallowing problems. There are likely other brands of liquid carnitine in development.

The pills or drops 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.

It is also smart to spread them out so that some carnitine is **available** throughout the day. Taking all at one time could result in taking in more than is immediately needed, and then excreting the extra … which then leaves people with no carnitine coming in to help run their bodies later in the day or evening. Later on, a person can tinker with how much and when they take it, but when trying to do a careful test to see if carnitine can help at all for a person struggling with some of the symptoms described, it makes sense to take it as described.

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.

Some People May Need More than 3000 mg Carnitine per Day

I have had some **very large patients** whose symptoms (hypotonia, excessive hunger, lethargy, excessive weight gain and poor endurance, etc.) have responded very well to carnitine supplementation, but an amount above the theoretical 3000 mg "top" was sometimes needed to bring the positive changes about**. 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.**

One pair of very heavy and fatigued adolescents responded beautifully to carnitine supplementation, but they required 6000 mg/day to bring about the changes we were looking for. Here is their story:

They would come home after school and go directly to bed. The sister told me that she walked through mud puddles instead of going around them because walking around is just too tiring. Both were very smart, very hungry, and very weak. The girl wanted very much to be a veterinarian although she expressed doubt that she could do it because of physical incapacity.

The 3000 mg was insufficient to result in the hoped-for changes, but instead of calling the trial a failure, we bumped the dosage up to do a trial on 6000 mg (with the approval of their physician, of course.) Happily, today both brother and sister continue on a (normal) maintenance dose of carnitine and they are now of normal weight. The sister is now a veterinarian with two children, and the brother just finished college. They were the first people for whom I ever suggested a trial on carnitine. I initially wrote this carnitine paper just for their physician, explaining why carnitine might help, and describing how to very safely do a trial. (They lived in a different state so we had to do everything via mail and phone.) My carnitine paper is substantially longer now…

[Note that I do not "order" anything … I suggest things (also described as "nag about things") but the health care provider (MD, PA, NP, etc.) is always the person who orders a trial on carnitine. I only do any of this in conjunction with one of these heath care professionals. I am the wrong kind of doctor for writing orders … I am a PhD and not an MD. ☺]

A number of patients I have seen (including the boy and girl described above) have been described in their medical charts as having **"familial hypotonia of unknown etiology."** This is not a diagnosis … it is just a description that means: "A person has low muscle tone for unknown reasons, and others in the family seem to have the same problem." It does not identify WHY they have such low muscle tone, or what might be done about it.

Many people who are in this situation have responded amazingly well to this therapeutic intervention even though as yet no one has ever 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.

Adjusting Carnitine as Children Grow.

When a pediatric patient demonstrates that supplemental carnitine is helpful, the level that seems to be effective needs to progress with growth (i.e., mg of carnitine per 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 the child 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. To facilitate this, the physicians write the order as "____ mg carnitine /kg body weight," so the carnitine dose can easily be progressed as baby grows without requiring a new prescription every five minutes.

Changing from a Therapeutic Dose to a Maintenance Dose

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 one 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. I have also had many patients who never smelled funny even at very high levels, suggesting that even at a very generous intake, there was not enough being given beyond actual requirements to produce this particular side effect.

Carnitine Inadequacy Can Be Found among People Who Have Other Medical Conditions.

Other conditions can be characterized by the same symptoms (lethargy, weight gain, hypotonia, etc.) Some of my patients with **Down Syndrome** or **Phenylketonuria (PKU)** have struggled with the same set of energy-related problems, and in several cases, the carnitine supplementation has helped tremendously. While it does not cure Down Syndrome or PKU, it has

been life-altering in a very positive direction. 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.

The exact nature of a person's carnitine insufficiency does not have to be known … one only needs to be alert to the symptoms. When the symptoms are not recognized, there is an unfortunate tendency to blame the parents and accuse them of serving unhealthful meals and allowing too much TV time when a child is severely overweight. Those are certainly contributory if the allegations are true. However, I saw one very memorable obese sixteen-year-old patient who illustrates our need to be suspicious of the possibility of contributory carnitine issues before leaping to that conclusion. Here is his story:

An Adolescent Boy Being Worked-up for Possible Bariatric Surgery:

A sixteen-year-old boy was very short and very round, as was his mother. His father was tall and very thin. The mother had been accused for years of causing her son's obesity by serving a high calorie diet. She had been referred several times to health professionals to learn how to serve a low calorie diet, and she had followed their advice although both she and the boy always felt very hungry. [Actually, their usual diet described was much lower in calories than average, although she also told me that no one believed that this was how she actually prepared food.

What crossed my mind initially when I met them was that mother and son looked amazingly alike in terms of being very obese and markedly short. They were very nearly round. If this scenario was caused by the food she served and she and the family ate, why was the father so thin if he ate the same foods? And he told me that he did … he described himself as having a hearty appetite. This raises questions about the possibility that some factor(s) other than Mom's cooking or general overeating might be in the picture.

The boy was currently being "worked up" to see if he was a candidate for bariatric surgery, which was just beginning to be done then to treat obesity in adolescents. [Please see the notes about carnitine issues in anyone having bariatric surgery at the end of this paper.]

I asked him about his ability to do endurance exercise with questions like "Can you run around the track with no problem?" He told me that he could do that easily and that he "exercised all the time" and that he was very physically active. So I explained that he was probably unlikely to have the kind of metabolic trouble for which people would see me. I explained that in general the people I may be able to help in a special way with weight are the people who could never easily run around the track and who struggle greatly with certain types of physical activity.

He started to cry … and sixteen-year-old boys don't usually do this. He said "I've been lying to you. I can't run around the track or do any of the things you asked about. But I keep getting told by everybody 'You need to get more exercise!' and I know that's true. But I just can't do it! So I just tell everybody "I'm exercising! I'm exercising!"

This story also has a very happy ending. A trial on carnitine was initiated, and bariatric surgery was cancelled. Now both he (and his mother!) are of normal weight for their height. Note that nobody, including me, has a clue what their underlying genetic problem might be, but the **symptoms** were suggestive that providing some extra carnitine might be helpful. And it was.

[Another clue about exercise tolerance problems is that while all the other kids in class tend to get better and better at this kind of activity, the child with relative carnitine inadequacy often simple fails to improve in spite of continued effort.]

Carnitine Supplementation for People with Prader-Willi Syndrome.

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 several 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 I have seen with PWS who receive carnitine 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 the (extremely expensive) 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. People with PWS also seem to benefit from supplemental CoQ10 along with the carnitine and growth hormone. (I do have a separate paper available just on PWS nutrition issues if you want to see more on that condition.)

Carnitine Inadequacy in Thin or "Normal-Weight" People with Low Muscle Tone, Weakness or Impaired Ability to Exercise.

For reasons that I cannot explain, some people apparently express relative carnitine inadequacy with muscle tone and weakness problems, or exercise tolerance problems, but they do not have the tendency to retain excessive fat or to experience excessive hunger. As a working model, I view this as possibly related to a carnitine problem only in certain tissues, but I am totally making up this explanation. **Here are examples of two real cases:**

A Toddler Who Demanded to be Carried Everywhere

A 16-month old boy was refusing to walk and cried to be carried everywhere. His muscle tone was "floppy" but he was not overweight nor did he ask for food with greater than normal intensity. His mother was accused of spoiling him by giving in to his demands. After ruling out other explanations (e.g. rickets,) his physician and I decided to do a trial on carnitine.

When one does this kind of trial it can be helpful to carefully note the situation prior to supplementation so that there is something concrete to compare the outcome with after supplementing. Otherwise, it can be quite hard to remember just how things were at the start. Not having these kinds of records can result in inappropriately continuing a therapy because you just can't tell if it helped or not. Or, a trial may be judged to be a failure even though it was actually helpful, for the same reasons.

In this child's case, I asked the mother "If you took him to the mall and went in the end by the food court, how far he would walk before putting up a big fuss and refusing to walk further. She said, "Oh, we would never even get half-way out of the food court!" So, that was one of our high-tech evaluation tools. After supplementation for only a few weeks, she took him to the mall for a comparison test. He walked all the way to the Penney's wing! (Trust me … that is an amazingly long way for a little guy to walk.) But he did it willingly … because now he could.

When I talk about carnitine at conferences for health professionals, people often come up afterword or email me to ask about the possible usefulness of carnitine supplementation for a family member or patient. We talk about it and then I give them this paper to take to that person's doctor … and sometimes the person interested and asking IS a doctor. One particular time an RD (a Registered Dietitian) came up and described her son. Here is his story:

The Oceanographer

The young man was finishing high school and looking at college. He had always dreamed of being an oceanographer, but he realized that his really limited exercise tolerance and major fatigue would make him a poor shipmate who could not pull his weight on board a ship. He just could not follow that dream.

He was VERY bright, and he told his mother that he would "probably have to be a calculus major and sit down at a desk all day." He was not at all fat, and he was actually considerably less hungry than the more average guys his age who often have what I call TBD … "Teenage Boy Disease." [Are you familiar with this condition? Symptoms of TBD include drinking a half gallon of milk in one big gulp while standing beside the refrigerator and leaving the door open and asking "what's for dinner?"]

Cutting to the chase: his doctor approved a trial on carnitine and the result was that his mother called me a month later and reported that "He's going to be an oceanographer!" How cool is that?!

Carnitine Issues in Managing Diabetes

Sometimes I talk about carnitine issues at conferences because it has applications to particular audiences. For example, when I talk at conferences for diabetes professionals, the research we focus on that describes the importance of assuring carnitine inadequacy is both very important and generally not well known.

As you can imagine, there are several places where relative carnitine inadequacy could affect diabetes and its management. A few examples:

- obesity is often associated with diabetes
- the need for exercise in diabetes management is very important
- experiencing excessive hunger can prevent people from succeeding at following a prescribed low calorie diet, and
- there is even fluctuation in blood sugar control among people using insulin because of inability to fast.

[For more on this, please see my paper called "Thinking about OTHER Nutrition Issues in Diabetes."]

Another function of carnitine:

Carnitine is now recognized as being a very potent antioxidant in addition to its role in fat metabolism. That means that assuring adequacy of carnitine is also a good idea because a generous antioxidant intake has benefits in a great many situations, including any condition that results in unusual metabolism and in excessive free radical production.

Generous antioxidant intake has the potential to make having inflammatory conditions hurt a person less, because although some of the cellular injury is due to the underlying condition, some is a secondary injury from excessive production of free radicals. Generous antioxidant intake assists in "quenching" the extra free radicals before they injure cell membranes.

There are <u>many</u> other applications being studied of supplemental carnitine that are showing benefit. These include: hypertriglyceridemia (a high amount of certain types of fat in the blood), 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. Stay tuned…

<u>Some Thoughts about BARIATRIC SURGERY in Individuals Who Have a Carnitine-Related Weight Problem:</u>

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 <u>do</u> 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. This 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 critical micronutrient issues is absent in many bariatric surgery programs. Often the only outcome of professional interest has been whether or not weight loss occurred, and whether there were improvements in dyslipidemias (like high cholesterol or triglycerides) or diabetes management. Careful study of most micronutrient issues is often not included, especially several years after the surgery.

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. The children do lose weight post-surgically … but they are likely to lose much more than weight unless overall nutrition is carefully monitored.

This is especially important because in children and teens one is inducing a LIFE-LONG impairment of micronutrient status that is potentially much more problematic than bariatric surgery on middle-aged adults who have already grown and had families.

One other reason for doing a trial on carnitine before moving on to surgery is that if patients do have an unrecognized carnitine-related weight problem they will continue to have it after surgery. 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.**

Quick Carnitine Fact List

1. Typical carnitine 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**. That is likely sufficient for a person who is very competent at making their own carnitine. But as you can see, amounts from **2000-6000 mg** can be needed in folks whose carnitine needs are higher or whose carnitine production is impaired.

The word carnitine comes from the Latin word for meat (as in "chili con carnitine" ☺) but the amount varies with type of meat. Also note that there is high variability in carnitine in commercial "complete nutrition" products.

2. Production:

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

3. 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 (growth), and also in a variety of other metabolic conditions.

People with liver or kidney problems may have difficulty producing it. Renal (kidney) patients may also be eating a low meat diet, so the diet is also 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** ("Depekene") impairs production of carnitine, but it also needs it to work. Inadequate carnitine reduces the **effectiveness** of the drug, and it greatly increases the potential for **liver toxicity**. The relative inadequacy of carnitine that results in this situation accounts for some of the **reported side effects** such as lethargy and weight gain associated with using this medication.

4. Beneficial Applications:

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

(For more information about specific carnitine issues in particular health conditions, please see my other papers that more throughly address the application of carnitine in helping to manage them. These include:

"Thinking about OTHER Nutrition Issues in Diabetes",
"Nutrition and Eye Health,"
"Nutrition Issues in Pregnancy,"
"Nutrition for Children with Special Health Needs," and
"Drug/Nutrition Interactions."

All my papers are available for free to anyone.

They represent my best guess at the time of writing, and they are updated regularly.

Much of the information they contain will be based on new research, so feel free to share them with your health care providers.

As always, my papers are not intended to take the place of the advice of your health care provider.