International Symposium on the Role of Tomato Products and Carotenoids In Disease Prevention: An Introduction

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The role of carotenoids in cancer prevention has been a matter of controversy since a series of intervention trials using β-carotene supplementation led to negative results (1). Most disconcerting was a study conducted in Finnish smokers that suggested an increase in lung cancer in smokers administered β-carotene supplements (2). Much soul-searching has followed (3) along with the growing awareness that antioxidants such as β-carotene can, under certain circumstances, serve as reactive pro-oxidants and therefore potential procarcinogens (4). Also arguing against the use of carotenoid supplements as cancer chemopreventive agents is the fact that 1) carotenoids are poorly bioavailable compared with other antioxidants such as vitamin E and vitamin C; 2) carotenoids have no specific cellular uptake mechanism; 3) blood and adipose tissue levels are poor markers of overall intake; and 4) blood levels are subject to lifestyle factors and such as smoking and exercise (5).

Reconsideration of the epidemiological evidence indicated that most of the data supporting a role for β-carotene in disease prevention came from studies associating yellow and green vegetables consumption, rather than β-carotene *per se*, with reduced cancer risk (6–9). Because β-carotene is only one of a variety of carotenoids consumed in fruits and vegetables by human populations, research has focused on carotenoid-rich foods and food groups and on carotenoids other than β-carotene (10). Interest in lycopene is based on the fact that lycopene, though largely ignored by researchers for years, is present in plasma and breast milk of Western populations at levels as high or higher than β-carotene (10). In addition, tomato consumption has been shown to be associated with decreased risk of several cancers, particularly cancers of the gastrointestinal tract, lung, and prostate (11) and because the major carotenoid in tomatoes is the acyclic, non-vitamin A precursor, lycopene, attention focused on lycopene as a potential chemopreventive agent (12). Supporting a role for lycopene as an anticancer agent are a variety of animal model studies and *in vitro* cell culture studies (see Cohen, this volume). Moreover, because reactive oxygen species have been shown to be associated with both carcinogenesis and coronary artery disease (12), there is a biologically plausible mechanism for lycopene action based on the fact that lycopene quenches singlet oxygen radicals to a greater degree than any other carotenoid (13).

Although the study of lycopene and cancer is still in its infancy, beginning in the 1990s there has been a rapid increase in peer-reviewed publications (Fig. 1). In part, this surge in activity has been due to the epidemiological studies of Giovannucci (11) and LaVecchia (14) and to the publication, in 1998, of the proceedings of an international symposium on lycopene and disease prevention (15). The present symposium was designed to stimulate further research and discussion by focusing on the most recent and innovative research on lycopene tomato carotenoids and cancer prevention and also on the protective role played by lycopene in other diseases including, coronary artery disease, age-related macular degeneration, and in lung function and physiology. The reports presented emphasized human studies with less attention focused on the intricacies of lycopene action at the cellular and molecular levels. The rationale for this approach was that it is more important to establish the effectiveness of lycopene in human settings, with some degree of certainty, before delving into the fine details of the effects of lycopene on intracellular signaling, cell cycle checkpoints, or gene expression.

The symposium has been organized around a multidisciplinary concept with epidemiology as its starting point, followed by animal model studies, clinical intervention studies, and concluding with current concepts on the mechanism of action in lycopenes. After an initial review by Khachik describing the chemistry and metabolism of lycopene, the epidemiological evidence for the role of lycopene and tomato consumption in cancer prevention is outlined by Giovannucci, and LaVecchia follows by a review of the status of animal model and *in vitro* studies by Cohen. Then, a series of clinical studies dealing with lycopene, tomato carotenoids, and prostate cancer are reviewed by Clinton, Kucik, and Bowen. Following this, Arab discusses her provocative work on the protection by tomato carotenoids against ozone-induced lung damage, and Rissanen and Rao review their studies indicating that lycopene plays a protec-

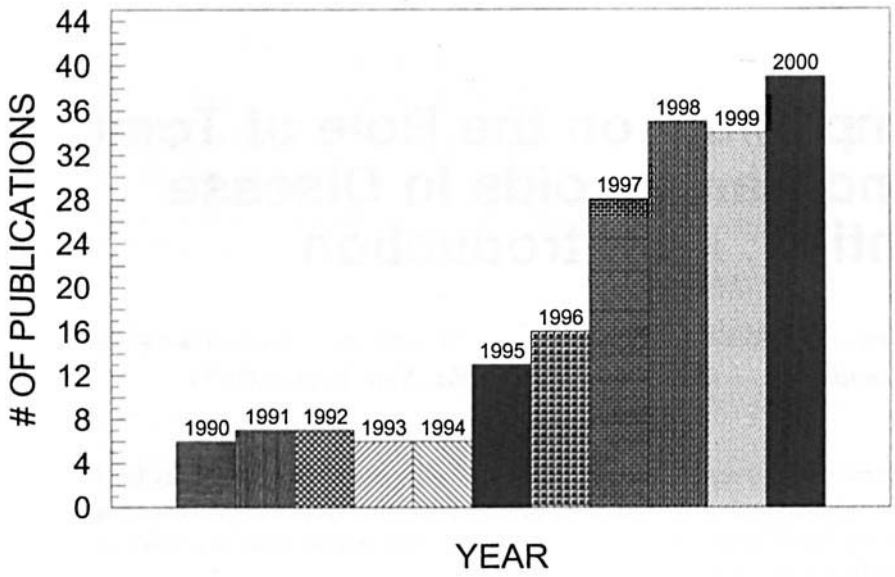

Figure 1. Publication trends: tomatoes, lycopene, and cancer data are from Medline (National Library of Medicine), Washington, DC.

tive role in coronary artery disease possibly *via* antioxidant functions. Schwartz and Erdman then update their studies on lycopene uptake from foods and the bioavailability of *cis-trans* isomers of lycopene. Last, the possible mechanism of lycopene actions and its interactions with other carotenoids are reviewed by Heber. Dr. John Weisburger closes this symposium with a summary of the proceedings. We thank Dr. Khor San Khoo, Carole Dichter, and Campbell Soup Company for their enthusiastic support and for providing an educational grant to the American Health Foundation to fund this important and timely symposium.

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