Conference: Prevention of Human Cancer

Introduction

Chemoprevention is a strategy to block cancer development through the use of chemical agents, some of which currently are considered nutrients and others which are clearly synthetic pharmacological compounds. Thus, chemoprevention is analogous to chemotherapy in the treatment of cancer. Hindrance or modification of each stage of the carcinogenic process—initiation, promotion, and progression—has been accomplished in vitro and in animal models. Translating this approach to human beings represents a formidable task. Although there is reason to believe that the general process of carcinogenesis should be similar in all species, several observations indicate that this assumption may have to be qualitatively and quantitatively modified for human beings:

- Metabolism of carcinogens by different species varies. Also, man is not an inbred species and therefore exhibits genetic and phenotypic heterogeneity in response to carcinogens;

- Acute one-time application of an initiator followed by multiple exposures to a promoter at relatively high to very high doses is the usual experimental carcinogenesis protocol. Actual interaction of chemicals with humans is unlikely to follow this convenient pattern. Exposure to multiple low doses of many carcinogens over a long period of time represents the more likely scenario;

- Dietary and environmental variables in animal experiments can be well delineated in appropriately designed trials. Modification of dietary and cultural variables in free-living individuals is very difficult;

- Compliance of cells or animals to the experimental plan is not an issue; adherence of subjects who are basically well, to a prevention protocol can be quite difficult.

In the early 1980s a number of investigators began to explore the feasibility of chemoprevention in human beings and several trials were launched. These trials represented formidable undertakings with sample sizes larger than most therapeutic phase III trials. Additionally, long follow-up times were needed for enough endpoints to occur that would allow for differences in the control and intervention arms of the trial to develop. New strategies have evolved to address the differences in experimental design, statistical evaluation, recruitment, agent selection, and outcome measurements inherent to chemoprevention trials.

The first conference in Tucson in 1982 dealt with vitamins as potential preventive or therapeutic anticancer agents; in 1985 the focus was primarily on the retinoids. The current conference in 1988 was directed toward exploration of the relevant scientific basis and methodological issues for chemoprevention in humans.
The papers which form these proceedings should provide an important resource for where we are in this field and where we need to go. Additionally, new investigators to this field will find the presented information useful and necessary as a basis for their own trials. We look forward to our next meeting in 1991 by which time our understanding of the biology of early transformation of human cancers will be more substantial, many chemoprevention trials should have matured to provide definitive answers, and new second-generation trials will have been launched.

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