

PERSONAL EXPERIENCE ONLY –

CADASIL TOGETHER WE HAVE HOPE CAN NOT SUPPORT TAKING L-ARGININE BUT HAVE PROVIDED THE INFORMATION FROM AN PERSONAL EXPERIENCE ONLY.

Local stores do not sell Cardio-Discovery anymore.

The manufacture now makes it for <http://advantagevitamin.com> toll free 1-800-328-1022

L-Arginine was introduced at the first ever CADASIL conference on January 2005 in Newcastle, England. No words can express the appreciation Jack Shields and his wife Joan has shown to me. A sincere Thank you to Jack who gave me L-Arginine to take home to the USA for Steve to try. This how Steve is doing

Steve states:

Prior to L-Arginine

I had trouble with motor functions (walking getting out of chairs) Blinding headaches vision disturbances, flashing lights, etc.

single tasked (one thing at a time)

Confusion with thinking skills

poor sleeping

could not swallow well

slurred speech when tired

pains in arms

trouble with trying to explain simple things

poor working memory TIA's/strokes

tingling in fingers/toes/faces drooling

high pulse rate

All of my above mentioned symptoms has subsided greatly or vanished since taking L-Arginine in January 2005. I take 12 gram per day (6 grams in morn and 6 grams in evening with water and blended very well.

Billie's states:

Prior to L-Arginine

Steve was not functionally very well and now he has fixed the kitchen sink.

He still needs to take his daily naps but otherwise he seems more alert. I

really thought that the L-Arginine would not work but I ate my words as

with Steve's other medicines they all work together.

Reference links - L-Arginine

Efficacy and safety of oral L-Arginine in acute myocardial infarction. Results of multicenter, randomized, double-blind, placebo-controlled ARAMI pilot trial.

Bednarz B, Jaxa-Chamiec T, Maciejewski P, Szpajer M, Janik K, Gniot J, Kawka-Urbaneck T, Drozdowska D, Gessek J, Laskowski H.

Postgraduate Medical School, Department of Cardiology, Grochowski Hospital, Warsaw.

Aims. L-arginine is a substrate for nitric oxide (NO) synthesis in vascular endothelial cells. NO bioavailability is decreased during myocardial infarction (MI). It might be expected that administration of L-arginine may maintain NO production and alleviate the course of MI. The aim of the study was to assess safety and effects of treatment with L-arginine on the clinical course of MI.
Methods and Results. 792 patients (mean age 64 years, 551 men) with ST segment elevation MI admitted within 24h after the onset of symptoms were randomized to oral L-arginine (3.0 t.i.d p.o. for 30 days) or placebo on top of routine therapy. The end point which was the composite of 30 day cardiovascular death, reinfarction, successful resuscitation, shock/pulmonary edema or recurrent myocardial ischemia occurred in 24% patients treated with L-arginine and 27% with placebo (OR 0.63, 95% CI 0.39-1.02, p=0.06). The end point was observed less frequently in 226 patients with hyperlipidemia (19 vs 31, p<0.05). No serious adverse effects were observed during L-arginine supplementation.
Conclusions. This study, which is the first attempt to use L-arginine in MI, showed that oral L-arginine supplementation was well tolerated. Beneficial nonsignificant trend was observed towards reduction of major clinical events.

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<http://www.docguide.com/news/content.nsf/news/8525697700573E1885256C54006B5BEA>

L-Arginine Minimises Stroke Damage in Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-like Episodes: Presented at ANA By Thomas S. May Special to DG News

NEW YORK, NY -- October 16, 2002 -- L-arginine therapy minimises tissue injury from ischaemia in the acute phase of mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS).

This is the conclusion of a study presented here October 15 at the 127th annual meeting of the American Neurological Association (ANA), by Dr. Yasutoshi Koga, from the department of paediatrics and child health, Kurume University School of Medicine, in Kurume, Fukuoka, Japan.

People afflicted with MELAS are vulnerable to small strokes during childhood and early adulthood. Based on the assumption that such strokes are caused by impairment of vasodilation in some segment of the intracerebral artery, the researchers administered L-arginine, a drug that helps control the expansion of blood vessels, to patients with MELAS in the acute phase of stroke.

Patients received 0.5gm/kg L-arginine in a 10 percent solution in six separate stroke-like episodes, and a placebo in another six episodes. The investigators analysed clinical symptoms, biochemical parameters, and intracranial haemodynamics by computed tomography before and after treatment.

They found that 30 minutes after L-arginine administration, all of the symptoms -- except teichopsia -- improved drastically.

There was also significantly increased uptake in the infarcted region compared with the contralateral regions, showing improvement in regional cerebral blood flow in the region of the fresh infarct. Levels of lactate and lactate/pyruvate ratio recovered to steady state levels 24 hours after L-arginine administration. The investigators concluded that L-arginine therapy improved microcirculation in the infarcted region and reduced tissue injury from ischaemia. L-arginine is the first drug that has been shown to rescue MELAS patients from the acute symptoms of stroke, the researchers contend.

"L-Arginine therapy also improved the blood flow in the area of the stroke, reducing tissue damage, and therefore constitutes a new potential therapy for use in the acute phase of stroke-like episodes in MELAS," Dr. Koga noted.

In 1988 researchers discovered that L-arginine's wide-ranging health benefits were due primarily to its role as a precursor to nitric oxide (NO). L-arginine stimulates the release of nitric oxide from the walls of blood vessels, helping them naturally expand to promote healthy circulation. So L-arginine is a particularly important amino acid for overall circulatory health.

Arginine [also L-Arginine]

An important anti-aging amino acid that fights cholesterol, promotes blood circulation in the brain, helps muscle growth, curbs appetite, and facilitates hormone production. The human body produces Arginine, and circulating levels can be increased through Arginine supplementation

A systematic review of nitric oxide donors and L-arginine in experimental stroke; effects on infarct size and cerebral blood flow.

Willmot M, Gray L, Gibson C, Murphy S, Bath PM.

Institute of Neuroscience, University of Nottingham, Nottingham, UK.

BACKGROUND: Nitric oxide (NO) is a candidate treatment for acute ischaemic stroke, however published studies in experimental stroke have given conflicting results. **METHODS:** We performed a systematic review of published controlled studies of L-arginine (the precursor for NO) and NO donors in experimental stroke. Data were analysed using the Cochrane Collaboration Review Manager software. Standardised mean difference (SMD) and 95% confidence intervals (95% CI) were calculated. **RESULTS:** Altogether, 25 studies(s) were identified. L-Arginine and NO donors reduced total cerebral infarct volume in permanent (SMD -1.21, 95% CI -1.69 to -0.73, $p < 0.01$, $s = 10$) and transient models of ischaemia (SMD -0.78, 95% CI -1.21 to -0.35, $p < 0.01$, $s = 7$). Drug administration increased cortical CBF in permanent (SMD +0.86, 95% CI 0.52-1.21, $p < 0.01$, $s = 8$) but not transient models (SMD +0.34, 95% CI -0.02 to 0.70, $p = 0.07$, $s = 4$). **CONCLUSIONS:** Administration of NO in experimental stroke reduces stroke lesion volume in permanent and transient models. This may be mediated, in part, by increased cerebral perfusion in permanent models. These data support clinical trials in stroke patients, although the presence of a narrow therapeutic time window may be a limiting factor.

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L-Arginine improves vascular function by overcoming deleterious effects of ADMA, a novel cardiovascular risk factor. Boger RH, Ron ES. Clinical Pharmacology Unit, Institute of Experimental and Clinical Pharmacology, Center of Experimental Medicine, University Hospital Hamburg-Eppendorf, Germany. boeger@uke.uni-hamburg.de.

There is abundant evidence that the endothelium plays a crucial role in the maintenance of vascular tone and structure. One of the major endothelium-derived vasoactive mediators is nitric oxide (NO), an endogenous messenger molecule formed in healthy vascular endothelium from the amino acid precursor L-arginine. Endothelial dysfunction is caused by various cardiovascular risk factors, metabolic diseases, and systemic or local inflammation. One mechanism that explains the occurrence of endothelial dysfunction is the presence of elevated blood levels of asymmetric dimethylarginine (ADMA)--an L-arginine analogue that inhibits NO formation and thereby can impair vascular function. Supplementation with L-arginine has been shown to restore vascular function and to improve the clinical symptoms of various diseases associated with vascular dysfunction.

Chapter from "The Arginine Solution" by Robert Fried, PhD & Woodson C Merrell, MD

ADNO (Arginine Derived Nitric Oxide) and the Brain

Put your fingertips together then spread your hands apart. The space created will give you a pretty good estimate of the size of your brain. Weighing in at under three pounds and sporting the consistency of firm oatmeal, this miracle of complexity is made up of billions of nerve and support cells that together affect the functioning of virtually every system in your body, from sexual performance to immune response.

The healthy brain consumes 25 percent of the body's oxygen supply and an astonishing 70 percent of its blood glucose. It also produces a bewildering array of chemicals. Cut off blood supply for more than a few minutes, and brain cells quickly begin to die. Even if blood flow is just slightly reduced, the resulting reduction in oxygen, if chronic, can contribute to a spectrum of mental disorders, from impaired thinking to disorders of senility.

Just as ADNO plays a key role in relaxing coronary arteries to guarantee a plentiful blood supply to your heart, so does this mechanism now appear to regulate blood flow to your brain. A 1993 animal study in Brain Research showed that inhibiting the enzyme used to make NO from L-Arginine cause constriction of the arteries supplying the brain. The body responded by elevating blood pressure to make sure enough blood still made it through. When the researchers then infused their animal subjects with L-arginine, the vessels dilated and blood pressure normalized. (1)

But what about blood flow within the brain's famously convoluted grey matter? You've probably seen high-tech brain scans that show different regions of the brain "lighting up" depending upon what kinds of activities a person is asked to perform. What these colorful images are actually revealing are changes in regional metabolic activity that accompany different cognitive tasks. In other words, the areas that are working hardest are also using up more oxygen and glucose to do their jobs. These areas that are "on break" require a reduced supply.

Brain researchers have for years been intrigued by the brain's ability to form these small functional activity networks and to shunt blood preferentially, via arterioles and capillaries, to the precise area where it's most required. In the vernacular of students of the cerebrum, this phenomenon is known as "cerebral microcirculation during neural activity". So what exactly regulates it?

To find out, neuroscientists applied low-intensity nerve stimulation to the paws of rats. As expected, this quickly produced increased metabolic activity in a specific area of the rat's brain. It also produced a 30-40 percent dilation in the arterioles that supplied this area. Remarkably, no such dilation occurred in adjacent arterioles that branched off from the same major artery and fed brain cells only a small distance away. The author of the study, Dr C Iadecola, concluded that the agent of such

precise vascular control was non-other than Nitric Oxide being produced by activated brain cells. (2)

But ADNO has other functions in the brain, too, besides orchestrating blood flow. The way different nerve cells "communicate" with one another is through the release of specific messenger chemicals called neurotransmitters. These are typically secreted in the synapse – the tiny gap that separates the end of one nerve cell from the beginning of a neighbor. Serotonin, noradrenaline, and dopamine are just three of the more famous examples of neurotransmitters, levels of which can be affected by drugs ranging from antidepressants like Prozac to Parkinson's treatments like levodopa. Recently, neuroscientists have learned that Nitric Oxide functions as a neurotransmitter, facilitating communication among nerve cells whether they are connected via synapses or not.

No one can yet say for certain what roles the ADNO neurotransmitter plays. One possibility may be the activation of memory storage. When you file a memory in long-term storage – say, your first kiss – the brain undergoes a complex process called long-term potentiation or LTP. In a sense, it's not unlike writing your self a note, then tracing it over back-wards to make sure the letters are nice and dark. This reverse tracing, neuroscientists suspect, requires a "retrograde messenger" – one that somehow work backwards to reinforce and "darken" nerve connections originally laid down when your lips first met. According to researchers at Stanford University School of Medicine, NO may well be this retrograde messenger. In fact, they were able to show that inhibiting the enzyme that makes ADNO in the brain interferes with long-term memory storage (3)

Other brain researchers have begun to examine the role of ADNO in diseases such as Alzheimer's and Parkinson's. In patients suffering either of these disorders, there is frequently a significant reduction in the Nitric Oxide being produced in their brain. Recent articles in both Nature and Journal of Neurological Sciences offered evidence that this reduction may hamper memory storage and reduces blood flow to the brain. (4), (5). The latter may at once contribute to and be exacerbated by deposits of a specific kind of plaque, called beta-amyloid, which is the hallmark of several degenerative brain diseases including Alzheimer's. This plaque, though chemically different from the atherosclerotic plaque that clogs heart arteries, seems equally damaging to endothelial cells in the small cerebral blood vessels. The Arginine Solution holds significant promise for restoring healthy levels of ADNO to the brain and, in doing so, enhancing its ability to function at its peak

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[New possibilities in treatment of atherosclerosis--increase of nitric oxide synthesis by L-arginine supplementation]

[Article in Polish]

Kielar M, Myrcha P, Pleban E.

Klinika Chirurgii Ogolnej i Naczyniowej II Wydzialu Lekarskiego Akademii Medycznej w Warszawie.

Diseases such as heart attack, stroke or critical atherosclerotic leg ischaemia are very common in the developed countries. It is estimated that they are the main cause of deaths in the age group over 40 years. Patients with advanced leg ischaemia can be treated surgically. However in distal disseminated occlusions, surgery is technically impossible. In such cases amputation is the treatment of choice, but postoperative death ratio in this group is still high. That is why new ways of atherosclerosis treatment are needed. Progress in vascular biology brings new methods of treatment. Discovering of vasodilatory effect of nitric oxide makes us seek for ways of increasing its endogenous synthesis in endothelium of blood vessels. Studies on angiogenic cytokine application, amplification of NO synthesis expression and other gene engineering techniques are carried out in order to increase the concentration of nitric oxide in endothelium. It has been found that an increase of nitric oxide synthesis can be achieved by administering L-arginine. Numerous trials suggest that supplementation of this amino acid can be of great therapeutic importance in patients with

various atherosclerotic diseases. Clinical effectiveness of L-arginine is comparable to conventional pharmacotherapy. It seems that in the near future L-arginine supplementation may contribute to better results of atherosclerosis treatment.

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Health Benefits of Arginine

By Harry Elwardt, N.D., Ph.D.

The following report, which is backed up by incredible scientific research, shows the many health benefits of increased arginine in the human body. Arginine is a semi-essential amino acid, which is produced in the liver and can be found in protein rich foods like red meat. Medical research has now shown that by simply supplementing with 3 to 6 grams of arginine everyday all the following is possible:

Aging Process

Arginine inhibits one of the primary mechanisms of the aging process (it inhibits the process of cross-linking) (1).

Arginine increases the release of the human growth hormone (HGH) (also known as the anti-aging hormone) from the pituitary gland (2)

Cardiovascular System

Arginine improves blood circulation, improves exercise capability and facilitates vasodilation in angina patients (3)

Arginine helps to prevent atherosclerosis and reduces the severity of existing atherosclerosis (4).

Arginine inhibits the adhesion of monocytes to the endothelium (an underlying event in the course of atherosclerosis) (5).

Arginine improves blood circulation (by stimulating the production of nitric oxide, an endogenous neurotransmitter that helps to prevent vasoconstriction and which initiates vasodilation by relaxing the smooth muscle cells of the blood vessels) (6).

Arginine helps to prevent abnormal blood clotting (by stimulating the production of plasmin and by increasing vasodilation) (7)

Arginine helps to prevent free radicals-induced damage to the lining of blood vessels (by enhancing the production of nitric oxide in blood vessels) (8)

Arginine significantly increases stroke volume and cardiac output (without effect on heartbeat rate) in congestive heart failure patients. It also increases vasodilation (leading to increased blood circulation) in congestive heart failure patients (9).

Arginine reverses consequences of coronary heart disease (10).

Arginine lowers blood pressure in some hypertension patients (by facilitating the body's production of nitric oxide (NO) and by inhibiting the angiotensin converting enzyme (ACE)) (11).

Arginine reverses adverse effects of high blood pressure (12).

Arginine decreases high blood pressure (13).

Arginine reduces pulmonary blood pressure and improves blood circulation in pulmonary hypertension patients (14).

Arginine increases walking distance in intermittent claudication patients (15).

Arginine restores normal endothelial function in hypercholesterolemia (16).

Arginine improves walking distance in peripheral vascular disease (17).

Arginine improves outcome after bypass surgery (18).

Arginine reduces blood clots and strokes (19)

Arginine helps prevent restenosis after angioplasty and bypass (20).

Arginine may give protection against size of heart attack (21).

Arginine improves heart failure (22)

Arginine improves peripheral vascular disease (23).

Digestive System

Arginine deficiency can cause constipation.

Arginine supplementation may decrease the incidence of gallstones.

Arginine reduces intestinal permeability (due to arginine's role in the production of nitric oxide) (24).

Arginine alleviates many cases of ulcerative colitis (by promoting the healing of the ulcers that occur in the colon of ulcerative colitis patients) (25).

Arginine may improve irritable bowel syndrome (IBS) (26).

Arginine reduces ulcers (27).

Arginine helps prevent post surgical damage after intestinal manipulation (28).

Arginine improves outcome in sepsis (29).

Excretory System

Arginine alleviates the pain and discomfort associated with interstitial cystitis (30).

Arginine significantly improves the function of the kidneys and helps to prevent age-related degradation of the kidneys (31).

Immune System

Arginine helps to prevent bacterial & viral diseases in persons with suppressed immune systems (32).

Arginine blocks the formation of some forms of cancer (arginine inhibits the cellular replication of 24 different types of cancer in animals) (33).

Arginine boosts the ability of the immune system to fight breast cancer (34).

Arginine lowers tumor protein synthesis and tumor growth rate in liver cancer patients (35).

Arginine inhibits the further growth of some types of sarcomas (36).

One of the means by which arginine counteracts cancer is by reducing the activity of ornithine decarboxylase, an enzyme that is associated with some types of cancer. * Caution: Arginine is also speculated to exacerbate some types of cancer, however this is not well proven.

Arginine improves outcome of cancer treatment (37).

Arginine (in non-excessive quantities) stimulates numerous aspects of the immune system (38):

Arginine stimulates the production of helper T-cells (39).

Arginine stimulates the activity of lymphocytes and also stimulates their production by the thymus gland (40).

Arginine increases the activity (cytotoxicity) of NK lymphocytes. (41).

Arginine stimulates the production of T-lymphocytes within the thymus and makes them more active and effective (42).

Arginine increases the size of the thymus, stimulates the production of lymphocytes by the thymus and restores the production of thymic hormones to youthful levels (43).

Arginine helps to counteract inflammation (44).

Arginine accelerates the ability of the immune system to recover from surgery (45).

Arginine improves sickle cell disease (46).

Metabolism

Alkalosis can occur as a result of arginine deficiency (47).

Arginine exerts antioxidant effects that scavenge superoxide free radicals (48).

Arginine lowers total serum cholesterol levels (49).

Arginine lowers serum low-density lipoprotein (LDL) levels (50).

Arginine inhibits the process of cross-linking (51).

Arginine reduces insulin resistance and improves blood sugar disposal in diabetes mellitus type 2 patients (52).

Arginine reduces insulin resistance (53)

Arginine improves diabetes and reverses damage caused by diabetes (54).

Arginine may prevent diabetes (55).

Arginine increases oxygen uptake in the lungs in persons with hypoxia (due to its role in the production of nitric oxide, which in turn improves blood circulation via vasodilation) (56):

Arginine increases oxygen uptake in the lungs in persons with altitude sickness (due to its role in the production of nitric oxide, which in turn improves blood circulation via vasodilation) (57).

Arginine improves asthma (58).

Arginine helps to detoxify the liver and alleviates cirrhosis. Liver malfunction can occur as a result of arginine deficiency (59).

Arginine lowers elevated serum triglyceride levels (60).

Arginine alleviates obesity and facilitates weight loss (by stimulating the release of human growth hormone (HGH) from the pituitary gland) (61).

Musculoskeletal System

Arginine facilitates the healing of fractures (62).

Arginine facilitates muscle growth (by inhibiting muscle loss) and is required for the transport of the nitrogen used in muscle metabolism (63).

Muscle weakness can occur as a result of arginine deficiency (64).

Arginine may prevent and alleviate osteoporosis (by stimulating the release of human growth hormone (HGH) which is an important mediator of bone formation and bone turnover; it also stimulates nitric oxide synthesis which is a potent inhibitor of osteoclasts that cause the resorption of bone) (65).

Arginine causes the relaxation of smooth muscle (by functioning as a precursor for nitric oxide production) (66).

Arginine improves muscle performance (67).

Arginine improves glucose uptake into muscle cells (68).

Nervous System

Arginine may be useful for the treatment of Alzheimer's disease (due to its ability to repair damaged axons by increasing polyamines levels) (69).

Arginine is essential for the regeneration of damaged axons of neurons (its role appears to be as an agent for degrading proteins that have been damaged through axon injury) (70).

Arginine facilitates the potentiation of long-term memory (by stimulating the production of nitric oxide (NO) - a neurotransmitter responsible for the potentiation (storage) of long-term memory (71).

Arginine improves memory and cognitive functions (72).

Arginine improves pituitary responsiveness and modulates hormonal control (73)

Sexual System

Arginine alleviates male impotence (by stimulating the production of nitric oxide, the endogenous chemical that stimulates erections in males) (74).

Arginine alleviates male infertility by improving sperm count and sperm motility (due to its involvement in the manufacture of endogenous spermidine) (75).

Arginine enhances (male and female) sexual desire (libido) (76).

Arginine enhances (female) sexual performance - due to its role in the production of nitric oxide in the clitoris (nitric oxide facilitates female orgasm in the clitoris) (77).

Arginine improves (male) sexual performance by providing nitrogen to the nitric oxide (NO) molecule that is integral to the achievement of erections - Arginine produces erections that are bigger, harder and more frequent. It also increases male sexual endurance, i.e. erections that last for a longer period of time (78).

Arginine improves sperm count and sperm motility (79).

Arginine may improve prostate function (80).

Arginine deficiency can cause atrophy of the testicles of the testes.

Skin/Hair

Hair loss (especially male pattern baldness) can occur as a result of arginine deficiency (81).

Arginine concentrates in the skin:

Arginine (applied topically) increases the level of vascular endothelial growth factor in the skin (82).

Arginine stimulates the proliferation of fibroblasts (skin cells) (83).

Arginine is essential for and accelerates the healing of wounds (by stimulating the release of human growth hormone (HGH), stimulating the production of collagen and by stimulating the proliferation of fibroblasts) (84):

Arginine accelerates the healing of burns (85).

Arginine dramatically accelerates the healing of wounds in people who have undergone surgery (86).

Arginine decreases post operative infection and length of hospital stay (87).

Arginine improves scleroderma (88).

Safety

Arginine has been shown to be safe in the above studies as well as thousands of others (89).

Arginine has been used safely in humans for the past 30 years. Thousands of professional athletes, as well as non-athletes, have used arginine supplements with no adverse side effects.

Research

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