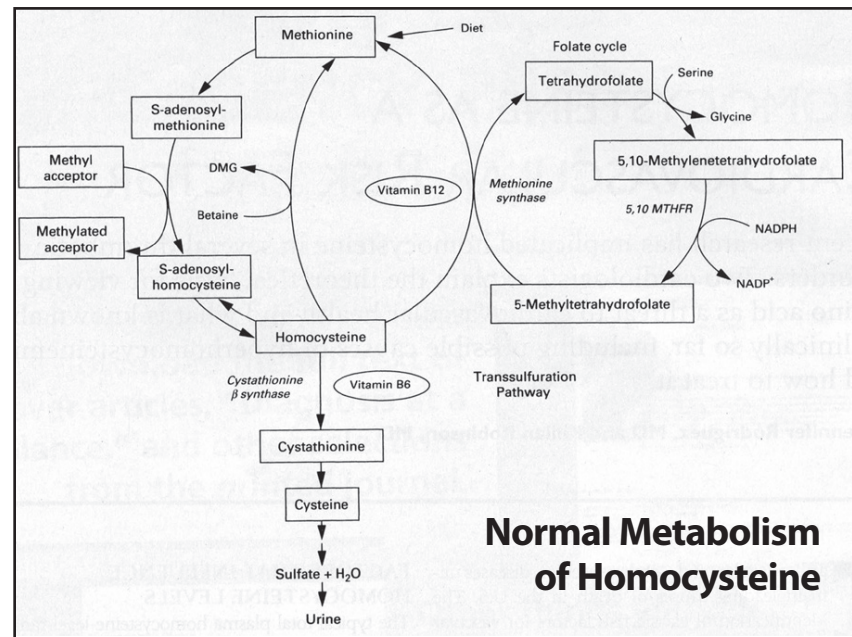


Besides faulty enzymes and genes, are there chemicals that cause faulty methionine conversion?

Yes, heavy metals. Mercury and lead are known to bind to these sulfur amino acids and interfere with the pathway. Mercury depletes B12 and may also interfere by causing a deficiency of this key methylator. The methylcobalamin form of B12 is responsible for remethylating folate so it can convert homocysteine back to methionine. However, too much emphasis on converting the pathway backwards does not allow the body to synthesize more cysteine if needed. Mercury toxicity creates a greater need for cysteine and glutathione. Chronic mercury inhalation from mercury fillings, with its great affinity to bind the sulfur-containing amino acids cysteine and methionine, can decrease the availability of these amino acids and affect the metabolism of both vitamin B12 and folate, making higher supplemental doses crucial. Cysteine is needed to synthesize glutathione, which helps the liver detoxify chemicals. High amounts of this antioxidant are used up to protect the body from heavy metals such as mercury. Glutathione prevents apoptosis, the dying of our cells due to excessive oxidative stress caused by heavy metals and chemicals, especially a problem in people who do not consume enough fruits and vegetables which contain antioxidants.¹³



Is methylation important?

Some of the toughest patients will not get effective lowering of homocysteine until choline is supplemented. Choline converts to betaine (see pathway) with the help of riboflavin and vitamin B2, and aids methylation in this step of the pathway. TMG (trimethylglycine) provides extra methyl groups. With the help of B2, betaine can convert back to glycine and aid the synthesis of creatine for muscle health. All of these necessary nutrients have been included in Homocysteine Supreme™, as well as zinc, which is a cofactor for enzymes in the pathway.¹³

The synergistic nutrients found in Homocysteine Supreme™ facilitate the homocysteine pathway, preventing toxic levels of

homocysteine from accumulating, and make it possible for a functioning pathway to provide necessary methyl and sulfur groups for a myriad of biochemical reactions, especially those needed for detoxification, immune system support, joint and cartilage repair, brain health and for reducing our risk of cardiovascular and other serious diseases.

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Homocysteine Supreme™

For the maintenance of healthy homocysteine levels



By Cristiana Paul, MS

THIS INFORMATION IS PROVIDED FOR THE USE OF PHYSICIANS AND OTHER LICENSED HEALTH CARE PRACTITIONERS ONLY. THIS INFORMATION IS INTENDED FOR PHYSICIANS AND OTHER LICENSED HEALTH CARE PROVIDERS TO USE AS A BASIS FOR DETERMINING WHETHER OR NOT TO RECOMMEND THESE PRODUCTS TO THEIR PATIENTS. THIS MEDICAL AND SCIENTIFIC INFORMATION IS NOT FOR USE BY CONSUMERS. THE DIETARY SUPPLEMENT PRODUCTS OFFERED BY DESIGNS FOR HEALTH ARE NOT INTENDED FOR USE BY CONSUMERS AS A MEANS TO CURE, TREAT, PREVENT, DIAGNOSE, OR MITIGATE ANY DISEASE OR OTHER MEDICAL CONDITION.

Why should a patient's homocysteine levels always be checked?

Excess homocysteine in the circulation can damage the lining of arterial walls, making them narrow and inelastic. Research suggests that a raised homocysteine level is an independent risk factor for hardening of the arteries, coronary heart disease, stroke, peripheral vascular disease and other conditions associated with abnormal blood clotting.^{1,2,19} Elevated homocysteine is also linked with a number of other serious medical conditions including depression, osteoporosis, Alzheimer's disease, multiple sclerosis, rheumatoid arthritis, spontaneous abortion, placental abruption, neural tube defects (spina bifida, cleft palate, etc), renal failure, and type II diabetes.^{9,11,16}

When homocysteine is elevated it reduces nitric oxide (NO) production, which can increase the risk of hypertension and erectile dysfunction. The synergistic nutrients included in Homocysteine Supreme™ facilitate the efficient metabolism of homocysteine, and prevent toxic levels of homocysteine from accumulating. Homocysteine Supreme™ allows the homocysteine pathway (which begins with methionine) to flow smoothly in any direction, producing its necessary and important end products, including the sulfur-containing amino acids taurine and cysteine and the neurotransmitters epinephrine, dopamine, and serotonin.¹³

What is homocysteine?

Homocysteine is produced by the demethylation of dietary methionine which comes from protein-containing foods. It is recycled back into methionine through a pathway that involves vitamin B12 in the form of methylcobalamin (which remethylates it) and folate. Homocysteine is simply an intermediate in a very important biochemical pathway. Plasma homocysteine can also travel another route which involves the passing of sulfur groups (transsulfuration). This is vitamin B6-dependent and results in the production of cysteine which can convert into glutathione, the most important antioxidant in the body.¹³

What causes homocysteine to become elevated?

Any roadblock in this pathway can cause homocysteine to elevate. When we intricately study the biochemistry of the homocysteine pathway we can see that it involves a series of conversions that require enzymes. Several nutrients, especially B vitamins, are needed for these conversions to occur.¹³ Stress can deplete B vitamins, as can many medications.

The Comprehensive Metabolic Profile (CMP) test offered by Designs for Health can pinpoint B vitamin deficiencies. It is also important to test the body's homocysteine levels. Performing both tests on women wishing to get pregnant could reduce the risk of neural tube defects and pregnancy complications. All patients with homocysteine levels above 7 are in need of intervention¹², with Homocysteine Supreme™ being an ideal recommendation. Patients with a family history of early heart attacks or depression are also prime candidates for such intervention.

Supplement Facts

Amount Per Serving	% Daily Value
Serving Size: 2 capsules Servings Per Container: 30	
Riboflavin (Vitamin B-2) (as Riboflavin-5-Phosphate)	50 mg 2940%
Vitamin B-6 (as Pyridoxine Hydrochloride and Pyridoxal-5-Phosphate)	50 mg 2500%
Folate (NatureFolate™ blend)	2400 mcg 600%
Vitamin B-12 (as Methylcobalamin)	1000 mcg 16670%
Zinc (TRAACS® Zinc Glycinate Chelate)	5 mg 35%
Trimethylglycine (TMG)	500 mg *
Choline	100 mg *
Serine	100 mg *
N-Acetyl-Cysteine (NAC)	100 mg *

*Daily Value not established.

Other Ingredients: Microcrystalline cellulose, vegetable stearate, silicon dioxide.



Homocysteine Level	Risk Level
0-6.9 micromol/L	Optimum (low risk)
7 - 9.9 micromol/L	Mild risk
10.- 12.9 micromol/L	Moderate Risk
13 - 20 micromol/L	High risk
Over 20 micromol/L	Very high risk

What are ideal homocysteine levels for patients?

Initially, levels between 8 and 15 micromol/L were considered ideal. Research suggests maintaining even tighter control as homocysteine levels above 6.9 micromol/L may be harmful for long-term health.¹² A rise in serum homocysteine of 5 micromol/L may increase cardiovascular risk by 20% to 30%. Homocysteine levels tend to rise with age; folate and B12 absorption decline in the elderly so they may require higher doses of these nutrients to lower their homocysteine levels effectively. Also, medications commonly taken by these individuals deplete folate, such as ibuprofen and other NSAIDs.

Homocysteine Supreme™ includes our proprietary NatureFolate™ blend of active isomer, naturally-occurring folates. Research shows that supplementing 2-7 mg of folates daily helps to reverse plaque and prevent stroke.^{12,18,19} Research also shows that doses above 1000 mcg of B12 get absorbed effectively even without intrinsic factor.¹⁵

How and how often should homocysteine levels be tested?

Patients with a personal or family history of coronary heart disease, or other CHD risk factors, or who have the MTHFR (methyltetrahydrofolate reductase) faulty gene should have homocysteine testing at least twice per year. Serum homocysteine can be ordered through any standard lab.

Testing for deficiencies of folate, B6 and B12 is very easy via bloodspot and/or urine collection. Designs for Health's Comprehensive Metabolic Profile (CMP) and Basic Metabolic Profile (BMP) tests will detect which of these are lacking. Serum or urinary methylmalonic acid (MMA) is the best marker of functional B12 status, while the formiminoglutamate (FIGLU) marker is best for folate. Kynurenine and quinolinic acid elevations show a deficiency of B6. Elevations of any of these markers on the CMP test may increase risk of homocysteinemia.¹³ Patients with hypothyroidism are at greater risk of hyperhomocysteinemia because hypothyroidism decreases hepatic levels of enzymes involved in the remethylation pathway of homocysteine.²⁰

How do we know that correcting these deficiencies will help longevity?

A meta-analysis of 12 randomized controlled trials suggested that supplementation with 0.5-5.7 mg folate per day could reduce elevated homocysteine levels by 25%, while adding 0.02-1 mg of vitamin B12 per day produced a further 7% reduction.¹⁰ In a study of 350 elderly people aged 65-75 years, folate supplements of 400-600mcg per day were needed to produce significant lowering of homocysteine levels compared to placebo. Due to reduced absorption in the elderly, it was estimated that a total intake of 926mcg per day was needed to avoid folate deficiency and lower cardiovascular risk. The addition of vitamin B12 is doubly important here as folate can mask early signs of vitamin B12 deficiency which might lead to subacute combined degeneration of the spinal cord.¹⁹

Have researchers done large-scale trials to assess whether interventions to lower homocysteine levels will reduce cardiovascular morbidity and mortality?

One analysis suggested that supplementation of B vitamins did not reduce the risk of cardiovascular events. This conclusion should not be considered valid because the subjects had previous cardiovascular events and the doses were not high enough for positive results considering the age of the subjects. There is adequate evidence that controlling homocysteine and adequately supplementing folate and B12 will improve overall health, reduce cardiovascular risk and increase longevity. Older women are also in need of higher doses of B vitamins. After menopause some women are less able to process homocysteine⁷, which may explain the higher risk of coronary heart disease in this group. Hormone replacement therapy, as well as oral contraceptives, deplete B vitamins. A survey in the US suggested that only 40 - 50% of people obtained enough folate from their diet to process homocysteine normally.

Why so much emphasis on converting homocysteine back to methionine?

The most common block in the homocysteine pathway is the conversion of cystathionine to cysteine, which requires vitamin B6 to activate the cystathionine beta-synthase enzyme, making B6 an important ingredient in Homocysteine Supreme™. Vitamin B6 is also required in the step that converts homocysteine into cystathionine.¹³

Serine, also included in the Homocysteine Supreme™ formulation, is needed along with vitamin B6 to help convert homocysteine into cystathionine. This part of the pathway synthesizes cysteine needed for glutathione synthesis, and taurine -which has multiple functions including preventing catabolism due to chronic stress and aiding insulin function; both of these nutrients are important for metabolic syndrome patients.

Due to the synergism of the ingredients, Homocysteine Supreme™ offers benefits no matter where the patient's block is in the pathway. By supplying folates and methycobalamin B12, this formula aids in the process of homocysteine being converted back into methionine in case the body is in need of converting methionine into SAME (S-adenosylmethionine), which is known to improve depression, synthesize neurotransmitters and support joint comfort, function and mobility in the spine, hips and knees. It is important to the joints because of its critical role in cartilage production. If SAME is supplemented in the absence of adequate B12, homocysteine levels may increase. Designs for Health supplies B vitamin cofactors in its SAME 200 mg capsules in order to prevent this.

Who should not take Homocysteine Supreme™?

Patients undergoing chemotherapy, radiation, or taking Methotrexate should not take high dose folate without consulting with their health care practitioner.