

Antineoplastic and Immunosuppressive Agents Part I

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Preface

Over the past two decades a number of attempts have been made, with varying degrees of success, to collect in a single treatise available information on the basic and applied pharmacology and biochemical mechanism of action of antineoplastic and immunosuppressive agents. The logarithmic growth of knowledge in this field has made it progressively more difficult to do justice to all aspects of this topic, and it is possible that the present handbook, more than four years in preparation, may be the last attempt to survey in a single volume the entire field of drugs employed in cancer chemotherapy and immunosuppression. Even in the present instance, it has proved necessary for practical reasons to publish the material in two parts, although the plan of the work constitutes, at least in the editors' view, a single integrated treatment of this research area.

A number of factors have contributed to the continuous expansion of research in the areas of cancer chemotherapy and immunosuppression. Active compounds have been emerging at ever-increasing rates from experimental tumor screening systems maintained by a variety of private and governmental laboratories throughout the world. At the molecular level, knowledge of the modes of action of established agents has continued to expand, and has permitted rational drug design to play a significantly greater role in a process which, in its early years, depended almost completely upon empirical and fortuitous observations. In addition, the rapid expansion in our knowledge of cancer etiology has begun to afford opportunities for the development of new types of agents with the capacity to inhibit the neoplastic process. Recent advances in our knowledge of viral carcinogenesis, and the consequent expansion of the field of cancer chemotherapy to agents which affect the processes of viral replication and virus-induced transformation of mammalian cells, are factors which are already having a profound influence on drug design and development. Modification and enhancement by pharmacological means of immune defenses to neoplastic growth is another area which is only beginning to be exploited by the chemotherapist. Many major advances still remain to be made to take full advantage of potential synergistic interactions between chemotherapy and surgery and/or radiation therapy: these three major modalities have developed almost independently despite the continuing efforts of several outstanding groups of investigators to bridge the gap between them at both the experimental and applied levels.

In addition to the rapid growth of these research areas, a second feature which strikes the editor who attempts to survey cancer chemotherapy and immunotherapy is the frequency with which, as in so many other areas of science, fundamental advances have been made unexpectedly, seemingly almost fortuitously. While such random progress may be expected to be a characteristic of the early development of any new research field, it appears to have played an unusually large role in cancer research, and the recent history of cancer chemotherapy shows that major findings have continued to emerge unpredictably, despite retrospective attempts of scientific historians to detect a previously discernable rationale in such developments. The unusually prominent role of chance in the development of antineoplastic and immunosuppressive agents may

be a reflection of the slow and difficult progress in our knowledge of cancer etiology: when the location of a target is still shrouded in darkness, it is probably inevitable that direct hits will continue to be a consequence of accident rather than design. It is to be hoped that current efforts of public and private research funding agencies to superimpose order and modern management techniques on the apparently random development of this and other biomedical sciences will not have the paradoxical effect of slowing the progress they are designed to enhance.

The volume is divided into two parts. The first, has two major sections on general considerations in the areas of antineoplastic and immunosuppressive agents, with chapters included on (a) test systems for both classes of drugs, (b) the clinical utility of both classes of drugs in suppressing the growth of cancer and the immune responses, (c) design of new agents in several major chemical and biochemical classes, (d) the role of cell cycle kinetics in the utility of these therapeutic agents, (e) pharmacologic factors of importance in their optimal utility, (f) selective toxicity, (g) tests predictive of cytotoxic potency, (h) mechanisms of resistance, (i) combination chemotherapy, and (j) among the related modalities, radiation therapy and immunotherapy.

The second part of the volume describes the agents of importance in the treatment of these disease states. It includes major sections on alkylating agents, hormones, antimetabolites and a variety of other cytotoxic compounds, including inhibitors of protein and RNA synthesis, antibiotics and alkaloids, a variety of important synthetic agents and cytotoxic metal-containing compounds.

The Editors wish to express their deepest gratitude to their collaborators who have not only contributed important chapters, but have cooperated fully in the final preparation of this volume. They are also most appreciative of the invaluable editorial assistance provided by Dr. BARBARA RENKIN and the important secretarial help they have received from Miss LENORA ANTINOZZI and Miss LYNN A. BON TEMPO. Special thanks go to Dr. WILLIAM A. CREASEY who has compiled the subject index for this volume. It is our deepest hope that research workers in cancer, immunosuppression and other scientific disciplines will find this volume of use in both their intellectual and laboratory endeavors and that it may aid in the accomplishment of further advances in science for the benefit of man.

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