

HOMOCYSTEINE

Researchers now believe homocysteine is over 40% more accurate to predict heart disease than cholesterol.

Cardiovascular disease causes and Alzheimer's dementia is expected to increase sharply as the population ages. Both cardiovascular and Alzheimer's disease have now been linked to the accumulation of a toxic amino acid called homocysteine. Vitamin supplement users have assumed they are being protected against homocysteine elevations.

Unfortunately, this is just not true. Treating high cholesterol with herbs and supplements is a great idea, but one needs to know that there is a very specific group of nutrients needed to work together.

Cholesterol

Cholesterol is a very important part of your biochemistry. It is needed to make hormones, Vitamin D3, it is needed for bile salts to digest fats, it acts as an antioxidant, protecting us from cancer and aging, and our cell walls would just not work or have the proper structure to protect their internal environment from the exterior medium. It has a huge role in memory, brain function and even the 'feel good' hormone, serotonin and the list goes on. You cannot live without it.

High cholesterol levels have been re-defined over the past few years to be lower and lower, resulting on more people being put on statin drugs. Adverse side effects from long term use of statin drugs are becoming more and more apparent.

As a result of unhealthy eating habits practiced these days, the essential nutrients, B6, B12, folic acid and trimethylglycine are in low levels and hence the correction of the homocysteine cycle is what is needed. These are all in natural substances used to lower cholesterol.

Homocysteine is formed by the body as a naturally synthesized byproduct of methionine (a very important amino acid in your body) metabolism. Like cholesterol, homocysteine performs a necessary function in the body, after which, if the right cofactors are present, it will eventually convert to cysteine (and this is one of the amino acids needed to produce glutathione, which is very critical in your detoxifications pathways.) and other beneficial compounds such as ATP, (the energy molecule of the body) and S-adenosylmethionine (SAME), creatine, choline, part of your RNA and DNA messengers and epinephrine. These are all critical elements of your healthy biochemistry.

The main sites of metabolism are in the kidney and liver and good levels of folic acid are required to keep homocysteine low.

When left intact, it enters the bloodstream and begins attacking blood vessel walls, laying the foundation for heart disease, stroke and other cardiovascular diseases.

The clear message from new scientific findings is that there is no safe 'normal range' for homocysteine. While commercial laboratories state that normal homocysteine can range from 5 to 15 micromoles per liter of blood, epidemiological data reveal that homocysteine levels above 6.3 cause a steep, progressive risk of heart attack (the American Heart Association's journal *Circulation*, Nov. 15, 1995, 2825-30).

One study found each 3-unit increase in homocysteine equals a 35% increase in myocardial-infarction (heart-attack) risk (*American Journal of Epidemiology*, 1996, 143[9]:845-59).

There are over 130 studies which show that increased homocysteine is a cardio vascular disease factor.

Many enzymes or catalysts are involved in the complete metabolism of homocysteine. If any of these enzymes is defective or functions inefficiently, the body is less able to successfully process

homocysteine. Although this enzyme dysfunction may be due to a mutated or defective gene, more often this breakdown in metabolism is due to deficiencies of certain nutrients, particularly B-6, B-12 and folic acid.

When this function is disordered, whether due to genetic defect or nutrient deficiency, homocysteine accumulates and enters the bloodstream where it promotes oxidation of lipids, causes platelets to stick together, enhances the binding of lipoprotein (a) to fibrin and promotes free radical damage to the inside of arteries.

Factors which increase homocysteine:

Males affected more than females	Increases with age
Hypothyroidism	Smoking
Alcohol	Menopause
Kidney Failure	Drugs ie Birth Control Pill, L-Dopa, etc
Enzyme Defects	Unchilled Blood
Genetic Defects	

Some have suggested that the obvious solution to reducing homocysteine would be to restrict methionine intake by restricting foods such as meats that are rich in methionine. But methionine is a sulfur-containing amino acid that is involved in the synthesis of protein, important in the maintenance of cartilage, and needed for the formation of other important amino acids such as taurine and carnitine. Methionine is not at fault and therefore restricting it will not be a sound strategy. The problem happens when homocysteine cannot be converted.

The good news is that elevated homocysteine levels, whether due to nutrient deficiencies or defective genes, can easily be normalized in

virtually all cases, simply and inexpensively, using a combination of nutritional supplements. The most effective defense against homocysteine buildup is a combination of vitamins B-6 and B-12, folio acid and trimethylglycine (TMG). So you have a way to naturally lower cholesterol.

There are three biochemical pathways used by the body to reduce homocysteine.

- In one pathway TMG donates a methyl group which detoxifies homocysteine. In this reaction, TMG is reduced to DMG (dimethylglycine), that familiar-product sold as a supplement for its energizing effects.
- In the other routes, folic acid, B12 and B6 convert homocysteine into nontoxic substances.
- Some people cannot utilize one or another of these pathways. That is why a combination of all these nutrients is most effective for lowering homocysteine. In some people vitamin B may not be efficiently converted to its active co-enzyme form, pyridoxyl-5-phosphate. In that case supplementing with pyridoxyl-5-phosphate would be necessary.

Good health depends on nutrition and yet many so called medical experts insist nutrition has nothing to do with overall health!

Trimethylglycine

Trimethylglycine (aka TMG) is the biochemical term for betaine. TMG is able to donate methyl groups (a methyl group is one carbon molecule and three hydrogens. Very, very important to our chemistries) to biochemical events and in the case of homocysteine this leads to the increased production of S-adenosyl-methionine (SAM or sometimes it is written S_AMe) which is the bioactive form of the amino acid methionine...also a methyl donor. SAM has been used successfully to treat problems such as cirrhosis of the liver, depression, osteoarthritis and Fibromyalgia.

Methyl groups are thought to protect cellular DNA from mutation, a process which is also helped by good antioxidants. As people age, they often do not have enough available methyl groups to safeguard DNA. Abnormal methylation patterns are found in many people with cancer. Eating foods that contain methyl groups such as beets, green leafy vegetables and legumes is helpful, but these must be eaten in relatively large quantities several times a week. Therefore, dietary supplements such as TMG may often be necessary to provide the body with sufficient protective methyl groups.

Betaine comes from beet sugar and is extracted through a very complex process. The betaine HCL that is seen in digestive supports is the same thing and it is not a good idea to substitute it for TMG because it is very acidic and not fit for long term use.

There are essentially two ways to lower homocysteine levels. One, the most common, would be to add methyl groups to it to convert it to methionine or SAMe.

This is accomplished, as mentioned, through TMG (which as its name suggests, has three methyl groups on each glycine molecule – glycine is another amino acid. They are transferred to homocysteine, but need the help of folic acid, vitamin B12, and zinc.

Another methyl donor of importance is choline and this remethylation of homocysteine does NOT need co-factors. One hitch, though, is that this process is only active in the liver and kidneys; so to protect the whole body, in particular the brain one should be sure to take a complex with all factors present.

The second pathway to lower homocysteine involves converting it into cysteine (a very important amino acid), which then through a cascade of chemistry becomes glutathione. This pathway is dependent on vitamin B6 and the exact amount needed to lower homocysteine from person to person can vary greatly.

It is only the amino acid methionine which can create homocysteine and the amount of that in someone's diet, really depends on the individual's diet. One higher in red meat and chicken would be higher in methionine and so this person would need more B6 (and the other co-factors for that matter) to ensure the clearing of homocysteine.

Elevated homocysteine can also be caused by a genetic defect that blocks the trans-sulfuration pathway (the path which ultimately changes it to glutathione) by inducing a deficiency of the vitamin B6-dependent enzyme cystathionine-B-synthase. In this case, high doses of vitamin B6 are required to suppress excessive homocysteine accumulation. Since one would not want to take excessive doses of vitamin B6 (greater than 300 to 500 mg a day for a long time period), a homocysteine blood test can help determine whether you are taking enough vitamin B6 to keep homocysteine levels in a safe range.

There are some people who lack an enzyme to convert vitamin B6 into its biologically active form, pyridoxal-5-phosphate. In this case, if low-cost vitamin B6 supplements do not sufficiently lower homocysteine levels, then a high-cost pyridoxal-5-phosphate supplement may be required.

For many people, the daily intake of 500 mg of TMG, 800 mcg of folic acid, 1000 mcg of vitamin B12, 250 mg of choline, 250 mg of Inositol, 30 mg of zinc, and 100 mg of vitamin B6 will keep homocysteine levels in a safe range.

But the only way to really know is to have your blood tested to make sure your homocysteine levels are under 7. If homocysteine levels are too high, then up to 6 grams of TMG may be needed along with higher amounts of other remethylation cofactors. Some people with cystathionine-B synthase deficiencies will require 500 mg a day or more of vitamin B6 to reduce homocysteine to a safe level.

For the prevention of cardiovascular disease, you would want your homocysteine blood level to be under 7. For the prevention of aging,

some people have suggested that an even lower level is desirable, but more research needs to be done before any scientific conclusions can be reached.

A Life Extension article (July, 1997), sites these cases of people with problems in these pathways. “People with these disorders frequently die of cardiovascular disease before reaching adulthood. In one case history report, a 16-year-old Japanese girl was unable to walk with or without support, and had severe peripheral neuropathy, muscle weakness and convulsions. Her vascular system was on the verge of collapse. B6 or B12 did not help. Folic acid lowered homocysteine, but did not improve her symptoms. Two months after adding TMG to the regimen, her homocysteine level dropped and she was able to walk with support. Seventeen months later, she was free from convulsions and able to walk normally again.

This case history demonstrates the seesaw relationship between homocysteine and SAM. The girl’s SAM levels went from undetectable to near normal after the first two months of treatment while her homocysteine levels fell dramatically.

If these nutrients can overcome a genetic disorder, consider how powerful they can be in reducing the risks associated with elevated homocysteine in the general population. Some people who have been taking this homocysteine lowering nutrient combination for more than a decade reported many benefits including fewer colds, more energy, increased endurance and lower blood sugar levels.

Also from the Life Extension article – “The homocysteine theory of cardiovascular risk was first tested and published by Dr. Kilmer McCully in 1969, but, with everyone focusing on cholesterol at that time, his findings were ignored. Finally, almost 30 years later, the word is out on homocysteine. In addition to NBC Nightly News with Tom Brokaw, articles have been published in Newsweek, The Wall Street Journal, The Los Angeles Times, Prevention magazine and more.”

Homocysteine levels rise as people age. Therefore, any anti-aging program must take homocysteine level control into consideration. Lowering homocysteine has benefits beyond heart protection.

- When the blood supply to the heart is blocked, a heart attack results
- When blood to the brain is blocked, a stroke results.
- If the penile artery is occluded, impotence results.
- Blockages in the extremities results in intermittent claudication or pain in the affected extremity.

Homocysteine's relationship to heart disease may explain some things that cholesterol never could. These B vitamins and homocysteine are so interrelated that homocysteine levels could be used to assess vitamin status.

- This could explain the increase in heart disease which has occurred in women over the past two decades which coincides with the use of birth control pills. Birth control pills deplete vitamin B6 and raise homocysteine levels.
- Smoking, a known risk factor for heart disease, also depletes vitamin B6 and smokers generally have low levels of folio acid and vitamin B12...all needed for homocysteine metabolism. It is not surprising that the statistics linking smoking to heart disease are similar to those linking high homocysteine levels to heart disease.

Methylation/Homocysteine and Other Disease

The importance of the process of methylation to our health and functions cannot be over emphasized. For one, it is essential to DNA repair, which if not repaired will result in breaks and mutation. This in turn leads to accelerated aging because of larger amounts of 'half-baked' or even dangerous proteins being produced. In fact, in a journal *Medical Hypothesis* (1998, 51[3]:179-221), it was suggested

that aging, period, could be a result of cellular demethylation, or in other words, a slowing of 're-methylation' needed to maintain and repair DNA. Methylation is a key process in the liver with respect to its ability to detoxify our bodies. It is needed for the growth of new cells, nerve sheath production (myelination) and a whole host of other critical processes.

Homocysteine is best for interfering with the whole methylation pathway. High homocysteine speaks to us of poor methylation in a patient. Homocysteine may also be causing damage through oxidative stress.

What if someone were to tell you that there was a measurable substance in your body that is theoretically the most important indicator of the health and adaptability of your body's total biochemistry and your risk of degenerative diseases? Sound intriguing – that's what is being said about Homocysteine. Recent research is discovering that high levels of homocysteine can damage arteries, the brain and DNA. Elevated homocysteine has been proven to increase the formation of plaques on blood vessel walls leading to clogging and hardening of the arteries. David Wald and colleagues from the Department of Cardiology at Southampton General Hospital (England) published in the British Medical Journal their findings of a study conducted on 20,000 people. They concluded that there is strong evidence demonstrating a causal relationship between homocysteine and cardiovascular disease.

If you lower your homocysteine level you reduce your risk of developing cardiovascular disease. In addition, with regard to brain degeneration, studies have shown that lowering your Homocysteine levels will significantly lower your risk of getting Alzheimer's disease by at least half. It has also been shown that high levels of homocysteine causes DNA damage. Since DNA damage is a precursor to cancer, lowering your homocysteine level will reduce your risk of getting cancer. Cancers linked to high homocysteine

levels include breast, colon and leukaemia. Other diseases linked to high homocysteine levels include diabetes and Rheumatoid arthritis.

There are risk factors that predispose individuals to being vulnerable to high homocysteine levels, they include; genetics (One in ten people carries a genetic mutation that makes them more prone to higher homocysteine levels than others), family history heart disease, stroke, cancer, Alzheimer's disease, schizophrenia or diabetes, foliate intake of less than 900 mcg/day, increasing age, male sex, estrogen deficiency, excessive alcohol, coffee or tea intake, smoking, lack of exercise, hostility and repressed anger, inflammatory bowel diseases, H. pylori-generated ulcers, pregnancy, vegetarian or vegan diet, high fat diet with excessive red meat, high fat dairy intake and high salt intake.

Homocysteine is naturally produced in most of the body's cells. It is derived from Methionine which is an amino acid found in dietary protein. It aids in tissue and cell growth and insulin formation and can act like growth hormone. The body turns homocysteine into glutathione and SAME. Glutathione is the body's most important antioxidant while SAME (S-adenosylmethionine) is a very important "intelligent" nutrient for the brain and body. Your antioxidant IQ is a measure of the glutathione and SAME inside your cells.

If you have suboptimal amounts of B vitamins in your diet, homocysteine cannot be converted and the levels rise dangerously.

The method of lowering Homocysteine involves a molecular process called 'methylation'. Methylation simply means that molecules add or subtract methyl groups. Methylation processes are necessary for the body to maintain optimal chemical balance. High levels of Homocysteine can be reduced by consuming substances that will donate methyl groups. These donated methyl groups will turn toxic homocysteine into SAME, which, as stated before, is an important nutrient for the brain. Choline and TMG (or betaine) is excellent

methyl donors which help reduce high homocysteine. Choline is found in eggs and lecithin while TMG is found in sugar beets and other vegetables. In addition, three vitamins, B6, B12 and Folate are required to metabolize homocysteine.

Other Supplement support

Guggul

Guggul is the name given to the yellowish resin produced by the stem of the mukul myrrh (*Commiphora mukul*) tree found throughout India. It has been used in Ayurvedic medicine for centuries in the treatment of arthritis, obesity, and one of its prime uses was for 'medoroga'. Medoroga is basically an ancient diagnosis for what we know as atherosclerosis. It was effective for this problem because of its ability to lower serum cholesterol and triglycerides.

Guggul extract isolates contain safe plant steroid compounds known as guggulsterones, which have been shown to lower lipid levels in your blood. They actually lower serum triglycerides and cholesterol, as well as LDL VLDL cholesterols (the 'bad' cholesterols) and as bonus raises HDL cholesterol (the 'good' cholesterols).

Guggulsterones also act as antioxidants in that they keep LDL cholesterol from oxidizing, protecting you further from atherosclerosis. Guggul also decreases the 'stickiness' of platelets, which of course also lowers the risk of coronary artery disease and stroke. There was a study which actually found guggul extract similar and even slightly better than clobfibrate for lowering cholesterol levels.

There are no real side effects associated with guggul. In earlier times, when the crude oleoresin was used, side effects such as diarrhea, anorexia, abdominal pain and skin rash were reported. The modern extracts are much more purified and this is no longer the case.

Niacin

For some time, some practitioners have been using high amounts of niacin (Vitamin B3) (also called nicotinic acid) to lower cholesterol. The problem with this is that at the doses needed, about 3 grams per day, divided dosing, patients experience side effects of flushing, headache, stomach pains and even chronic liver damage, diabetic responses, gastritis or stomach inflammation, eye damage and even gout. The other common form of B3 – niacinamide (also called nicotinamide) – does not help lower cholesterol levels.

An acceptable variation on niacin called Inositol hexaniacinate has more recently been prescribed for cholesterol treatment without the unwanted effects of niacin. It is used at the 500 to 1,000 mg. taken three times per day. It is newer and fewer studies have been done, so if one takes it, make sure you have your cholesterol monitored to evaluate its effectiveness and have liver enzymes, uric acid and glucose levels checked just to be sure you are not one of the people prone to problems with B3 therapy.

Beta-Sitosterol

Guggul is a phytosterol or plant steroid. Not, like the harmful steroids of pharmaceutical fame, though. Another, Beta-sitosterol alone and with other plant sterols, lowers blood levels of cholesterol. This probably happens because beta-sitosterol blocks the absorption of cholesterol. Beta-sitosterol (and others such as campesterol, stigmasterol, etc.) are found in high levels in rice bran, wheat germ corn oils and soybeans.

Vitamin C

Vitamin C plays a very important role in lowering homocysteine. Vitamin C cannot be produced by humans but plays a very important role in almost all aspects of human life. It has among other things the unique ability to recycle the vitamins, thus acting as a force multiplier.

Garlic

Garlic roasted and eaten or added as a paste to garnish cooked food will be far more effective in the fight to lower cholesterol and triglycerides.