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Editor's Correspondence

Multivitamin Supplements Are Effective and Inexpensive Agents to Lower Homocysteine Levels

Omland et al¹ validate once more the 30-year-old theory regarding the direct association between serum homocysteine levels and cardiovascular diseases and death. The authors suggest that there is merit in "stratifying patients into groups that are more or less likely to benefit from homocysteine-lowering therapy" based on serum homocysteine levels.

Such "therapy" effectively consists of recommending a multivitamin-mineral supplement with somewhat higher-than-daily-value amounts of several of the B vitamins (pyridoxine hydrochloride [B6], cyanocobalamin [B12], and folic acid). Therapy with, for example, 25 mg of B6, 100 µg of B12, and 400 µg of folic acid is simply obtained in a high "potency" (no-iron) multivitamin that can be bought in the United States for as little as \$0.10 a day. Such supplements usually also contain several other nutrients important in homocysteine metabolism (eg, zinc, which is a factor in the betaine-homocysteine-lowering pathway).

Since none of the methods in homocysteine therapy involve drugs but simply micronutrients that are effective and, especially in combination, benign at much higher-than-daily-value levels, it is time to recommend an over-the-counter multivitamin to anyone at risk for cardiovascular conditions. My guess, based on NHANES III² and other studies³ is that about half of the US readership already takes a multivitamin, and it is time to evaluate and recommend proper supplementation to all those at risk.

In addition to the aforementioned 3 vitamins, the authors do not mention homocysteine lowering with betaine, which is the only pathway unimpeded by known genetic enzyme dysfunctions. Betaine is a methylator found in beets, spinach, whole grains,⁴ and in several other foods, and it is cheaply produced industrially from beet molasses. In doses of several grams it also seems harmless (common doses for hyperhomocysteinuria therapy are 6 to as high as 20 g/d).

The authors are right that there are no "conclusive" studies that demonstrate a beneficial effect of lowering homocysteine levels (and there may be no such data for decades). However, it is certain that a good multivitamin will lower serum homocysteine levels in everyone, and it should in fact move most in the highest quintile to the lowest quintile. There

are hundreds of studies suggesting that such over-the-counter multivitamin therapy is both cheap and safe and also carries probable benefits, especially in very high-risk patients like those in the group studied.

From a patient or consumer point of view (for both convenience and low cost), a no-iron, over-the-counter multivitamin with daily-value amounts or higher of 19 nutrients can be purchased for \$0.10 to \$0.20 per day, while most single-nutrient supplements retail for about half as much. The no-iron multivitamin with the aforementioned amounts of B vitamins is sold in 180-capsule containers without childproof caps, which gives a good indication of the very low total toxicity of homocysteine-lowering therapy by means of such common nutritional supplements.

Eddie Vos, MEng
Sutton, Quebec

1. Omland T, Samuelsson A, Herlitz J, et al. Serum homocysteine concentration as an indicator of survival in patients with acute coronary syndromes. *Arch Intern Med.* 2000;160:1834-1840. [ABSTRACT](#) | [FULL TEXT](#) | [PDF](#) | [MEDLINE](#)
2. Balluz LS, Kieszak SM, Philen RM, Mulinare J. Vitamin and mineral supplement use in the United States: results from the third National Health and Nutrition Examination Survey. *Arch Fam Med.* 2000;9:258-262. [ABSTRACT](#) | [FULL TEXT](#) | [PDF](#) | [MEDLINE](#)
3. Frank E, Bendich A, Denniston M. Use of vitamin-mineral supplements by female physicians in the United States. *Am J Clin Nutr.* 2000;72:969-975. [MEDLINE](#)
4. Vos E. Whole grains and coronary heart disease [letter]. *Am J Clin Nutr.* 2000;71:1009. [MEDLINE](#)

In reply

We thank Mr Vos for his interest in our manuscript. In his comments, Mr Vos argues that "it is time to recommend an over-the-counter multivitamin to anyone at risk for cardiovascular conditions." We are unconvinced that existing data justify a general recommendation of this kind. Indeed, our own data suggest that in patients with unstable coronary syndromes, only a homocysteine level greater than the upper normal level is associated with increased risk of premature death.¹

Although a multivitamin tablet containing 0.4 mg of folic acid is likely to decrease circulating homocysteine levels in most subjects, the effect of homocysteine-lowering therapies on cardiovascular morbidity and mortality remains unproven. However, several large-scale clinical trials are under

way to test the hypothesis that homocysteine-lowering therapy will reduce cardiovascular morbidity and mortality. The results of these trials will probably be available, not in "decades," as stated by Mr Vos, but within the next 2 to 4 years. Until clinical trial data are available, we would consider prescribing homocysteine-lowering therapy to patients with high homocysteine levels and evidence or a family history of early-onset vascular disease, but we do not recommend its use in subjects with unknown or low homocysteine levels.

Torbjørn Omland, MD, PhD
Marianne Hartford, MD, PhD
Kenneth Caidahl, MD, PhD
Gothenburg, Sweden

1. Omland T, Samuelsson A, Hartford M, et al. Serum homocysteine concentration as an indicator of survival in patients with acute coronary syndromes. *Arch Intern Med.* 2000;160:1834-1840. [ABSTRACT](#) | [FULL TEXT](#) | [PDF](#) | [MEDLINE](#)

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