Clarifying the evidence: vitamin E, vitamin A, and folate

After reading the article “Health benefits of selected vitamins,” we would like to clarify the evidence regarding the effect of supplementation with vitamin E, vitamin A, and folate on cardiovascular disease (CVD) and mortality. The theory that antioxidant vitamins prevent CVD is well known but not supported by higher-level evidence (randomized controlled trials, systematic reviews, and meta-analyses).

As possible evidence of benefit, the authors point to the Cambridge trial, in which patients taking 400 to 800 IU of vitamin E had a significant reduction in non-fatal myocardial infarction. It did not, however, show a reduction in cardiovascular death as the authors suggest, but rather a non-significant increase in cardiovascular death and all-cause mortality. As well, these patients had proven coronary artery stenosis, and the authors previously acknowledged that clinical trials had not demonstrated benefit in patients at increased risk. More to the point, a number of randomized controlled trials and meta-analyses, including secondary- and primary-prevention patients with and without risk factors, have failed to show benefit of vitamin E on CVD. In fact, a recent meta-analysis demonstrated that doses of ≥400 IU of vitamin E are associated with a significant increase in all-cause mortality (number needed to harm [NNH] 257, confidence interval [CI] 136-3334). Unless future evidence suggests benefit, patients should be advised that vitamin E does not prevent CVD and is potentially harmful in high doses (≥400 IU).

In Table 1, the authors indicate that “possible health benefits” of vitamin A include “General health, including immunity” and then in the text indicate that caution is “recommended because of some evidence that high intake of carotenoids might be harmful to some groups, such as smokers.” The evidence indicates, however, that all-cause mortality is increased not only in smokers but also in primary- and secondary-prevention patients in a variety of populations (NNH 326, CI 140-∞).

The observed link between increased homocysteine levels and better cardiac outcomes has led to the hypothesis that, by reducing the surrogate marker of homocysteine through folate and B₁₂ supplementation, cardiac outcomes will be improved. In the high-risk population of patients who have had percutaneous coronary intervention, one trial has shown benefit while another has demonstrated harm from folate supplementation. Secondary prevention trials of folate supplementation used by stroke patients and stable coronary artery disease patients have failed to show benefit. At present, the assumption that “folic acid supplementation greatly affects homocysteine levels, and hence, coronary artery disease” is an exaggeration beyond the available evidence.

There are examples throughout medicine where theory, extrapolation of effects through surrogate markers, and weaker levels of evidence have led to harmful consequences for our patients. We should focus on proven preventive therapies, such as blood pressure control, before advocating potentially harmful therapies.

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References

Sexual consequences of prostate cancer treatment

Your July 2005 issue seems mislabelled. There are indeed sexual consequences of advanced and aggressive prostate cancer, but the tragedy is that the largest part of the epidemic of male sexual depredation is a result of treatment, not disease.

Your issue would better be titled “Severe Sexual Consequences of Aggressive Treatment of Prostate Cancer.”

Offering editorial comment1 from a urologist is like inviting a logger to discuss the preservation of old-growth forests. The surgeon advises family physicians to explain to patients that they “might experience changes in ejaculation.”

Might? What truthful family physicians will tell their patients is, “This means the end of sex as you know it for almost all men treated. And by the way, as many as four in 10 of you will end up wearing a diaper at least some of the time.”

Then, truthful family physicians will make sure their patients understand that aggressive screening and treatment of prostate cancer might, at best, prolong their lives a few months. (See Tom Pickles’s review of the lack of proven benefit with current therapies.)2

Surely avoiding prostate-specific antigen screening in asymptomatic patients and restricting surgical and radiation interventions to clinically obvious cancers is the plan family physicians providing evidence-based care should follow.

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References

Make your views known!

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