The present status of antioxidant vitamins and β-carotene¹,²

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In October 1989, an international conference on the topic of antioxidant vitamins and β-carotene in disease prevention was held in London and the proceedings appeared as a supplement to The American Journal of Clinical Nutrition [1991;53(suppl):189S-396S], edited by the late TF Slater and G Block. At that time, the conference participants presented papers in the broad categories of free radical formation and tissue damage; prevention of cancer, cardiovascular disease, and cataracts; and antioxidant vitamins and β-carotene: their roles in the future. In his concluding remarks, Slater (1) referred to the conference as “stimulating, timely, and scientifically very valuable” and summarized that the criteria for a successful agent are that “the scavenger (antioxidant) must get to the right site, at the right time, and in the right concentrations; moreover, it must have acceptable low intrinsic toxicity for use under conditions in vivo.”

How far have we come in the 5 years since the first conference was held? In an attempt to answer that question the Second International Conference on Antioxidant Vitamins and β-Carotene in Disease Prevention was convened in Berlin in October 1994. The following 34 presentations represent the most current attempts to evaluate the relation between antioxidants and β-carotene and the prevention of diseases. It is no longer necessary to begin conferences of this nature with papers about free radicals and tissue damage because these processes are so well documented and accepted. A great deal of interest now focuses on the mechanisms whereby scavengers, or antioxidants, can prevent or intercept potentially harmful radical reactions (2), although we must bear in mind that some of the effects of these scavengers may be expressed through effects that are not related to their antioxidant functions (3–5).

The observational epidemiologic studies continue to accumulate impressive evidence that foods rich in the antioxidant vitamins (6) and β-carotene (7) have an important role in the prevention of cardiovascular disease, as well as in cancer prevention (8, 9). But of even greater interest are the human intervention studies that are underway, as well as those that have been completed. These studies are based on the assumption that the protective effect of dietary fruit and vegetables can be ascribed to the antioxidant vitamins C and E, as well as to β-carotene (or other carotenoids); thus, these three micronutrients have been used as supplements in an ever-increasing number of studies worldwide.

The Linxian Study continues to offer new evidence of the effectiveness of a β-carotene, vitamin E, and selenium intervention in the case of decreasing proliferation in esophageal cancer (10), decreasing cerebrovascular mortality in men (11), and enhancing the T lymphocyte response (12). Bear in mind that the study population has one of the world’s highest rates of esophageal cancer, which may be partially attributed to a poor diet.

The Alpha-Tocopherol Beta-Carotene (ATBC) Study was discussed at great length during the conference and is addressed by Albanes et al (13) as well as in the panel discussion, which is summarized by Blumberg (14). When the results of this carefully controlled, double-blind intervention trial were reported (15), indicating that there was a significant, 18% increase in lung cancer mortality in the group supplemented with β-carotene, there was a great deal of surprise in the scientific community, for this finding seemed to refute a great deal of the epidemiologic evidence. A subsequent analysis of the data suggests that the lung cancer excess in the β-carotene group was evident primarily among men consuming more alcohol (13). However, even the ATBC Study reported that the men with the highest concentrations of both dietary and serum β-carotene and vitamin E at baseline had the lowest lung cancer rates (15).

Other intervention studies reported at this conference included the protective effect of vitamin E in patients being treated with aspirin for recurrent strokes and transient ischemic attacks (16), the clinical regression of oral leukoplakia by both vitamin E and β-carotene (17), the positive effects of β-carotene in a phase II trial of cervical intraepithelial neoplasia (18), and the absence of an effect of β-carotene (plus vitamin A) in altering the incidence and prevalence of premalignant cells in the sputum of asbestos workers, who are at a very high risk for developing lung cancer (19).

The intervention model, however, is not uniformly accepted. Block (20) presents her argument that clinical trials alone cannot answer the question of the role of nutrients in preventing chronic disease, and that further analyses of the laboratory and epidemiologic data are required to move forward in our understanding of the nutrient-disease question. This issue was fully addressed in the panel discussion, which is summarized by Blumberg (14). The focus of the discussion is what consti-

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tutes scientific substantiation for a role of the antioxidant vitamins and β-carotene in disease prevention. The conclusions of this panel are that the available evidence is still not sufficient to make public health recommendations regarding the efficacy and safety of these compounds for preventing human diseases. Even those studies that have clearly indicated that protection is only observed in groups taking supplements (21), caution is voiced until large-scale intervention trials are completed.

Although the completed and ongoing intervention trials continue to hold great interest and expectation, other studies suggest that we should be looking beyond cancer and cardiovascular disease for evidence for the role of antioxidant vitamins and β-carotene. In fact, other carotenoids may play a particularly important role in certain specialized conditions. The recent report of a protective effect against the onset of the neovascular form of age-related macular degeneration by diets rich in lutein and zeaxanthin, summarized by Snodderly (22), and the role of antioxidants in the development of cataracts (23) indicate that the eye is an organ that may be especially sensitive to micronutrient status.

It is clear that we will require at least a third international conference on antioxidant vitamins and β-carotene (and other carotenoids) in disease prevention in a few years time to help us decide if we can make public health recommendations based on the totality of the available evidence.

REFERENCES