Homocysteine is a byproduct of normal protein metabolism. It is formed from the conversion of the amino acid methionine. Since high levels of homocysteine is not a good thing for our health, the body has a built-in mechanism to partially convert it back into methionine and other beneficial, non-toxic amino acids. If, however, this process is out of whack a bit, homocysteine builds up in bodily fluids and tissues, with serious ramifications. Luckily, there are some specific nutriceuticals that have been shown to effectively reduce homocysteine levels. This article will address the ramifications of high homocysteine, as well as the nutriceuticals that can be used for effective treatment.

Ramifications of High Homocysteine
Cardiovascular Disease

The most well-known ramification of high homocysteine levels is cardiovascular disease. In fact, moderately high levels of homocysteine can raise heart disease risk independent of other known risk factors such as elevated serum cholesterol and hypertension. In a study comparing 750 people with clogged arteries and 800 whose blood vessels were healthy, those with homocysteine levels in the top 20 percent of the study had a vascular disease risk twice as high as the other volunteers. Homocysteine appears to affect a significant number of individuals (about 21 percent of the population has elevated homocysteine levels) who don’t have other standard risk factors. In addition, high homocysteine levels have also been linked to a common type of hypertension in the elderly, called ISH (isolated systolic hypertension). ISH (20 percent of people over 60 have ISH) also increases the risk of stroke and heart attacks. It is suspected that lowering homocysteine levels may help prevent hardening of the arteries, ISH, and ultimately, strokes and heart attacks.¹ ²

Depression

The American Journal of Psychiatry³ published a study examining 3,884 elderly people for depressive symptoms, homocysteine blood levels, as well as folate and vitamin B12 levels. Results showed that high homocysteine levels were related to depressive disorders. Vitamin B12 deficiency and folate deficiency (to a lesser extent) were also related. Additional research also found similar results in late-life depression.⁴ This was consistent with a review in the American Journal of Psychiatry⁵ which hypothesized that high levels of homocysteine may cause depression of mood. The mechanism of action is that homocysteine may alter neurotransmitters.⁶⁷
Fibromyalgia
A study on 12 women who had both fibromyalgia and chronic fatigue syndrome were found to have increased homocysteine levels in the cerebrospinal fluid. This study found a significant positive correlation between the increased homocysteine levels and fatigueability, and that the levels of vitamin B12 in cerebrospinal fluid also correlated significantly with fatigueability. Since vitamin B12 deficiency is associated with increased homocysteine levels, the researchers observed that the low level of vitamin B12 found in their patients probably contributed to the increased homocysteine levels.

Alzheimer’s Disease and Vascular Dementia
High homocysteine has been causatively linked to Alzheimer’s disease and vascular dementia in old age. A close examination of research has verified that individuals with Alzheimer’s disease and vascular dementia do indeed have higher homocysteine levels than controls; however, a causal relationship between high-homocysteine level and risk of developing dementia is not clearly supported. More prospective studies and randomized controlled trials are required to test the therapeutic benefits of lowering homocysteine levels in these disease states. Meanwhile, it seems logical to take measures to lower homocysteine in people with Alzheimer’s disease and vascular dementia.

Eye Health
Higher plasma total homocysteine concentration was observed in diabetic individuals with retinopathy than in those without retinopathy. In addition, elevated serum homocysteine along with deficiencies in folate and vitamin B12 were found to be associated with the incidence of deficiencies predicted increased risk of incident age-related macular degeneration.

Other Homocysteine-related Disorders
Elevated homocysteine levels are also implicated in the development of venous thromboembolic disease (i.e., blood clots), neural tube defects and early pregnancy loss, and possibly chronic renal failure and preeclampsia (high blood pressure and protein in the urine during pregnancy). In addition, two studies have demonstrated that increased homocysteine levels significantly raise the risk of both hip fracture and other broken bones resulting from osteoporosis.

Nutraceuticals for Treatment
The most widely studies nutraceuticals for reducing homocysteine levels are betaine anhydrous, folic acid, vitamin B12 and B6. Following is a summary of the homocysteine-related research on these nutraceuticals.

Betaine Anhydrous
Betaine anhydrous (aka, trimethylglycine or TMG, not to be confused with betaine hydrochloride) is a methyl derivative of the amino acid glycine that occurs naturally in the body, and is found in foods such as beets, spinach, whole grains, liver, eggs and seafood. Supplementation with betaine has shown significant reductions in homocysteine levels. A daily dose of 6 g of reduced homocysteine by 15 percent, although significant reductions were also seen at a dose of 1.5 g daily. Since a reduction in fasting homocysteine by 5μmol/L is associated with a 20-30 percent reduction in cardiovascular disease, a 15 percent reduction in homocysteine would translate to a 1.5 μmol/L decrease, or a 6-9 percent reduction in cardiovascular disease. In addition, research has also demonstrated that betaine supplementation has effectively lowered homocysteine levels in patients with end-stage renal failure. This is important since high homocysteine levels is a complication in 80 percent of end-stage renal failure patients and may contribute to the progression of atherosclerosis among these patients.

Folic Acid, Vitamins B12 and B6
A substantial body of scientific evidence suggests that generous intakes of folic acid can help lower homocysteine levels. Vitamin B12 has been shown to have additive benefit, and to a lesser extent vitamin B6. To ascertain the lowest dose of folic acid associated with the maximum reduction in homocysteine concentrations and to determine the additional relevance of vitamins B12 and B6, the Homocysteine Lowering Trialists’ Collaboration conducted a meta-analysis. The results were that proportional reductions in plasma homocysteine concentrations with folic acid occurred when homocysteine was higher and when folate (folic acid) concentrations were lower before starting therapy. Folic acid reduced homocysteine levels by 13-25 percent, with daily doses of 200-800 mcg and as high as 5 mg. Vitamin B12 (500 mcg/day) offered an additional 7 percent reduction in homocysteine levels, but there was a lack of significant effect with an average daily dose of 16.5 mg vitamin B6. However, other studies have found that taking pyridoxine supplements in combination with folic acid (and sometimes B12) was effective for lowering homocysteine levels.

A 2004 meta-analysis examining the effectiveness of folic acid in the treatment of depression concluded that the “evidence suggests folate may have a potential role as a supplement to other treatment for depression.” Additional research also showed that supplementation led to a statistically significant improvement in depressive symptoms. Likewise, patients with celiac disease who were treated with 500 mcg vitamin B12, 2 mg vitamin B6, and 800 mcg folic acid for six months experienced a drop in homocysteine levels, and statistically significant improvements in well-being, notably anxiety and depressed mood. Furthermore, folic acid together with conventional antidepressants was found to improve treatment response.

Conclusion
High homocysteine levels are associated with cardiovascular disease, depression, fibromyalgia, Alzheimer’s disease and vascular dementia, diabetic retinopathy, age-related macular degeneration and other homocysteine-related disorders. The use of betaine anhydrous, folic acid, vitamin B12 and B6 may help lower homocysteine levels, and in some instances have a mitigating effect on these disease states.

References:
2. Bestrom AG, Silbershatz H, Rosenberg IH, et al. Nonfasting plasma total homocysteine levels and all-cause and cardiovascular disease mortality in elderly