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Selenium and Vitamin E Supplementation for Cancer Prevention

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LETTERS

Selenium and Vitamin E Supplementation for Cancer Prevention

To the Editor: The Selenium and Vitamin E Cancer Prevention Trial (SELECT) by Dr Lippman and colleagues[1] reported that selenium or vitamin E alone or in combination did not prevent prostate cancer. The negative results of this trial confirm the outcomes in the Nutritional Prevention of Cancer (NPC) Trial for those participants with the highest baseline plasma selenium concentration prior to supplementation with selenized yeast.[2] The conclusion from both NPC and SELECT should be that daily selenium supplementation will not benefit all persons. Cancer risk reduction with selenium should be expected only in men with low or suboptimal levels prior to supplementation.

A U-shaped dose-response relationship between selenium intake and cancer risk, as suggested by studies in dogs,[3] is consistent with the results of SELECT and NPC. At baseline, the average participant in SELECT had selenium status within the trough of the U-shaped curve, ie, not low or suboptimal. After supplementation with 200 µg per day of selenium as selenomethionine, the average SELECT participant achieved selenium levels that far exceeded the high postsupplementation values of men in NPC in the highest baseline-selenium tertile. Those NPC participants experienced no prostate-cancer risk reduction and an almost 3-fold increased incidence of diabetes.[2,4] In SELECT, there was no reduction in prostate-cancer risk and a statistically nonsignificant increased diabetes incidence. We therefore consider the results of SELECT and NPC to be consistent, not contradictory.

We believe that it is time to move beyond the belief that any particular agent administered at the same dose to all participants will benefit the overall population and instead attempt to individualize cancer prevention.[3] Subsets of individuals should be identified who are more likely to benefit from supplementation, such as persons with low selenium concentrations or perhaps those with the selenoprotein-P genotype that is associated with prostate-cancer risk.[5] This stance is distinct from claiming knowledge of which types of cancer will or will not be prevented by selenium.

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Financial Disclosures: Dr Rayman reported receiving grant support from Wassen International, a manufacturer of nutritional supplements, including selenium. Dr Waters reported that he is director of the Murphy Cancer Foundation, a not-for-profit research institute that, in collaboration with Bostwick Laboratories, markets a toenail test for selenium. Dr Waters reported that he has no financial interest in Bostwick Laboratories and no financial relationships with any manufacturers of selenium supplements. Dr Combs reported no disclosures.

1. Lippman SM, Klein EA, Goodman PJ, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA*. 2009;301(1):39-51.
2. Duffield-Lillico AJ, Reid ME, Turnbull BW, et al. Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: a summary report of the Nutritional Prevention of Cancer Trial. *Cancer Epidemiol Biomarkers Prev*. 2002;11(7):630-639.
3. Waters DJ, Chiang EC, Bostwick DG. The art of casting nets: fishing for the prize of personalized cancer prevention. *Nutr Cancer*. 2008;60(1):1-6.
4. Stranges S, Marshall JR, Natarajan R, et al. Effects of long-term selenium supplementation on the incidence of type 2 diabetes: a randomized trial. *Ann Intern Med*. 2007;147(4):217-223.
5. Cooper ML, Adami HO, Grönberg H, Wiklund F, Green FR, Rayman MP. Interaction between single nucleotide polymorphisms in selenoprotein P and mitochondrial superoxide dismutase determines prostate cancer risk. *Cancer Res*. 2008;68(24):10171-10177.

To the Editor: Dr Lippman and colleagues[1] concluded that "selenium, vitamin E, or selenium + vitamin E (at the tested doses and formulations) did not prevent prostate cancer." We believe that this statement is potentially misleading because the data relate to the effects of *L*-selenomethionine supplementation only in a selenium-replete population. The effects of selenium are species specific, with some forms of selenium having greater anticancer benefit than others,[2] so the null effect of *L*-selenomethionine supplementation on prostate cancer risk should not be applied to selenium in general.

In addition, the effects are dependent not only on the dose and form of selenium but on the initial baseline selenium status of the population. In a previous study, selenium supplementation was only effective against prostate cancer in volunteers (with a previous history of skin cancer) whose plasma selenium was less than 120 µg/L (to convert to µmol/L, mul-

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