

ELEVATED HOMOCYSTEINE-IS IT A CARDIOVASCULAR RISK FACTOR OR JUST ANOTHER HYPE?

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 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 hyperhomocysteinemia with an elevated risk of cardiovascular disease. The independent risk of cardiovascular events conferred by mild elevated serum homocysteine levels and the association of elevated levels with a deficiency of folic acid and vitamin B12 was thought to be a unique target for a preventative approach. In the Women's Antioxidant and Folic Acid Cardiovascular study, it was shown that supplemental folic acid and B vitamins do not lower the risk for important vascular events even though they lower homocysteine levels. The Vitamin Intervention for Stroke Prevention showed that although there was a dose dependant reduction in homocysteine levels, there was no reduction in vascular events. In the Norwegian Vitamin Trial (NORVIT) showed that there was no significant effect of folic acid and B12 on the risk of recurrent heart attacks or sudden death from coronary artery disease. There was, however, a trend toward more heart attacks. The HOPE-2 was a prevention trial that showed that treatment consisting of vitamin B12, vitamin B6, and folic acid for 5 years was associated with a reduction in homocysteine levels. Once again, there was no reduction in heart attack, stroke, or death from cardiovascular causes.

Maybe the answer lies in why patients with elevated homocysteine are at risk for CVD. There has never been a definite, accepted reason explaining the CVD risk seen in patients with high homocysteine. Is homocysteine the atherogenic culprit or is it simply a marker of some other pathologic process? It has been proposed that homocysteine is simply indicative of impaired renal function, a major CVD risk factor, and perhaps treatment should be directed at the kidney and not the homocysteine per se.

The truth is we really are not as smart as we think we are about most cardiovascular risk factors and so far have failed to discover others. It is speculative at best to predict what therapeutic manipulation of a given risk factor will do until it is subjected to properly designed, prospective, blinded outcome trials. It took many years before homocysteine was accepted as a risk factor and it took a decade of excellent clinical trials to prove that treating it with B-vitamin and folic acid is no longer justified. As usual, most of the previous data was from studies of men, but now we also have the answer in women. Therefore, if B-vitamin and folic acid therapy is null, screening patients

with expensive homocysteine assays and following the levels over time is no longer justified. Likewise, the monies spent on vitamin therapy can be directed at better-proven therapies, including balanced diets to provide these supplements.