

Comprehensive Textbook of
ONCOLOGY
Volume Two

Comprehensive Textbook of **ONCOLOGY**

Volume Two

Second Edition

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Accurate indications, adverse reactions, and dosage schedules for drugs are provided in this book, but it is possible that they may change. The reader is urged to review the package information data of the manufacturers of the medications mentioned.

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Foreword

Oncology is no longer an orphan discipline. It has provided the stimulus for turning upside down the traditional ways of thinking and of organizing knowledge about important questions of human biology. It has become the paradigm for change in basic and clinical science, and in many fields of medicine apparently unrelated to oncology. The Special Virus program of the early 1970s of the National Cancer Institute, for instance, may not have resulted then in discovering any well-characterized oncogenic viruses, but it did result in the definition of the tools that have not only done so, but have been applied to many other avenues of investigation. These have put oncology in the front line of discovery.

So, too, has the clinical approach to cancer both been changed and been the stimulus to change. Our approaches to the diagnosis and treatment of malignant disease have been altered from the sequential and uncoordinated application of individual disciplines to a prospective, multidisciplinary approach that is now rapidly incorporating the research laboratory as well as the statistical model into approaches to solving everyday, practical, clinical problems. The lessons learned from the need to evaluate scientifically new drugs for cancer have also been building blocks for practitioners of experimental therapeutics and drug development in all fields of medicine. Merely reading the contents pages of this text will convince even the most casual reader of the truth of these observations. It is not enough, however, that a textbook deal only with the facts of pathophysiology and the responses of the systems that unwillingly coexist with disease.

Increasingly, it is necessary to be aware of what kind of a disease the patient has, and how that disease impacts not only the patient, but also on the family and the society in which he or she lives as well as how society responds to the illness and its causes. No doubt the chronology of our scientific and clinical advances and their relation to each other and to other diseases would be enough to stimulate another edition of the *Comprehensive Textbook of*

Oncology. This book, however, extends its concerns and fields of scholarship not only to considerations of science and clinical medicine, but to all aspects of patient care. There are many human problems encountered by the cancer patient that new knowledge has created. Coping with getting well again is now as much of a problem as coping with the threat of dying. Coping with living while physically or psychologically disabled is now a significant hazard for an increasing fraction of patients. The fear that the advances in diagnosis and treatment, although real, might not apply to the individual patient, is another growing problem. Chapters in this book address these questions as part of the editors' view of a comprehensive approach to oncology. Seventy-three chapters have been added to deal with the growing body of scientific, medical, and social information that oncologists need for reference.

Finally, the editors have chosen to extend their concerns even further to those of the impact of our system on the economics of care, and vice versa. It is one of the challenges of our times that the health care delivery system is gradually restricting access to the benefits of progress through failure to insist on health insurance for all or failure of that insurance to grant approval for the application of the new technologies discovered. Is it in this arena that the explanation for the higher mortality among certain minorities and the aged lies? Or is it that our system offers with one hand what it withholds with the other? Thus, economic issues facing the oncology community, both physicians and patients, are believed by the editors to be pertinent for inclusion in this text. So, it is with this broad philosophy of comprehensiveness that the second edition of the *Comprehensive Textbook of Oncology* is offered. It provides a philosophy of content and organization that, it is hoped, will be stimulating and informative to all.

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Preface

About 8 years ago, we made our initial decision to embark on producing a truly comprehensive textbook of oncology, one that would be of value to specialists and subspecialists alike in medicine, surgery, pediatrics, and obstetrics/gynecology and that would be of use both to the practicing clinician and to the student of oncologic disease management. We were personally delighted at the exceptionally fine quality of chapters that our invited authors produced; we were equally pleased with the expertise and enthusiastic relationship that was built with Williams & Wilkins; and we were particularly pleased with the public reception of *Comprehensive Textbook of Oncology*. This combination of personal gratification coupled with the exceptionally rapid pace of fruitful and exciting research that has, is, and will lead to major diagnostic and therapeutic breakthroughs has lead us to editing a second edition. We are extremely fortunate that, for this edition, Drs. Austin Doyle, Mark Green, and Richard Kaplan have joined us as Associate Editors. Their combined expertise in basic laboratory science, clinical trials, and the association between basic science, clinical science, and clinical medicine have all combined to enrich this second edition substantially.

The second edition follows the same basic format as the first edition. We begin with introductory chapters in Part I on the basic biology of cancer. These chapters are entirely new, and we are very pleased and proud to have authors who present basic biologic science in a clear, crisp, and meaningful fashion for those of us who are not immersed day to day in the laboratory. Part II continues with chapters on approaches to diagnosis and individual chapters on each of the major approaches to cancer therapy appear in Part III. Once again, each of these chapters is almost entirely new given the rapid pace of progress. Part IV, the next and largest part, deals with each of the tumor types, giving a thorough yet concise description of the epidemiology, pathophysiology, diagnostic and therapeutic approaches, avenues for prevention, and commentaries for future directions. Once again, with rare exception, these chapters have been either extensively reworked or are entirely new. The complications of neoplasia and its treatment follow in Part V with specific guidelines for patient management. The ethical and socioeconomic issues are discussed in Part VI. Finally, a series of appendices has been inserted in this second edition for rapid, practical reference to staging, drug regimens, and the treatment of oncologic emergencies.

Cancer increasingly affects all of medicine and does so in increasingly diverse fashions. The population is aging and with it comes an absolute increase in people with cancer. The numbers of socioeconomically deprived indi-

viduals has increased and with it an increasingly complex problem of bringing prevention and early treatment to a chronically underserved population. More and more people are surviving for greater periods of time, but in the process are subjected to debilitating surgery, radiation, or drug therapies. Thus, attempts to improve the quality of life and address issues such as **community resources**, no-code status, reconstructive surgery, and the like become increasingly paramount in the overall clinical practice of oncology. The pace of basic research discoveries despite concerns of inadequate federal funding has been truly astronomical in the past decade. From this research have come new agents such as the biologic response modifiers, including interferon and interleukin, tumor necrosis factor, and the hematopoietic growth factors. These are already having important practical applications for patient therapy. Similarly, gene probes are changing the entire concept of tumor diagnosis and new approaches to molecular genetics and cytogenetics in leukemia, for example, have shown major prognostic gradients unrelated to longstanding light microscopy classifications. All of these advances and many more are dealt with in breadth and depth in this comprehensive text. As these words are written, the first FDA-approved gene therapy is being attempted. The basic science that has led to this possibility is found in this text and with it the promise of many new approaches for therapy. The issues of bioethics are developing and, as such, may provide the potential for a possible third edition. Future editions of this text almost undoubtedly will describe not only gene therapy but totally new approaches to patient management, such as techniques to prevent development of metastases, drug carrier systems that will attach to targeted cells, and perhaps, most importantly, new and effective approaches to cancer prevention.

A text of this size and complexity obviously implies that we owe a debt of gratitude to many. First and foremost, we must thank our 239 authors who have willingly given of their time and expertise, responded to our queries and our proddings, our requests for changes and our urgings to hurry, and have done so with chapters that are clearly comprehensive while remaining concise and clear. Second, we need to thank our Associate Editors, Drs. L. Austin Doyle, Mark R. Green, and Richard S. Kaplan, who have worked tirelessly to assure the utmost standard of quality. Our friends and colleagues at Williams & Wilkins who have suffered with our idiosyncrasies have been essential. While there are many behind the scenes whom we have never met, we would like to express thanks in particular to Timothy Satterfield, our Editor; Barbara Felton, our Production Coordinator; and Victoria Vaughn, our Associate Editor. Our assistants, most notably, Paula Rosen

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and Rachel Ramiro, deserve outstanding praise, for we recognize that without them this text could never have come to fruition. Paula deserves special mention for cross-checking every copyedited manuscript against the final page proofs and picking up many errors. We are thus pleased to present this second edition with thanks to those who

have contributed to its success and yet with recognition that any errors are borne by us.

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