Letter to the Editor


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We read with great interest the paper by Goodman et al. (1) reporting on a small clinical trial investigating the effects of β-carotene and α-tocopherol on bleomycin-induced chromosomal damage. However, we must take exception to the assertion that vitamin C supplementation in vivo has been shown to reduce the number of bleomycin-induced breaks per cell. In 1997, we published results of a large clinical trial designed to evaluate in vivo ascorbic acid supplementation and modulation of bleomycin-induced chromosomal damage (2). This was a double-blind study with 228 individuals randomized into four arms: placebo and 1, 2, and 4 g of ascorbic acid. We found that there was no significant difference between treatment and the level of bleomycin-induced chromosomal damage. Furthermore, we found that there was no direct dose-response relationship between serum ascorbic acid concentrations and bleomycin-induced chromosomal damage. On the surface, it would appear that these two clinical trials support the contention that mutagen sensitivity cannot be modulated by dietary supplements.

However, we would like to stress an important point made by a coauthor on both papers, T. C. Hsu (1, 2). In the discussion of our paper, Dr. Hsu comments on the in vivo/in vitro nature of this particular study design. The agents of modulation (ascorbic acid, β-carotene, and α-tocopherol) are given in vivo, but the mutagen (bleomycin) is introduced several days after the culture has been established. Hsu pointed out that ascorbic acid can pass freely in and out of the cells, whereas the mutagen cannot. We estimate that during the culture process, the ascorbic acid levels are diluted to ~10% of the serum levels. Although clearly there is a physiological difference between the water-soluble ascorbic acid and the fat-soluble β-carotene and α-tocopherol, we believe that a similar mechanism may be in place. β-Carotene and α-tocopherol, although present in the parent cells at the time the culture was established, are not necessarily present in daughter cells at the same concentration after 72 h of cell growth. A discussion of these potential "culture effects" in the context of the Goodman study would be of interest.

The joint findings of our study and those of Spitz et al. (3), Cloos et al. (4), and Goodman et al. (1) support the lack of relationship between supplement and this cellular phenotype. However, careful consideration of these culture effects must be included in the interpretation of these findings.

References


T M King, S Hursting, J Contois, et al.