INTRODUCTION

Perspectives in Cancer Prevention (44163AA)

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This issue of the *Proceedings of the Society for Experimental Biology and Medicine* presents a forum that assesses the status of cancer prevention *via* 18 critical reviews of the elements that impact on carcinogenesis. Each article is written by a leading authority in the field of cancer prevention. Contributors were also selected with the goal of providing a broad-based view of the many facets of cancer prevention. We believe that, in addition to presenting the current state of knowledge in cancer prevention, the reviews also facilitate an appraisal of where current research in carcinogenesis is likely to lead in the coming years. Thus, we hope this issue of the *Proceedings* will prove to be a valuable reference for readers now and in the future, as the various ideas presented begin to unfold.

The reviews emphasize that effective use of chemopreventive agents, whether naturally occurring or synthetic, will be realized only in the context of a fundamental understanding of the processes of carcinogenesis and tumor biology. They also illustrate why success in preventing cancer will be enhanced by improved methods for identifying people at increased risk for different types of cancer. The importance of understanding and minimizing barriers that limit the inclusion of high-risk individuals in cancer prevention trials, while communicating our understanding of chemoprevention to those it is intended to benefit, is considered.

The first section of this special issue of the *Proceedings* focuses on general perspectives for prevention of cancer. Mechanisms by which cancer can be prevented, even when the exact causative factor(s) is unknown or cannot be removed from the environment, are reviewed, as are the use of epidemiologic methods to identify risk factors in specific types of cancer. Also discussed in Section I are the properties of intraepithelial neoplasia relevant to cancer prevention and the development of surrogate end points for clinical trials.

The second section deals with the major determinant of cancer: permanent acquired damage to cellular DNA. A major goal of chemoprevention is to inhibit this type of damage, so it becomes important to know how to measure damage to DNA and how to use evidence of damage to monitor the efficacy of chemopreventive therapy. Target populations have been assessed for the presence of specific adducts with DNA from cells in peripheral blood and exposed tissues. It is hoped that the clinical and public health impact of quantitative measures of DNA damage will be enhanced in the future as refinements in detection methods occur. The current understanding of heritable traits that govern carcinogen metabolism is provided in this section, too.

The review of carcinogenesis induced by *N*-nitrosamine, and of how this specific problem can be modulated, provides an example of what can be achieved through specific knowledge of the enzymology of carcinogen metabolism. Information regarding enzyme systems that protect the host is also detailed. Thus, besides inhibiting the synthesis of proximate carcinogens, chemoprevention can be effected by enhancing the capacity to detoxify such metabolic products. The last article in this section reviews evidence for a relatively new approach to modulating cancer risk by downregulating synthesis of prostaglandins. Several candidate approaches for achieving this goal are discussed; emphasis is given in this review to altering the amounts and functional states of the cyclooxygenases, especially for the inducible isoform (designated Cox-2).

The cancer prevention strategy that has caused the most interest in recent years is diet. Several perspectives on diet-dependent modulation of cancer risk are provided in the final section. These reviews discuss the effects of a variety

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of dietary factors, ranging from fatty acids to polyphenols in tea. It is also emphasized that specific diets can affect tissue types differentially.

The problem of cancer prevention is more complex, of course, than simply understanding biochemistry and molecular biology. Public acceptance of the idea of chemoprevention, on the one hand, and individual responsibility for decreasing cancer risk, on the other, are crucial societal problems. Consequently, important methodologic issues related to design of clinical trials are emerging. The reviews in Section IV address the many complex considerations in the design and conduct of chemoprevention trials—for instance, the recruitment of populations that are generally healthy; the low tolerance of such individuals to side effects of the agents; means for enhancing awareness and willingness to participate in clinical protocols; and inclusion in trials of high-risk populations, which exist usually within medically underserved communities. Behavioral sciences thus will become increasingly significant in chemoprevention research. A conundrum is apparent here. The science of carcinogenesis and the need to control the many variables that can confound trial results lead to more complex trial design; and this complexity may serve, conversely, to limit enthusiasm for participation by patients and physicians. Broad-based participation must be encouraged, however, and international efforts that allow for enhanced recruitment of participants need to be explored and assessed.