Practical Gynecologic Oncology

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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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To our wives, Deborah and Estelle,
whose patience and support made this
endeavor possible; and to our children,
Jonathan Micah, James, and Jessica;
Geoffrey, Graeme, and Sharon.

Foreword

Close to the beginning of this century, William Osler observed that "The practice of medicine is an art, based on science." That brief characterization of our profession rings true even as we approach the next century in the midst of brilliant, accelerating scientific discovery.

Some aspects of the art—including compassion and the basic skills of history taking and physical examination—are, or should be, common to all physicians and remain largely unchanged by a century of research. In other ways the "art," which can also be translated as "craft" from the original Greek word "techne," has been greatly enlarged and diversified by science and technology. Thus the special skills required by a gynecologic oncologist derive not only from experience and practice, but also from the proliferation of knowledge in many branches of science. Indeed, it is mainly the contributions of science from obstetrics and gynecology—and from some other disciplines—that have evolved the clinical subspecialty of gynecologic oncology.

The art and the science are connected not only by ancestry, however. Their relationship continues to be an interdependent one. It is one of the ever-expanding glories of medicine that what is learned in the laboratory can enhance learning at the bedside, and what is learned from experience with patients helps to shape and direct scientific inquiry.

Doctors who remain lifelong students are exhilarated by these interconnections and make the best teachers of clinical medicine. It is in this scholarly tradition that Jonathan S. Berek and Neville F. Hacker, with contributions from distinguished colleagues in their own discipline and in fields that bear upon it, have brought together the salient information required to develop the acumen and skills that enable clinicians to understand and to care for women suffering from tumors.

Practical Gynecologic Oncology reflects the indivisibility of art and science in medicine. The two editors—one in Los Angeles and one in Sydney—worked and studied together for seven years in the same hospital and laboratories and remain mutually helpful intellectual allies on opposite shores of the Pacific Ocean.

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Preface

Gynecologic Oncology was officially recognized as a subspecialty of Obstetrics and Gynecology in the United States in 1973, and subsequently almost 360 gynecologic oncologists have been certified by the American College of Obstetricians and Gynecologists. The specialty is established in some centers in Europe and has recently been given official recognition by the relevant colleges in Britain and Australia. Hence, an increasing number of physicians are devoting their professional careers to the management of patients with gynecologic malignancies.

Since the development of the subspecialty, there has been a proliferation of societies and journals devoted to gynecologic cancer, and the field has been the subject of more intense clinical and basic research than ever before. New treatment strategies are constantly being devised, and many traditional concepts have been challenged. For example, radical vulvectomy is no longer considered necessary for all patients with early vulvar cancer, and unilateral salpingo-oophorectomy is now considered appropriate for selected patients with ovarian tumors. Individualization of treatment is regarded as desirable, and an increasing emphasis is being placed on the quality of the patient's life. It is not surprising that such issues as pelvic reconstruction and sexual rehabilitation are increasingly becoming legitimate concerns of the practicing gynecologic oncologist.

This book was written to provide a practical guide to current evaluation and treatment strategies for patients with preinvasive and invasive malignancies of the female genital tract. It is a culmination of our collaborative teaching, clinical, and research activities during the 7 years we worked together in the Division of Gynecologic Oncology at the UCLA School of Medicine. We undoubtedly have interjected some personal biases but have tried to justify our points of view with adequate reference to the literature.

We have made no attempt to cover basic research issues, but have included chapters on principles of cancer therapy, as an understanding of these principles is mandatory for proper patient care. The bibliography is not intended to be exhaustive but rather to be sufficiently comprehensive to allow each subject to be adequately reviewed. Similarly, the brief descriptions of some surgical procedures are not intended to replace a large surgical atlas. They are intended merely to help facilitate a better understanding of the basic steps involved in the particular operation.

The text has been written primarily for fellows undertaking postgraduate training in gynecologic oncology, but should also be of interest to gynecology residents, consultant gynecologists, and physicians in allied fields whose practice involves a significant component of gynecologic oncology.

The book is divided into three sections. The first section discusses general principles of oncology, particularly as they relate to gynecologic malignancies. This section includes chapters on chemotherapy, radiation, immunology, pathology, and biostatistics. The second section deals with the primary disease sites, while the third section presents topics of special interest to the gynecologic oncologist. Such topics include relevant aspects of medicine, surgery, nutrition, and psychology.

We would like to acknowledge the contribution of our colleagues who have written chapters for this book. All are respected authorities in their particular fields. We are most grateful to Gwynne Gloege for her outstanding illustrations and to Norman Chang for preparing the photography. Drs. Yao S. Fu and Fredrick Montz provided valuable suggestions regarding the preparation of the manuscript. Special thanks are due to Monique Etcheverry, who superbly coordinated and performed most of the initial word processing, and to Kathleen Ann Agbayani who, with considerable finesse, prepared the final manuscript. Additional manuscript preparation was performed by Chris Poirier.

Finally, we are most grateful for the encouragement and support we have received over the years from our mentors, Dr. Sherman Mellinkoff, Dean Emeritus of the UCLA School of Medicine; Dr. J. George Moore, former Chairman of the Department of Obstetrics and Gynecology at UCLA; and Professor Eric Mackay, Chairman of the Department of Obstetrics and Gynecology at the University of Queensland.

We trust that this book will make a contribution toward the improved care for women with gynecologic malignancies.

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Contents

Section I General Principles of Oncology

1 Chemotherapy

Robert C. Young

General Principles

Selection of Chemotherapy

Drugs capable of the relatively selective destruction of malignant cells now are used routinely in cancer patients. A wide variety of such agents are available and the selection of drugs is often difficult. Furthermore, because the vast majority of antineoplastic agents have a narrower therapeutic index than drugs of other types, careful thought should be given to the factors outlined in Table 1.1 prior to the institution of antineoplastic chemotherapy.

It is important to understand clearly the natural history of each patient's malignancy. The use of chemotherapeutic agents should be restricted to patients whose malignancies have been biopsy proved. In some instances, second opinions regarding definitive histologic diagnoses should be obtained prior to institution of chemotherapy. When doubt exists concerning the diagnosis, it is preferable to delay initial therapy and not use response to chemotherapy as a diagnostic trial.

The decision to use chemotherapy is also dependent on a thorough knowledge of the extent of the patient's disease as well as the rate of progression of that disease. Limited evidence for metastatic spread or documented slow disease progression may warrant withholding chemotherapy for a period. Because all chemotherapeutic agents produce toxicity, it is important that the physician have an evaluable tumor so that one can assess response. It is inappropriate, in general, to administer antineoplastic agents unless one can determine objectively patient benefit. Thus, except in rare instances, the determination of tumor response to chemotherapy is an important factor in treatment decisions.

The patient's particular circumstances may play a major role in decisions regarding chemotherapy. The extent of previous therapy, the patient's age, general health, and other complicating illnesses form an important part of the physician's decision and may affect substantially tolerance

Table 1.1.
Issues to Be Considered Before Using Antineoplastic Drugs

1. *Natural History of the Particular Malignancy*
   a. Diagnosis of a malignancy made by biopsy
   b. Rate of disease progression
   c. Extent of disease spread
2. *Patient Circumstances and Tolerance*
   a. Age, general health, underlying diseases
   b. Extent of previous treatment
   c. Adequate facilities to evaluate, monitor, and treat potential drug toxicities
   d. The patient's emotional, social, and financial situation
3. *Likelihood of Achieving a Beneficial Response*
   a. Cancers in which chemotherapy is curative in some patients, e.g., ovarian germ cell tumors
   b. Cancers in which chemotherapy has demonstrated improvement in survival, e.g., epithelial ovarian cancer
   c. Cancers that respond to treatment but in which improved survival has not been clearly demonstrated, e.g., cervical cancer
   d. Cancers with marginal or no response to chemotherapy, e.g., melanoma

to antineoplastic drug treatment. In addition, the patient's emotional, social, and even financial status must be respected and evaluated prior to a final decision.

Chemotherapy should not be used unless facilities are available for careful monitoring and treatment of the resulting toxicities. If such facilities are not available and chemotherapy clearly is required, the patient should be referred to a physician or another facility that has that capability.

The decision to use chemotherapy depends heavily on the probability of achieving a useful response. Not all cancers respond to chemotherapy in similar quantitative and qualitative ways. Nevertheless, tumors can be grouped into four categories by their likelihood of chemotherapeutic response:

1. In the first group of tumors, antineoplastic therapy is curative for most patients, e.g., ovarian germ cell tumors, choriocarcinoma. Obviously, a decision not to treat patients with diseases known to be curable with chemotherapy is, with rare exceptions, inappropriate. Even substantial toxicity is acceptable if the probability of cure is high.

2. In the second group, chemotherapy improves patient survival, but does not restore a normal life expectancy, e.g., epithelial ovarian cancer. Patients with these tumors usually benefit from chemotherapy, and it should be offered unless there are exceptional circumstances.

3. In the third group, responses to chemotherapy occur, but improved survival has not yet been achieved for a significant number of patients, e.g., cervical carcinoma, uterine sarcoma.

4. In the fourth group, few if any responses to chemotherapy are seen, e.g., melanoma. In such patients, the use of che-