



# Stroke Recovery Nutritional Treatment

**Dr. Steve Haltiwanger, MD, CCN**

*Ed. Jimmie Holman & Thomas Drake*

*From multiple viewpoints (philosophical, nutritional) it makes sense that when there has been bodily injury to an organ it becomes necessary to provide dietary compounds that the body naturally uses/requires in self-regeneration to repair that organ.*

It is medically impossible to use only one compound to repair a tissue when multiple compounds are needed. This is like using concrete as the only building material to build a house. While it may be possible to live with concrete furniture in a house without windows it becomes impossible when you expect your concrete lights, refrigerator, stove and phone to work. These appliances require other materials besides concrete to operate electrically.

Ischemia is the reduction or absence of blood supply to an organ or tissue in the brain, also known as a stroke. The etiology of ischemia may be obstruction of blood supply by a blood clot, atherosclerotic plaque, traumatic disruption of the vascular supply or hypoxemic vasoconstriction.

Ischemia has damaging effects on energy production. The cells of the body are dependent upon an uninterrupted blood flow, which guarantees delivery of nutrients and oxygen for the continual production of cellular energy (ATP). Ischemia causes microcirculatory blockages; a change in tissue metabolism where the cells are no longer able to produce ATP by aerobic metabolism and oxidative stress that damages multiple cellular components. When cellular oxygen levels fall because of failure of the circulatory system to deliver oxygen instead of oxygen-dependent aerobic metabolism, the cells switch to glycogenolysis and anaerobic glycolysis. These metabolic processes lead to the intracellular accumulation of NADH, lactate and H<sup>+</sup>-ions and a reduction in intracellular levels of reduced glutathione. The accumulation of these substances and loss of reduced glutathione creates intracellular acidosis and a change in cellular redox status. If the ischemic process is prolonged the accumulation of acids, lactate and nicotinamide adenine dinucleotide (NADH) inside of the cells eventually inhibits even anaerobic energy production.

With loss of a continual supply of cellular energy the energy-dependent metabolic functions of the cell grind to a halt. Within minutes cell membrane disruption and organelle dysfunction occurs. Protein, fat and carbohydrate catabolism and synthesis are also inhibited, as is control of intracellular mineral concentrations. When the energy supply is compromised to the point that it is inadequate to even meet survival needs the cells die.

### **Pathophysiological issues that are common in ischemic neurological conditions, (like strokes), that need to be addressed include:**

- excitotoxicity – a main issue creating neurodegeneration
- oxidative stress – a main issue creating neurodegeneration
- free radical production – avoid all acetaminophen it lowers glutathione
- inflammation
- damage to cell membranes
- damage to mitochondria
- Impaired cell membrane transport of nutrients



## Treatments must be able to address the pathophysiology

- Improve or modulate long-term synaptic plasticity - to facilitate learning and recovery of function in damaged neural tissue thru the use of proper fats and lipids.
- Repair nerve cell membranes by addressing fatty acid synthesis and metabolism
- Control excitotoxicity by blocking glutamate receptors with magnesium and other compounds
- A number of antioxidants have been shown to inhibit glutamate-induced cytotoxicity (excitotoxicity) including: alpha lipoic acid, and individual flavonoids from fruits and raw vegetables.
- Control oxidative stress – with magnesium, melatonin and antioxidants.
- Address dietary antioxidant availability
- Support mitochondrial energy production
- Address mineral imbalances – magnesium, zinc and other trace minerals
- Supply compounds that support cerebral energy production – creatine, ribose and ketones in coconut oil as an alternative fuel source for spinal cord tissue

## General diet and environmental recommendations:

- Eliminating **all** sugar and high-fructose containing foods or drinks
- Never use aspartame or MSG
- Try to eliminate sucralose – this may be hard because most of the idiot protein shake manufacturers are putting this crap in all their shakes and food bars. So you need a 100% whey protein.
- Eliminating other white foods - refined carbohydrates, hydrogenated and partially hydrogenated fats
- Control hypoglycemia with frequent meals
- Increase complex carbohydrates use lots of fresh vegetables including yams
- In general avoid or reduce intake of high glycemic foods
- Increase proteins and oils and use some with every meal and snack – fish, nuts and eggs might be nice. In general avoid soy unless it is fermented.
- Avoid all processed foods – No junk food at all
- Use whole foods especially raw foods including fresh fruits and vegetables
- Protein shakes – at least once a day
- Vitamin therapy both fat and water soluble
- Mineral therapy – I will suggest magnesium and zinc

A major issue with nutrients is **overcoming impaired transport into tissues and intracellular sites**. Response can occur when the cellular deficits of nutrients like thiamine (vitamin B1), B6 (pyridoxal-5-phosphate), methyl B12 and methyl folate are corrected by using enough to optimize/saturate the metabolic pathways that are compromised due to impaired absorption in the gut, and impairment in transport across the cell membranes.

I see the same issues are involved with B12, B6 – impaired conversion to P-5-P, B2, B3, glutathione, **poor intracellular transport of magnesium and zinc** and many other essential nutrients. Just giving the RDA of nutrients fails to account for biochemical individuality, genetic polymorphism, GI tract malabsorption, impaired transport into and through the blood stream by dysfunctional carrier mechanisms, dysfunctional cell membrane structures (due to bad fats + lack of essential fatty acids + disrupted sterol metabolism) and free radical damage (to membranes, mitochondria, membrane bound proteins/carriers/transport mechanisms, metabolic enzymes and damage to RNA and DNA. In addition, toxins that are not removed also affect all of these mechanisms and create uncoupling in the mitochondrial electron transport chain + disrupt DNA activity and DNA repair. Use of synthetic coal tar derived vitamins and poorly absorbed mineral preparations also complicate these issues. When the body cannot convert a synthetic B-complex to an active coenzyme

form a clinician often thinks he has addressed an issue when he has completely missed the boat. I see many people suffering from both subclinical and overt nutrient deficiency syndromes who are taking the very substance that they are functionally deficient in.

Any effective nutritional ischemic protocol must address nucleotide synthesis, ATP synthesis, nucleic acid synthesis, NAD synthesis, FAD synthesis and S-adenosylmethionine synthesis. The body will lose zinc, magnesium, and vitamin C in the urine during stress and the nervous system will upregulate glucose utilization which results in depletion of the coenzyme forms of B-vitamins. The adrenal glands will also be taxed and will produce more cortisol which depletes the body of vitamin C again plus coenzymes of B- vitamins especially vitamin B5, B6 and B3.

When brain cells or spinal cord cells are subjected to low levels of oxygen, low essential nutrient availability and excessive free radical production during strokes or microvascular ischemia, These conditions produce excessive amounts of cell damaging free radicals that attack and destroy the DNA, proteins, and mitochondria of neural cells. The persistence of symptoms indicates that some degree of brain injury is still present. An ongoing inflammatory process is very likely present. Oxidative stress, which arises from increased free radical production, is a significant mechanism that is involved in the pathology of neurodegenerative diseases. When free radicals are poorly controlled damage occurs to sensitive structures like cell membranes, DNA and enzymes.

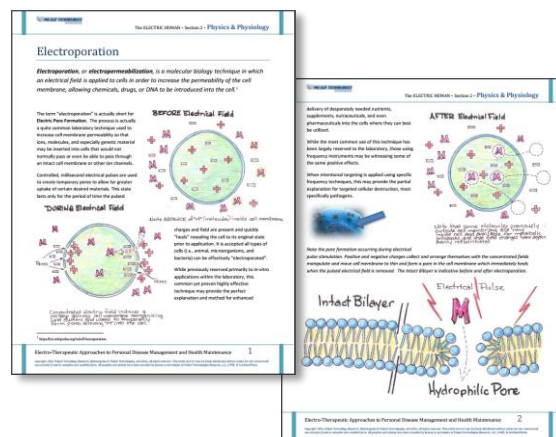
A number of nutritional compounds can be used to control free radical production and inflammation in the brain and spinal cord such as vitamin C, vitamin D, vitamin E, lipoic acid, acetyl-L-carnitine, melatonin, curcumin and krill oil.

Brain and spinal cord neurons are highly susceptible to damage from free radicals and inflammation because their membranes contain large amounts of polyunsaturated fatty acids. When neuronal cell membranes are damaged by free radicals the membranes can become stiff due to lipid peroxidation and they can become depleted of critical phospholipids. This is why I recommended choline, krill oil and L-Serine, which helps rebuild the phospholipids of the cell membranes. Cell membrane damage affects many functions of the cells including genetic expression, energy production, **and nutrient transport.**

Other nutrients that are very important to reverse the ongoing damage to the brain from strokes include many antioxidants, (specifically glutathione), alpha-lipoic acid, selenium, and melatonin. The B vitamins, acetyl-carnitine, ribose and magnesium are all known nutrients that can support the mitochondrial system, from which all the energy of the cells is made.

*Editors' Note: Efficiency and uptake may be greatly enhanced utilizing resonant frequency and/or electrical concepts.*

*For important related article see:*



<http://www.pulsedtechresearch.com/wp-content/uploads/2015/01/2-1-Electroporation-Aug2015.pdf>

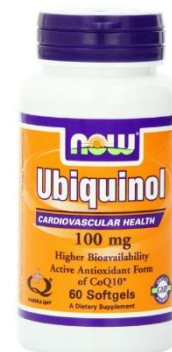


## SUPPLEMENT REGIMEN

### Coenzyme Q10

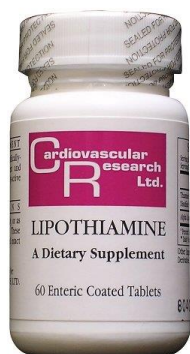
**use the Ubiquinol form 100 mg twice a day.** [www.amazon.com](http://www.amazon.com)

CoQ10 or Coenzyme Q10 is naturally produced by the human body. CoQ10 is both an antioxidant and is required for energy production. Statin drugs lower this essential nutrient. Ubiquinol is the most effective form of CoQ10.



### Lipothiamine

**2 tablets twice a day** from "Cardiovascular Research Ltd." [www.amazon.com](http://www.amazon.com)



Contains Vitamin B1 (Thiamine Tetrahydrofurfuryl Disulfide) 50 mg

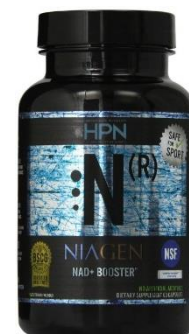
Lipoic acid 7.5 mg

This is a fat-soluble thiamine, combined with alpha-lipoic acid. The body's ability to absorb and metabolize conventional thiamine supplements is very limited. No matter how much thiamine you take plasma levels don't increase beyond about the first 12 milligrams of the dose. Very little thiamine actually makes it into the cells where it is needed. This is why you need a form of thiamine (Lipothiamine) that can get into nerve tissues. B-complex vitamins, including thiamine as well as niacinamide, are absolutely vital for nerve cell health. Where pathology already exists, unusually large quantities of vitamins are needed to repair damaged nerve cells.

### Niagen

**250 mg 2 capsules twice a day** must be HPN Niagen brand, find on [www.amazon.com](http://www.amazon.com) this is a form of vitamin B3 helpful for spinal cord and brain trauma

Niacinamide, also known as vitamin B-3, is a key to the successful treatment of nerve diseases. Niacinamide, say researchers at Harvard Medical School, "profoundly prevents the degeneration of demyelinated axons."<sup>1</sup> Niacin or vitamin B3 can be supplied in the diet as either nicotinic acid or nicotinamide. I use the Niagen brand because of its' many beneficial effects. Niacin is required for the synthesis of the active coenzyme forms of vitamin B3, nicotinamide adenine dinucleotide (NAD+) and nicotinamide adenine dinucleotide phosphate (NADP+). These coenzymes function as cofactors for a number of dehydrogenases such as lactate dehydrogenase and malate dehydrogenase. A recent study demonstrated that a single dose of Niagen resulted in statistically significant increases in the co-enzyme nicotinamide adenine dinucleotide (NAD+) in healthy human volunteers. Studies have shown that nicotinamide riboside switches "off" the genes of aging, extends life span, increases endurance, improves cognitive function and enhances cellular energy.



There are some general treatments that apply to all neurologic disease. The supplements that I emphasize, that support nerve and brain tissue, are the B vitamins, especially B1 (thiamine), B6, B3, folic acid, and B12. Essential fatty acids, both omega 3 and omega 6, are components of the nerve cell membrane and the myelin sheath that surrounds the nerve. Phospholipids, specifically phosphatidylcholine and phosphatidylserine, are also important parts of the cell membrane and the myelin sheath.

<sup>1</sup> Hoffer, Abram, & Andrew W. Saul. Orthomolecular Medicine for Everyone: Megavitamin Therapeutics for Families and Physicians. Laguna Beach, CA: Basic Health, 2008. Print. Copyright 2016, Steve Haltiwanger & Pulsed Technologies Research, LLC, all rights reserved.

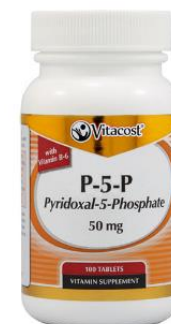
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## Pyridoxal-5-phosphate

**50 mg once per day** from [www.amazon.com](http://www.amazon.com) or [www.vitacost.com](http://www.vitacost.com)

Pyridoxal-5-phosphate is the active form of vitamin B6. B6 is a required coenzyme for transamination enzymes, which are involved in the synthesis and catabolism of the amino acids. Pyridoxal, pyridoxamine and pyridoxine are all forms of vitamin B6. These compounds must be changed to the biologically active form of vitamin B6, pyridoxal-5-phosphate. Pyridoxal-5 Phosphate (P-5-P) is the bioavailable coenzyme form of Vitamin B6 and in my opinion it is the preferred form of this vitamin for individuals who need optimal absorption and effective cellular activity of this critical B vitamin. In general P-5-P is essential for proper metabolism of amino acids and it is involved in the production of many neurotransmitters. It is also important for immune function and this coenzyme is an essential cofactor for scores of enzymatic reactions. An interesting observation is that a deficiency of the active form of vitamin B6 will also impair the body's ability to make sufficient amounts of certain essential fatty acids, which are needed for brain and spinal cord repair. It also helps reduce inflammation along with curcumin and krill oil.



Many people cannot convert the standard form of vitamin B6 into its active coenzyme form, so taking standard B6 supplements is generally a waste of time and money. B6 has to be converted in the cells to its bioactive form called pyridoxal-5 phosphate. The conversion of B6 to P-5-P is mediated by an enzyme called pyridoxal kinase. Many drugs and toxins and even inherited genetic abnormalities can interfere with the action of this enzyme in the cells of the body. When the activating enzyme is blocked in the liver the ability to metabolize some drugs and many toxins is impaired. This results in individuals becoming chemically sensitive to numerous substances. When the activating enzyme is blocked in the heart it interferes with the heart's ability to make energy. When it is blocked in the intestines the actions of the intestines are compromised. When the activating enzyme is blocked in the brain the production of neurotransmitters becomes impaired and a person develops imbalances in their neurotransmitters. Neurotransmitter imbalances are generally dealt with by doctors by adding on more and more psychiatric drugs thus compounding the problem. The end result is that because of a variety of factors some people develop a functional B6 deficiency in various organs despite adequate dietary B6. In the cells the activating enzyme pyridoxal kinase requires mineral cofactors in order to properly function. It is generally thought that adequate levels of cellular magnesium are important in the heart, liver and intestines. I recommend use of a specific form of magnesium to get adequate magnesium into neural tissues, (**Magnesium Orotate**). However Dr. Jon B. Pangborn in his publications has pointed out that zinc may also be a critical activating mineral. In order to get zinc into the spinal cord I recommend using a compound called **Zinc Orotate**. This substance is a mineral transporter and is superior to many other supplement forms of zinc for many conditions.

## L-methyl folate

**10mg one daily** also known as 5-MTHF from [www.amazon.com](http://www.amazon.com). **Take daily for 2 weeks then use twice a week.**

L-methylfolate is indicated for the distinct nutritional requirements of individuals who have suboptimal L-methylfolate levels in the CSF, plasma, and/or red blood cells. L-methylfolate increases the production of neurotransmitters. Studies also show that the effectiveness of 5-MTHF can be further enhanced by co-supplementing with methylcobalamin (the active form of vitamin B12) and vitamin B6. Some individuals do not effectively methylate and convert folic acid into its bioactive form thus are still at risk of deficiency. L-5-MTHF, an active, methylated form of folate, requires no additional metabolic steps to be used by the body, thus it is often the preferred choice of a folic acid supplement. Oxidative stress in the CNS can produce a regional brain deficiency of B vitamins such as B12, B6, folate, and thiamine (B1), which I have included in this protocol.



## Biotin

**5 mg 1 daily** from [www.amazon.com](http://www.amazon.com)

## Vitamin C

**500 mg 2-3 times a day** (no photo – everyone should already have some!)

## Methyl B12

**5000 mcg use two sublingual tablets daily** from [www.amazon.com](http://www.amazon.com)

I recommend the Kirkland brand 300 tablets

## Choline and Inositol

**500 mg 2 capsules twice a day** --- buy the NOW brand from [www.amazon.com](http://www.amazon.com)

Choline is a precursor to the neurotransmitter acetylcholine. Therefore, choline is believed to have neurological effects. Choline, a constituent of phosphatidylcholine (PC), is a component of cell walls and membranes and is needed for nerve cell repair.

## 100% Whey Protein with no artificial sweeteners but stevia is fine + Ribose Powder + Creatine Powder

**Add 5 grams of ribose powder and 5 grams of creatine to whey protein shake**

You can get these from [www.vitacost.com](http://www.vitacost.com) or [www.amazon.com](http://www.amazon.com)

Ribose and creatine are energy compounds for the nerve tissues. Creatine typically comes as a powder and was made popular as a supplement for enhancing athletic performance. However, research on creatine has recently been extended to neurologic illness. Much of the study on creatine has been on animals. But one human study, though it did not demonstrate big gains in motor function, did show improvement in mood and depression. Due to its safety record, creatine should be considered, with dosages starting at 5 g daily.

Ribose is a natural pentose sugar used by the cells in energy production. Ribose is also used by the cells to synthesize nucleic acids, nucleotides and glycogen. Ribose is created in the cells from conversion of glucose in the pentose phosphate pathway, which is also known as the phosphogluconate pathway. Ribose is a precursor of PRPP, which in turn is a precursor of ATP, adenine nucleotides and nucleic acids. In ischemic conditions ATP and adenine nucleotide pools are depleted because the production of PRPP is limited by the rate limiting activity of the enzyme glucose-6-phosphate dehydrogenase. Supplements that increase PRPP levels reestablish the production of ATP and adenine nucleotide biosynthesis. Production of ATP in ischemic tissues can be enhanced by nutrients that affect both mitochondrial ATP production as well as cytoplasmic ATP production. Activation ribose and orotate mineral transporters and support of purine and pyrimidine nucleotide synthesis by orotates, aspartates and glycine also restores depleted adenine nucleotide pools as well as nucleic acid and protein synthesis.

When a stroke occurs to the brain or spinal cord the vascular supply to a portion of the tissue is compromised. Some neural tissue will die while other tissue around the infarcted area survives, but has reduced energy production due to restricted oxygen and nutrient supply. This tissue also goes into a hibernation state with reduced production of ATP and adenine nucleotides. Ribose is can assist in correcting these metabolic disturbances by increasing cell levels of ATP.



## Coconut Oil

**1-2 tablespoons twice a day** more is better than less

It would take too long to discuss all the benefits of coconut oil but it provides a source of energy to brain and spinal cord cells that cannot use glucose and you can improve neural function.



## Magnesium Orotate

**500 mg 2 tablets capsules twice a day** 800-222-7157

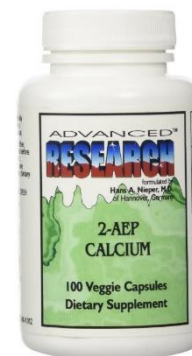


Magnesium is the main regulator of calcium flow in the body. Magnesium is involved in ATP (energy) production, is a factor in over 300 chemical or enzyme reactions in the cells of the body, and is vital for the normal function of nerves and muscles. Deficiencies of magnesium are extremely common and cause muscle weakness with tremors and leg cramps, irregular heart rhythms, heart muscle spasms with heart attacks, insomnia, fatigue, anxiety, depression, and confusion. Calcium 2-AEP, magnesium orotate and zinc orotate are mineral transporters. The mineral-transporter complex remains stable in the blood stream with low dissociation, and the minerals are not released until the mineral-transporter complex enters the target tissues/cells. The attachment of minerals to carrier molecules forms electrically neutral stable complexes that allow selective direction of minerals to particular tissues that metabolically use the carrier molecules. This form of directed mineral nutrition also enhances mineral entry even into cells that have disturbed cell membranes. Damage to cell membranes is a major issue in spinal cord ischemia, which impairs nutrient transport into damaged cells. These are the very cells that need the nutrients the most.

## 2-AEP Calcium

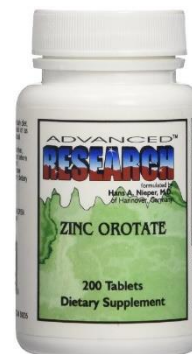
**500 mg 4 capsules twice a day** 800-222-7157

2-AEP Calcium plays a dual role both as a mineral carrier that releases calcium on the cell membrane surface and as a cell membrane repair material. Calcium 2-AEP was considered by Dr. Hans Nieper to be a cell membrane integrity factor. When the AEP is incorporated into the cell membrane, it binds fatty acids to preceding and following peptide chains in cell membranes helping in the repair of membrane structure. Calcium 2-AEP enhances normal membrane activity by assisting the cell membrane in maintaining its electronic function allowing for proper production of cellular capacitance. The capacitance of cell membranes is a reflection of the amount of charge in the membrane. Healthy cells are able to maintain their membrane charge whereas unhealthy and damaged cells have structural membrane abnormalities and imbalances of intracellular mineral concentrations which results in lower membrane capacitance. One of the most important electronic roles of the cell membrane is creation of charge, maintenance of charge and the transfer of that charge to genetic material, which facilitates cellular protein synthesis. Reestablishing cell membrane structure in damaged cells and maintaining a healthy capacitance of the cell membranes is critical in the repair of damaged nerve cells.



## Zinc Orotate

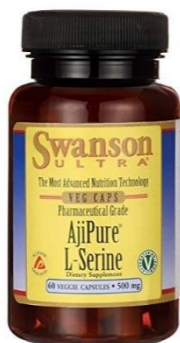
**1 daily** 800-222-7157





## L-Serine

**4 capsules twice a day** – cheapest price is at [www.swansonvitamins.com](http://www.swansonvitamins.com)



Serine is not made by neurons when they differentiate (mature). It must be supplied by astrocytes, which means a CNS serine deficiency is very possible. Serine plays a critical role in the production of tryptophan which in turn makes the neurotransmitter serotonin. Patients with low urinary serine have predominant neurological symptoms and increased severity of pain. Serine helps form the phospholipids needed to make cell membranes. It is also involved in the function of RNA and DNA, fat and fatty acid metabolism, muscle formation, and the maintenance of a healthy immune system. The proteins used to form the brain, as well as the protective myelin sheaths that cover the nerves, contain serine. Without serine, the myelin sheaths could fray and become less efficient at delivering messages between the brain and nerve endings in the body, essentially short circuiting neural functions.

## DejaVida

**2 capsules twice a day**. You can get this from [www.vitacost.com](http://www.vitacost.com) or [www.amazon.com](http://www.amazon.com)

This is a bioactive form of curcumin that can get into the central nervous system to help reduce inflammation in the brain and spinal cord. Curcumin has anti-inflammatory and antioxidant effects and the proper form can enter the tissues and control oxidative stress. Curcumin can also up regulate antioxidant gene expression. The DejaVida brand has the proper type of extract. If the wrong extract of curcumin is used it is poorly absorbed, rapidly metabolized, and rapidly eliminated so it exhibits poor bioavailability. This supplement also contains vitamin D3 and niacinamide (a form of vitamin B3).



## Melatonin

**6 mg at night** before sleep. You can get this from [www.vitacost.com](http://www.vitacost.com) or [www.amazon.com](http://www.amazon.com)

Melatonin is an effective neuroprotective agent for treatment of brain and spinal cord ischemia. Melatonin is an ideal neuroprotective agent as it readily crosses the BBB and lacks toxicity and has both antioxidant and anti-inflammatory effects in ischemia.

## Acetyl-L- Carnitine

**500 mg two capsules twice a day**

Acetyl L-carnitine (ALC) is an anti-aging nutrient to protect energy starved brain and myocardial cells from degeneration due to age- related decline in cellular energy production, since ALC increases the rate of mitochondrial energy production by transporting fatty acids into the mitochondria. Researchers at the UCB University of California Berkley reported in 2002 that combining alpha lipoic acid with ALC improved energy (mitochondrial function). Acetyl L-Carnitine has been found to be helpful in stroke recovery.



Combining carnitine, coenzyme Q10 and lipoic acid is synergistic in increasing cellular energy production. L-carnitine use can increase cardiac output and exercise endurance, and reduce the incidence of irregular heartbeats. According to Packer 1999 combining L-carnitine with the antioxidant alpha-lipoic acid can improve mitochondrial production of

energy in nerve cells, heart and skeletal muscles. Lipoic acid also recycles many of the body's other antioxidants such as vitamins C and E, glutathione, and CoQ10 ref assists in glucose transport into the cells.

## Krill Oil

**3000 mg daily (500mg capsules 3 twice day)**

[www.amazon.com](http://www.amazon.com) Vita Pure Krill Oil Per Serving Softgels, 1000 mg, 360 Count

When the brain or spinal cord is damaged by any condition motor and sensory functions are impaired studies have shown that neural functions can be improved by supplementing with omega-3 fatty acids. In the case of omega-3 fatty acids they work by improving the functions and repair of damaged neural synapses as well as by increasing the production of dendritic spines on neurons. Dendritic spines are part of a nerve cell's interface with the communication grid of neural networks. The more dendritic spines there are the greater the connectivity and free flow of information. Evidence shows that omega-3 fatty acids can directly cross the blood-brain barrier (BBB) and enter neural tissue. It also has an anti-inflammatory effect.



## Chlorella

**10 tablets twice a day** either [sunchlorellausa.com](http://sunchlorellausa.com) brand or **Swanson Kyoto** brand (chlorella growth factor)



Chlorella growth factor supplies the body with nucleic acids as do sardines. However, chlorella growth factor isn't just about nucleic acids. It also includes special polysaccharides known as beta glucans, which play a particular role in immune system health.



Nucleotides are the precursors to DNA and RNA, which in turn control protein synthesis. Nucleotides are critical energy carrying molecules particularly ATP and GTP. Nucleotides according to the Third edition of Lehninger's Principles of Biochemistry are also components of the enzyme cofactors NAD, FAD and S-adenosylmethionine as well as coenzyme A. Nucleotides can be produced by either de novo pathways or through salvage pathways. De novo synthesis of nucleotides requires adequate cellular availability of the precursor amino acids and ribose 5-phosphate. The pyrimidine ring of pyrimidine nucleotides is first synthesized as orotate, which is then attached to ribose phosphate and then converted to the common pyrimidine nucleotides that are used in nucleic acid synthesis.