The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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Preface

The importance of vitamins and other micronutrients in the maintenance of health has been appreciated for nearly a century. Information about the role of vitamins as basic modulators of biological and biochemical functions has been accumulated steadily but slowly. A heightened interest in vitamins and their derivatives as potential anticancer agents has taken place in the last 5-10 years, which reflects both an increase in our knowledge about the biochemical basis of biological processes such as differentiation and cancer and an increased interest in non-cytotoxic modification of cancer.

The mechanism(s) via which vitamins effect their action(s) in vivo have been clarified in part by a careful study of biochemical strategies utilized by these compounds. Discrete modulatory effects on cell function have been identified at the membrane, enzymatic, and nuclear levels, and binding to specific proteins may play an important effector role for several vitamins in mediation of cellular change. Predictable positive changes in hormonal and cellular immunological function are also produced. To understand the mechanism of action of vitamins, intensive investigations of the effect of individual vitamins on biochemical processes will be required. Our understanding of the interaction of vitamin A and its derivatives with cells has increased tremendously over the past decade, and this knowledge has provided the basis for new strategies to biological problems such as differentiation, carcinogenesis, and cancer.

We ask: Do different vitamins share similar biochemical effectors (specific cellular receptors, incorporation into membranes, inhibition of key regulatory enzymes)? Can one vitamin
potentiate the effect of another? Do vitamins modulate complementary immunological pathways?
Epidemiological observations about vitamins and other nutritional principles and laboratory investigations provide the background for asking several questions about the future of vitamins and cancer in humans:
(1) Numerous epidemiological studies suggest that the incidence of several types of epithelial cancers is inversely related to the level of serum vitamin A and/or -carotene. Extensive data indicates that vitamin A is critical for normal epithelial cell differentiation. Synthetic derivatives of vitamin A also inhibit cell proliferation and frequently stimulate cell differentiation and have an improved therapeutic index (efficacy/toxicity ratio) based on animal studies. Are intervention studies in humans at high risk of epithelial cancers or who already have preneoplasias warranted at this time? If so, in what conditions or diseases? With what agents - -carotene, vitamin A, synthetic retinoids, other vitamins or compounds?
(2) Basic principles of chemical and physical carcinogenesis have been formulated over the past two decades, and modifiers of both the initiation and promotion phase have been identified. Many substances including vitamins A, C, and E may be modifiers of these processes. Does the data indicate that intervention studies in high risk individuals are warranted? If so, with what group of individuals? With what agents?
(3) Laboratory investigations in vitro and in vivo indicate that the growth of many transformed
cells can be inhibited by biological response modifiers including vitamins, and in some cases evidence for differentiation was apparent. Also, several investigations in animals and a few in humans indicate that these compounds favorably affect the immune system. Should vitamins be studied clinically for activity in the adjuvant setting or against advanced cancers? If so, which vitamins? In combination with other immune modulators or chemotherapeutic drugs?

A large group of investigators from the sciences of cell biology, biochemistry, nutrition, epidemiology, and oncology have contributed to the broadening base of knowledge about vitamins. Individuals from these different disciplines only infrequently interact and, therefore, an interdisciplinary meeting which would provide a forum for interchange and collaboration seemed timely. This First International Conference on the Modulation and Mediation of Cancer by Vitamins was held in Tucson, Arizona, from February 23 to 27, 1982. The series of papers in these proceedings in part represent the key information exchanged, although they only hint at the intensity of this developing field of inquiry.

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