Dr. Shari Lieberman

Dedicated to the Scientific Pursuit of Better Health

Special Edition

December, 2004 Newsletter

Dr. Shari Lieberman's Nutritional & Integrative Therapy Review Newsletter

Welcome to my newsletter. Each month I review the cutting-edge research in the field of nutritional and integrative medicine and give you my commentary. At the end of each newsletter, I give a specific nutritional protocol for a specific disorder. The newsletters and nutritional protocols can also be found on my website. You may also visit my website to view my numerous Powerpoint presentations given at medical conferences and visit my Q & A, library and more. As an ongoing commitment to excellence in product development, you can also view products I have developed and co-developed with leading experts all over the world.

The results of a vitamin E meta-analysis were released to the press prior to the publication of the results in the Annals of Internal Medicine. The results of this analysis suggest that high intakes of vitamin E can increase mortality (death). These results have been sensationalized throughout the media with little explanation as to how such bizarre results could be obtained. I have included the abstract of the analysis exactly as it appears in Medline and if you are interested in reading the **entire paper, click this link**.

I have received countless emails and communications asking for a rebuttal to the results of this meta-analysis. My friend and co-author James Gormley beat me to the punch. He has given me permission to use his excellent "Letter To the Editor" that was just submitted to the Annals of Internal Medicine (let's see if they publish it). In addition to his letter that

follows the abstract below, I also offer some additional information that the researchers clearly overlooked.

Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E.
Ann Intern Med. 2004 Nov 10; [Epub ahead of print]

Abstract:

BACKGROUND: Experimental models and observational studies suggest that vitamin E supplementation may prevent cardiovascular disease and cancer. However, several trials of high-dosage vitamin E supplementation showed non-statistically significant increases in total mortality. PURPOSE: To perform a meta-analysis of the dose-response relationship between vitamin E supplementation and total mortality by using data from randomized, controlled trials. PATIENTS: 135,967 participants in 19 clinical trials. Of these trials, 9 tested vitamin E alone and 10 tested vitamin E combined with other vitamins or minerals. The dosages of vitamin E ranged from 16.5 to 2,000 IU/d (median, 400 IU/d). DATA SOURCES: PubMed search from 1966 through August 2004, complemented by a search of the Cochrane Clinical Trials Database and review of citations of published reviews and meta-analyses. No language restrictions were applied. DATA EXTRACTION: 3 investigators independently abstracted study reports. The investigators of the original publications were contacted if required information was not available. DATA SYNTHESIS: 9 of 11 trials testing high-dosage vitamin E (>/=400 IU/d) showed increased risk (risk difference > 0) for all-cause mortality in comparisons of vitamin E versus control. The pooled all-cause mortality risk difference in high-dosage vitamin E trials was 39 per 10,000 persons (95% CI, 3 to 74 per 10,000 persons; P = 0.035). For low-dosage vitamin E trials, the risk difference was -16 per 10,000 persons (CI, -41 to 10 per 10,000 persons; P > 0.2). A dose-response analysis showed a statistically significant relationship between vitamin E dosage and all-cause mortality, with increased risk of dosages greater than 150 IU/d. Limitations: High-dosage (>/=400 IU/d) trials were often small and were performed in patients with chronic diseases. The generalizability of the findings to healthy adults is uncertain. Precise estimation of the threshold at which risk increases is difficult. CONCLUSION: High-dosage (>/=400 IU/d) vitamin E supplements may increase all-cause mortality and should be avoided.

Commentary by James Gormley:

Dear Editor,

As you know, a paper on vitamin E by Miller et al. was just released on November 10th in the *Annals of Internal Medicine.*

The authors of this paper pooled data from 19 studies, 18 of which were statistically insignificant. This, however, didn't discourage the authors from concluding that their number-crunching yielded an increased risk of mortality from vitamin E.

The authors, significantly, admitted that they cannot "evaluate the generalizability of our findings to healthy adult populations." Nevertheless,

that did not stop them from stating that, "On the basis of our study, high-dosage vitamin E supplementation is clearly unjustified […] Policymaking bodies, which currently do not recommend antioxidant vitamin supplement use to the general population should also caution the public against the use of high-dosage vitamin E supplementation."

It is shocking how, on the basis of flimsy findings, such sweeping and definitive pronouncements are being made. It is likewise unfortunate that so many media outlets (print and broadcast) have seen fit to uncritically provide a platform for misplaced hysteria over interpretation of this weak data.

What does the established body of research on vitamin E really show?

A number of landmark epidemiological studies have, in fact, established that vitamin E supplementation reduces cardiovascular disease progression and, in fact, improves mortality.

In the Cambridge Heart Antioxidant Study (CHAOS) (Lancet, 1996), investigators wanted to see if supplementation with 400 or 800 I.U. of vitamin E for roughly 510 days would reduce risk for myocardial infarction (MI) and cardiovascular death in 1,035 patients with ischemic heart disease (967 other people received a placebo). The findings were that high-dose vitamin E supplementation significantly reduced the risk of cardiovascular death and non-fatal MI.

In a study by Boaz et al. (Lancet, 2000), hemodialysis patients with cardiovascular disease (aged 40 to 75 years) received either 800 I.U./day of vitamin E or a placebo for approximately 519 days. The results? There was a significant decrease in cardiovascular disease (endpoints) and myocardial infarction.

In another study from 2000 (Salonen et al., J Int Med), a combined supplement of both vitamin E and slow-release vitamin C reduced the progression of atherosclerosis in men by 74 percent over a three-year period of supplementation.

In the Nurses' Health Study (Stampfer, 1993), which looked at 87,000 female nurses over eight years, among the 13 percent of women who regularly used vitamin E supplements (of at least 100 I.U. per day) there was a 31 percent reduction in relative risk for nonfatal myocardial infarction and death from cardiovascular disease compared with women who did not take vitamin E..

In a study by Rimm (1993), in which 39,000 male health professionals were studied for four years, 17 percent of the men took vitamin E supplements. Those who took the highest doses (median of 419 I.U. per day) had a 40 percent reduction in the relative risk for nonfatal myocardial infarction or death from coronary heart disease..

That's what the science really shows. .

Responsible media outlets will (1) run a follow-up story on this putting the Annals interpretation of data into perspective-and with as much fanfare as the original "story" received from certain outlets and will (2) in the future work hard at not following the example of the outlets which "blew it" with

this story in the first place in not critically looking at what the real story was behind the hype..

Thank you. .

James J. Gormley, Policy Advisor, Citizens for Health (www.citizens.org); Editor-in-Chief, Better Nutrition, 1995 - 2002; Former managing editor, American Journal of Surgery & American Journal of Medicine; Health book author, journalist and consumer advocate;
Mail to **james gormley..**

Dr. Shari Lieberman's Commentary:

While many of you do not have a background in statistics - this is very easy to get. There are THOUSANDS of studies on vitamin E - including animal and human data. Many of these studies demonstrate statistically significant results, such as the ones James described above. Studies range from prevention/treatment of macular degeneration to cancer to heart disease, just to name a few. There are even studies on dry vitamin E (d-alpha tocopherol succinate) that show it can both prevent and treat many types of cancer including cancers of the breast and prostate. This specific type of vitamin E has also been shown to be synergistic with many forms of conventional therapies. The problem that remains with respect to vitamin E studies is that in the majority of studies, synthetic vitamin E (d,l-alpha tocopherol) was used. Synthetic vitamin E has approximately 1/8 the activity of the natural (d-alpha tocopherol), which does explain why some researchers get positive results while others get negative results. Also, the doses used in studies vary greatly. Nonetheless, there are still thousands of statistically significant studies to choose from for any meta-analysis. To use studies with non-significant results in a meta-analysis flies in the face of credible science. If I had done this for my doctoral dissertation, I would not have received my Ph.D. Annals of Internal Medicine is a peer reviewed medical journal - were the reviewers sleeping or clueless?