

VITAMINS / SUPPLEMENTS

Homocysteine

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In the last few decades our knowledge about the causes of heart disease, our nation's number-one killer, has increased dramatically. We know that the level of cholesterol, as well as the types and ratios, can affect cardiac disease risk factors. Researchers have discovered that genetics, diet, exercise and stress can contribute in either positive or negative ways to a person's risk factors. We have also been frustrated when people with theoretically low risk factors, such as moderate or low stress and cholesterol under 200, suffer heart attacks and strokes. With the homocysteine theory of heart disease, we now have a likely explanation for some of these "idiopathic" cases and another important piece of the puzzle that determines a patient's cardiovascular status.

History

Last year Kilmer McCully, MD, published a book called The Homocysteine Revolution. In his book he describes the link between homocysteine and a variety of diseases, the most important of which is heart disease. Dr. McCully first noticed a possible connection almost 30 years ago while studying homocystinuria, a hereditary disease which is the second-most-common error of inborn amino acid metabolism. This disease causes premature strokes and heart attacks by initiating and accelerating the atherosclerotic process. Dr. McCully theorized and later helped prove that blood levels of homocysteine not previously considered pathologic may be high enough to damage a person's cardiovascular system over time and, thus, increase the risk factor for developing atherosclerosis. At least five studies are currently underway to determine if lowering homocysteine will reverse the effects of previously elevated levels. In the meantime, given the ease and safety of lowering homocysteine, most experts recommend that patients with elevated levels begin a program to lower them now.

Homocysteine Biochemistry

Homocysteine is an intermediate amino acid utilized by our body for protein synthesis. It comes from the essential acid methionine. When methionine is activated, it provides methyl groups for many compounds, including betaine, choline, creatine, epinephrine, and melatonin. When methionine loses its methyl groups to form these various substances, homocysteine is formed. Homocysteine can then be metabolized in two ways (this will be discussed in the Nutrition Connection section).

The Heart Disease Connection

- 1. Elevated levels of homocysteine can lead to an increase in platelet stickiness, which then leads to the formation of arterial and venous thromboses.
- 2. Elevated homocysteine acts as a pro-oxidant. Cholesterol does not damage arteries until it is oxidized. Homocysteine can oxidize cholesterol, thus forming dangerous cholesterol oxides.
- 3. Elevated homocysteine leads to scarring on the inner lining of arteries. This scarring injures endothelial cells, which produce a substance called endothelial-derived relaxing factor (EDRF). EDRF keeps vessel walls loose and blocks plaque formation by preventing

substances like platelets and cholesterol oxides from adhering to artery walls.

Laboratory Data

Not every laboratory tests for homocysteine, although the number is increasing. Homocysteine levels are measured in micromoles per deciliter. The normal range is 4 to 17. Males with 15.8 or higher triple their risk of cardiovascular disease. At this time, optimal levels appear to be less than 12. It should be noted that some patients who take the test may not have high blood levels of homocysteine after fasting; however, when given a methionine challenge, hyperhomocysteinemia develops.

A Nutrition Connection

Folic acid, vitamin B12, and vitamin B6 are the key micronutrients involved in homocysteine metabolism. The two ways homocysteine is broken down are:

- 1. Methylation. Folic acid and vitamin B12 facilitate the donation and transfer of their methyl groups to homocysteine to reform methionine. The majority of homocysteine is metabolized this way.
- 2. Transulfuration. Vitamin B6 helps convert homocysteine to cysteine. It is also the treatment of choice (along with folic acid) for people who develop high levels of homocysteine following a methionine challenge test.

Recommendations

- 1. All patients (males age 40, females age 50) with a family history of cardiovascular disease, or those who already have cardiovascular disease, should have their homocysteine levels measured.
- 2. High-risk patients who take a homocysteine test should also take the methionine challenge (this eliminates false negatives).
- 3. All patients should continue to follow a plant-based diet rich in fruits and vegetables that is low in fat, cholesterol and total calories.
- 4. All patients should continue to follow a regular exercise program.
- 5. All patients should continue to monitor stress levels.
- 6. All patients should regularly monitor their blood pressure.
- 7. All patients should make sure they are getting enough B vitamins, including 50 mg of vitamin B6, 100 mcg of vitamin B12, and 400 mcg of folic acid per day. Good multivitamins (not the one-pill-a-day type) will usually provide adequate amounts of these nutrients.
- 8. Patients with elevated fasting homocysteine should take at least 650 mcg of folic acid and 400 mcg of B12 daily.
- 9. Patients with elevated homocysteine following the methionine challenge should take at least 100 mg of B6 and 5000 mcg of folic acid daily.
- 10. Nutritional dosing will vary and co-management with a cardiologist is strongly recommended.

Resources

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