



## Your Monthly Update

*Dear Colleague*

Welcome to the April 2013 newsletter from Pure Bio Ltd.

### **Did you know:**

Research in Sweden has shown that supplementing with CoQ10 and selenium halves the risk of heart attack in those over 70 years of age (*Int J Cardiol, 2012; 10.1016/j.ijcard.2012.04.156*)

Don't forget our website on [www.purebio.co.uk](http://www.purebio.co.uk). We always welcome feedback and suggestions.

## Elevated Homocysteine

Protocol Summary

Ranking	Nutritional Supplements	Botanical Medicine
Primary	Vitamin B6 Folic acid Vitamin B12	
Secondary	Betaine (Trimethylglycine) Lecithin (Phosphatidyl choline) Vitamin B2 (riboflavin)	
Other		

**Primary** – Reliable and relatively consistent scientific data showing a substantial health benefit.

**Secondary** – Contradictory, insufficient, or preliminary studies suggesting a health benefit or minimal health benefit.

**Other** – An herb is primarily supported by traditional use, or the herb or supplement has little scientific support and/or minimal health benefit.

## Introduction

Homocysteine is an amino acid that cannot be synthesized by the human body. It is synthesized from the essential amino acid called methionine in the body. An essential amino acid means that it is indispensable for life. Methionine must be supplied in the diet. High levels of methionine can be found in sesame seeds, brazil nuts, fish, meats (particularly red meat) and some other plant seeds. Most fruits and vegetables contain very little of it. Most legumes are also low in methionine.

Although at first not generally accepted, epidemiologic trials conducted over the past 25 years have provided ample support for the association of mild hyperhomocysteinaemia (elevated levels of homocysteine) with an elevated risk of cardiovascular disease.

High homocysteine is associated with low levels of vitamin B6, B12, and folate and renal disease.

## Causes

- Homocysteine is chemically transformed into methionine and cysteine (similar amino acids) with the help of folic acid, vitamin B12, and vitamin B6. This transformation utilizes a set of mediator molecules (called enzymes) and happens via a delicate sequence of specific steps.
- Therefore, insufficient amounts of these vitamins in the body can hamper the natural breakdown of homocysteine. In addition, if there are any related enzymatic, the breakdown is also hampered. This will invariably lead to homocysteine accumulating in the blood because its breakdown is slow and inadequate.
- Homocysteine levels in the blood may be elevated due to genetic causes. Homocystinuria, is caused by an enzymatic deficiency in the complicated homocysteine breakdown pathway. This leads to severely elevated levels of homocysteine. This rare condition is also associated with developmental delay, osteoporosis, visual abnormalities, formation of blood clots, and advanced atherosclerosis. This condition is generally diagnosed in childhood.
- Milder genetic variations are more common causes of elevated homocysteine levels. In these conditions, the enzymes malfunction and are less efficient because of minor abnormality in their structure. They also lead to elevation of homocysteine levels by slowing down its breakdown.
- The other more common (5%-7% of the population) and less severe type of elevated homocysteine level may be caused by nutritional deficiencies in folate, vitamin B6 and vitamin B12, chronic (long-term) kidney disease, and cigarette smoking.

## Signs and Symptoms

Elevated homocysteine levels in the body do not cause any symptoms.

- Elevated homocysteine levels affect the interior lining of blood vessels in the body, increasing the risk of atherosclerosis or narrowing of blood vessels. This can result in early heart attack and stroke.

- There is a relationship between the levels of homocysteine in the body and the size of the carotid arteries that supply the brain with blood; the higher the level of homocysteine, the narrower or more stenosed the carotid artery.
- The risk of deep vein thrombosis and pulmonary embolism may also be linked to elevated homocysteine levels in the body.
- There may be a relationship between elevated homocysteine levels and broken bones, especially in the elderly.
- Alzheimer's disease and other types of dementia may be more frequently seen in patients with increased homocysteine in the blood.
- In pregnancy, homocysteine levels tend to decrease. Elevated homocysteine levels may be associated with some foetal abnormalities and with potential blood vessel problems in the placenta, causing abruption. There may also be an association with pre-eclampsia.

## **Lifestyle Modification**

According to a recent study, both cigarette smoking and coffee consumption were associated with increased homocysteine levels. These findings are consistent with studies that have found both smoking and caffeine consumption to be associated with an increased risk of both cardiovascular disease and osteoporosis.

In one study, a diverse group of people participated in a week-long program that included a strict vegan diet, stress management and spirituality enhancement sessions, group support, and exclusion of tobacco, alcohol, and caffeine. B vitamin supplements known to reduce blood homocysteine levels were not provided. After only one week in the program, the average homocysteine level fell 13%.

## **Dietary Modification**

High-risk patients with elevated homocysteine levels should increase their intake of B-vitamins in their diet. These vitamins can be found in a wide variety of fruits, green, leafy vegetables, as well as grain products fortified with folic acid.

A study of men with heart disease demonstrated that consumption of whole-grain and legume powder at breakfast, instead of their usual breakfast cereal, resulted in a significant reduction in homocysteine levels.

Since homocysteine is produced from methionine, intake of large amounts of methionine will tend to increase homocysteine levels. (In fact, ingestion of supplemental methionine is used experimentally as a way to increase homocysteine levels). Foods high in methionine include meat, poultry, fish, shellfish and egg whites.

A controlled trial showed that eating a diet high in fruits and vegetables containing folic acid, beta-carotene and vitamin C effectively lowered homocysteine levels. Healthy people were assigned to either a diet containing a pound of fruits and vegetables per day, or to a diet containing three and a half ounces of fruits and vegetables per day. After four weeks, those eating the higher amount of fruits and vegetables had an 11% lower homocysteine level compared with those eating the lower amount of fruits and vegetables.

## Nutritional Supplement Treatment Options

**Folic Acid, Vitamin B6, and Vitamin B12 - 400 to 1,000 mcg of folic acid daily, 10 to 50 mg of vitamin B6 daily, and 50 to 300 mcg of vitamin B12 daily.** Vitamin B6, folic acid, and vitamin B12 all play a role in converting homocysteine to other substances within the body. By so doing, they consistently lower homocysteine levels in research trials, a finding that is now well accepted. Several studies have used 400–1,000 mcg of folic acid per day, 10–50 mg of vitamin B6 per day, and 50–300 mcg of vitamin B12 per day.

Of these three vitamins, folic acid supplementation lowers homocysteine levels the most for the average person. It also effectively lowers homocysteine in people on kidney dialysis. In 1996, the US FDA required that all enriched flour, rice, pasta, cornmeal, and other grain products contain 140 mcg of folic acid per 3½ ounces. This level of fortification has led to a measurable decrease in homocysteine levels in the USA. However, even higher levels of food fortification with folic acid have been reported to be more effective in lowering homocysteine, suggesting that the FDA-mandated supplementation is inadequate to optimally protect people against high homocysteine levels. Therefore, people wishing to lower their homocysteine levels should continue to take folic acid supplements despite the FDA-mandated fortification program.

Elevated blood levels of homocysteine have been linked to risk of stroke in most studies. Supplementation with folic acid, vitamin B6, and vitamin B12 generally lowers homocysteine levels in humans. In a pooled analysis (meta-analysis) of eight randomized trials, folic acid supplementation in varying amounts (usually 0.5 mg to 5 mg per day) reduced stroke risk by 18%.

In another double-blind study, daily supplementation with folic acid (2 mg), vitamin B6 (25 mg), and vitamin B12 (400 mcg) for three months improved symptoms of schizophrenia compared with a placebo. All of the participants in this study had elevated blood levels of homocysteine. Based on this study, it would seem reasonable to measure homocysteine levels in people with schizophrenia and, if they are elevated, to supplement with folic acid, vitamin B6, and vitamin B12.

**Betaine (Trimethylglycine)- 1.5 to 6 grams daily.** Betaine (trimethylglycine) (6 grams per day) and choline (2 grams per day) have each been shown to lower homocysteine levels. Choline at a dose of 2.6 grams per day (provided as 34 grams per day of soy lecithin) has also been shown to lower homocysteine levels in a double-blind trial<sup>9</sup> More recently, 1.5 grams of betaine per day, an amount similar to that in a typical diet, also has been found to lower homocysteine levels. The results of this study point to the potential benefit of increasing one's intake of foods rich in betaine (such as whole wheat, spinach, beetroot, and other plant foods).

**Lecithin (Phosphatidyl Choline) - 2 grams daily choline or 34 grams daily lecithin.** As above.

**Vitamin B2 - 1.6 mg daily.** Vitamin B2 (riboflavin) supplementation (1.6 mg per day) has been shown to lower homocysteine levels by 22 to 40% in a subset of the

population that has a certain genetic variant of an enzyme involved in folic acid metabolism (the 677Cà T polymorphism for the methylenetetrahydrofolate reductase gene). Approximately 15 to 20% of the population carries this gene and could benefit from taking riboflavin. Since genetic testing is expensive and not readily available, it would seem reasonable for all people trying to lower their homocysteine levels to include riboflavin in their regimen of B vitamin supplementation.

**Vitamin B6 and Folic acid** - taken under the supervision of a qualified practitioner. The relationship between folate status and the risk of miscarriage is also somewhat unclear. In some studies, women who have had habitual miscarriages were found to have elevated levels of homocysteine. In a preliminary study, 22 women with recurrent miscarriages who had elevated levels of homocysteine were treated with 15 mg per day of folic acid and 750 mg per day of vitamin B6, prior to and throughout their next pregnancy. This treatment reduced homocysteine levels to normal and was associated with 20 successful pregnancies. It is not known whether supplementing with these vitamins would help prevent miscarriages in women with normal homocysteine levels. As the amounts of folic acid and vitamin B6 used in this study were extremely large and potentially toxic, this treatment should be used only with the supervision of a doctor.

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