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Nutritional Supplements & Death

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Two recent studies refute popularly held beliefs that nutritional supplements are not dangerous. The first, published in Archives of Internal Medicine, concluded that vitamin and mineral supplements *increase mortality* in older women. It received over-the-top publicity, but, based on the study design and actual results, the multi-billion dollar supplement industry doesn't have much to worry about.

The Iowa Women's Health Study followed 38,772 women, with a mean age of 61.6 at the start, for twenty two years. The investigators checked in with the women at years eleven and eighteen to see if they took supplements and if they had died. By year twenty-two, 40.2% had died. The risk of death was slightly higher in supplement users.

Multi-vitamins increased risk of death by 2.4%, zinc by 3%, magnesium by 3.6%, iron by 3.9%, vitamin B_6 by 4.1%, folic acid by 5.9%, and copper by 18%. Because of the large numbers of subjects, these small death rate increments were statistically significant but, except for folic acid and copper, they don't look that impressive.

The problem with this type of study is that not enough variables are known. Since it was observational, rather than a controlled intervention, any number of differences in the two groups could account for the results. The women weren't queried about their health at the start of the study. We don't know their reasons for taking supplements. What if a significant proportion of women who took supplements were doing so because they were already sick or had a strong family history of early death, and they hoped that supplements would ward off disaster. At best the supplements didn't succeed as well as the dead women had hoped. Did supplements hasten death? We just can't tell from this data.

For most of the implicated nutrients, there is no inkling from other research of why taking extra would kill someone. The scientists didn't ask about dosage, so we don't even know if the women who died were taking small doses or large. Many vitamins assume toxic side effects at very high, non-physiologic doses. For example, 500 mg of niacin, used to lower blood fat levels, causes flushing, stomach upset, high glucose levels and liver irritation, none of which we see at the 15-19 mg daily requirement.

Folic acid and copper were the two nutrients which showed the strongest association with death. We know that high dose supplements might actually be dangerous. I've wrote about folic acid in DrG'sMedisense Vol 4-2, June 2009 (www.healthychoicesformindandbody.org). Both theory and experimental data link high dose folic acid supplementation to colon and possibly other types of cancer.

Yes, folic acid has crucial purposes in the body, but eating green vegetables and whole grains should provide enough without supplements. For Americans who don't eat enough of those foods, food manufacturers fortify grain products with folic acid. They started fortification to prevent devastating neural tube birth defects, but everyone benefits. The risk of over-dose came in the 1990's, when cardiologists started to prescribe high dose folic acid to correct homocysteine excess, even when patients had normal folate levels and folate had nothing to do with their high homocysteine.

Copper is a tough one. We need *enough* copper to facilitate iron usage. At *physiological* levels (i.e. those obtained from food) copper raises HDL-cholesterol (the good one). Copper helps to maintain a healthy anti-oxidant/oxidant balance, but just a little too much copper shifts the balance to pro-oxidant, which isn't healthy. We don't know if this or some as yet undiscovered effect of copper supplements is the reason for the high risk of death.

Iron excess can also shift the oxidant/anti-oxidant balance to pro-oxidant. Also, at least when given intra-venously, it impairs the immune system's ability to fight infection. For a while, cardiologists blamed at least some of the heart disease epidemic on iron surplus. Compared to pre-menopausal women who lose iron monthly with their periods and have low cardiac risk,

men and post-menopausal women have higher iron levels and worse risk.

Countering the recent scare linking calcium to hardened arteries, the women in this study who took calcium supplements died *less* often. Both of these findings need more research, to figure out exactly what is going on and what people should do about supplements.

Zinc interferes with other minerals' absorption, but would that kill people? Magnesium can cause diarrhea and high blood levels retard muscle and heart contraction, but that really only occurs in people on humungous doses or with kidney failure. Any rational individual would cut back on a supplement that was causing miserable diarrhea.

The second study concludes that vitamin E supplements increase prostate cancer risk. Vitamin E (400 Units), selenium (200 mcg), both, or no supplements were taken by 35,533 North American men for up to 10 years. Those taking vitamin E alone had a 17% greater risk for prostate cancer. Even the investigators don't have a clue why.

What's even more confusing is that, while selenium slightly increased risk by 9%, combining the two somehow attenuated vitamin E's effect: The two together only increased cancer risk by 5%. Perhaps this is another example of anti-oxidants regenerating each other, in order to prevent them from becoming pro-oxidants. (When an anti-oxidant neutralizes an oxidized molecule, it gives up a hydrogen or otherwise neutralizes a free electron. In doing so, it loses its ability to anti-oxidize something else. It must be regenerated, e.g., get its hydrogen back, to regain that ability.)

The take-home lesson from these two studies is that there is a lot we don't know. We should avoid high dose supplements until we know that doses higher than those needed to maintain physiological levels are safe.