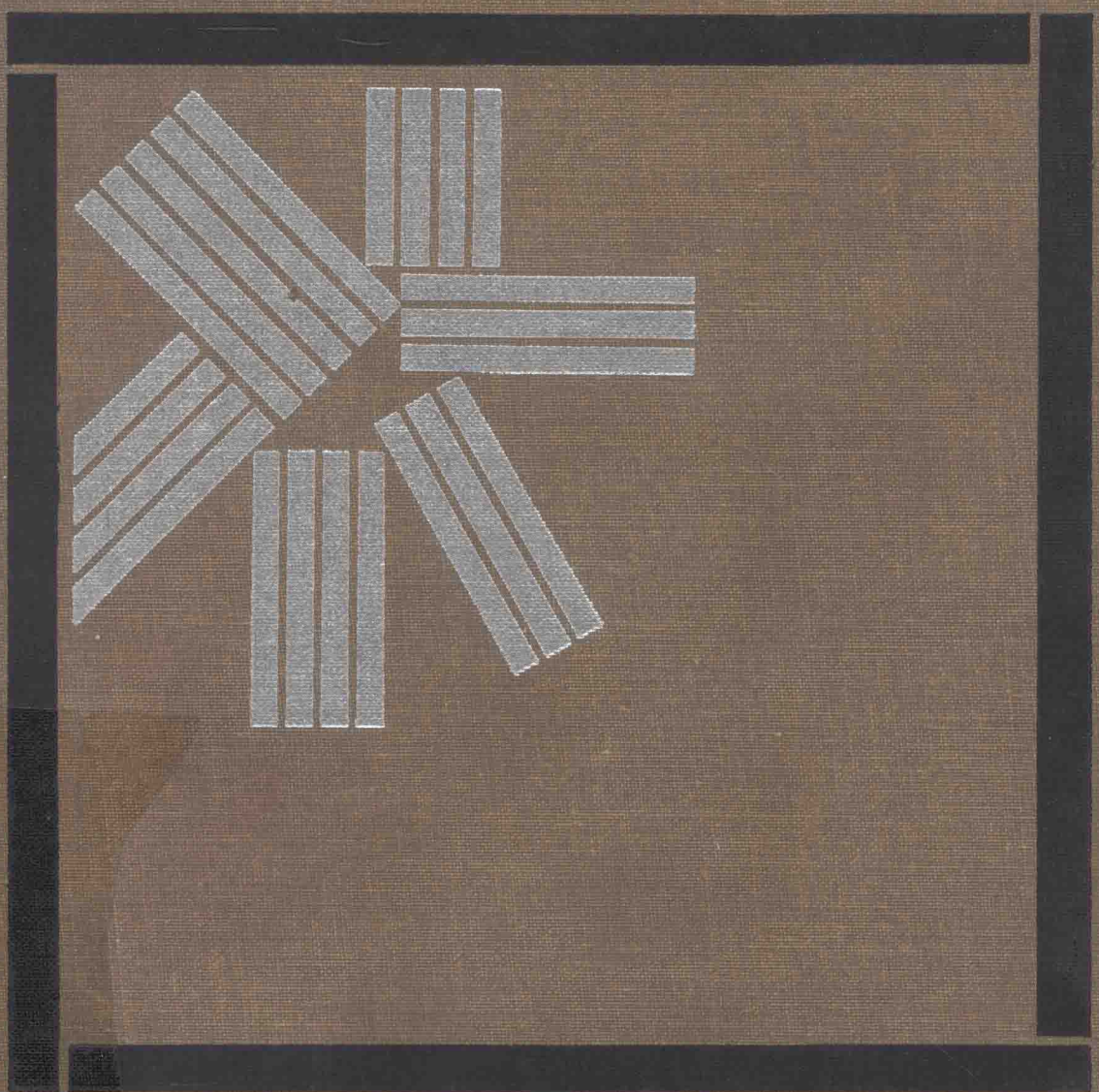
Clinical Cancer Medicine

Treatment Tactics

Edited by Jacob J. Lokich, M.D.



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The authors and publisher have worked to ensure that all information in this book concerning drug dosages, schedules, and routes of administration is accurate at the time of publication. As medical research and practice advance, however, therapeutic standards may change. For this reason, and because human and mechanical errors will sometimes occur, we recommend that our readers consult the *PDR* or a manufacturer's product information sheet prior to prescribing or administering any drug discussed in this volume.

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Clinical Cancer Medicine

Treatment Tactics

Also by Jacob J. Lokich:

Primer of Cancer Management

To my daughter Emily from whom I took the time

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Preface

With the development of medical oncology as a medical subspecialty, an authoritative and comprehensive text about cancer, *Cancer Medicine* by Holland and Frei, has appeared to explain the bridge between this field and the clinical sciences. In addition, the individual therapeutic disciplines in oncology have developed clinical texts in surgery, radiation, pediatric, and medical approaches to the neoplastic diseases. These texts serve as compendia of information organized and structured for presentation by organ.

This book adds to the growing list of oncologic texts but focuses on pratical tactics in the management of cancer and its complications and incorporates this author's individual philosophy and approach to the cancer patient. In this context, the primary care physician without special training in oncology may find the book a useful reference. A major purpose of preparing the text is to provide an instructional guide for those physicians in training and in practice who are not oriented toward oncology. The organization and structure of this text are designed to reinforce the principles of cancer management and to augment the educational experience.

Initially, this book was conceived specifically to describe the clinical approach to oncologic emergencies. It is clear, however, that those complications of cancer that are not life threatening are equally unique and complex in their management. Furthermore, such complications bridge many of the subdisciplines in medicine and surgery. Thus, the extension from oncologic emergencies to cancer complications at individual organ sites was a natural evolution and one which required collaboration and interaction among the major disciplines of medicine and surgery.

It is hoped that this book will add to the expanding list of oncology texts and will be both an educational tool and a management guide for the treatment of the cancer patient.

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Part I Introduction

Chapter 1

General Concepts in Cancer Management

J. Lokich

1.0 Introduction

The complications of cancer are myriad, and for those complications with life-threatening potential, the perspective of the therapeutic clinician has been, by and large, one of nihilism. Such an approach has been based on the assumption that the cancer patient will inevitably die and that the acute complication may obviate a long period of suffering. Consequently, it is common for the patient with cerebral metastases, for example, to be allowed to drift into coma without treatment with corticosteroids or for the patient with pneumonia not to receive antibiotics. For many patients, however, adequate therapy for the acute oncologic emergency may result in a prolonged period of disease-free survival without major treatment-related morbidity. Substantial morbidity of a complication in advanced cancer may cause pain or disability over a protracted period, and treatment for the complication may prevent the morbidity of the disease. For example, early treatment of spinal cord compression can prevent paraplegia with prolonged survival. For the less than life-threatening complications of cancer, excessive morbidity can be a consequence of inadequate treatment.

The goals for treatment of the acute complications of cancer are both to improve the quality of life and to extend the duration of life. The patient with hypercalcemic coma, acute brain syndrome, or superior vena cava syndrome may be returned to a completely functional state with minimal morbidity through specific therapy. Effective management of these cancer complications achieves prolonged survival, although the therapy is almost never curative.

2.0 Therapeutic decision-making

Cancer complications from primary or metastatic tumors involve therapeutic de-

cisions that must be based on characteristics of both the host and the tumor. The host characteristics that play a major role in determining therapy include age, performance status or functional activity, and the presence or absence of concomitant serious disease. Another morbid disease, such as renal failure, chronic heart failure, or cirrhosis, may influence the therapeutic modality to be employed and is often a critical determinant in the choice of specific treatment.

In addition to the host factors, four tumor factors critically influence treatment decisions (Table 1.1). The pathologic category of the tumor—mesenchymal, epithelial, or lymphoma, for example—and the primary site or origin—for example, lung, breast, or colon—greatly influence the therapy by indicating the tumor's potential responsiveness. A second crucial factor in determining therapy is the stage or extent of disease. In patients with extensive, local tumor bulk or multiple sites of metastasis, systemic therapy is the treatment of choice unless local complications dominate the clinical picture.

Table 1.1 Host and tumor features that influence therapeutic decision-making

Tumor

1. Primary tumor source and pathologic features
2. Stage or extent of disease (quantitative host-tumor burden)
3. Biologic activity of disease (growth rate)
4. Responsiveness or resistance to therapy (prior therapeutic reaction)

Host

1. Age
2. Performance status (functional activity)
3. Other morbid disease
4. Visceral distribution of metastases and functional reserve of organ system

Third, the biologic activity of the tumor—as reflected in growth rates and measured by doubling times for pulmonary nodules, or as measured by the interval from the primary diagnosis to the development of metastasis—may reflect the aggressiveness of the tumor as well as its potential responsiveness to therapy. The fourth determinant of therapy is the potential responsiveness to individual therapeutic modalities. Tumors notoriously resistant to radiation and drug treatment include renal cell carcinoma, colon cancers, and lung cancers. On the other hand, lymphomas and sarcomas become increasingly responsive to both of these modalities. Responsiveness to treatment also depends on response to prior therapy. For example, patients responding to hormonal therapy or chemotherapy are more likely to respond again than patients who have established resistance to one modality or another. Nonetheless, so-called "second-line" therapy is always less likely to induce a response, even in tumors generally responsive to treatment. For example, in advanced ovarian cancer, "first-line" therapy is successful in 40 to 60 percent of patients, while second-line therapy at the time of relapse may induce tumor regression in less than 10 percent of cases.

Second-line therapy is less likely to be successful because of established tumor resistance, increased tumor burden, and decreased host resistance.

First-line therapy contributes to the limitation of response to subsequent therapy not only because of potential induction of tumor cell resistance, but also because

of host effects limiting the amount of secondary therapy to be administered. One such example is the reduction of bone marrow reserve by first-line therapy. The corollary to this principle is that tumors which do not respond to primary or first-line therapy also generally fail to respond to the secondary therapy.

These general therapeutic principles relating to features of the tumor are guides, however, and not definitive principles. A common misconception in cancer management is that tumors that are pathologically anaplastic with a high mitotic index are more sensitive to chemotherapy than are well-differentiated tumors. The fact is that such tumors are more likely to develop resistance to therapy more rapidly than do slowly growing tumors, and the initial response will likely be of short duration. No data in humans currently indicate that rapidly growing tumors are more responsive tumors. The most important consideration is tumor type.

The problem of therapeutic decision-making in cancer management is the general question of when to treat, and specifically when to employ chemotherapy or radiation therapy. Combined modality treatment employs complementary methods such as preoperative radiation for rectal cancer or chemotherapy for responsive tumors. Chemotherapy may also be used preoperatively to permit less surgery for patients with locally inoperable tumors that are chemotherapy responsive. Preoperative chemotherapy for soft tissue sarcomas of the extremities has been introduced to promote limb-sparing tumor surgery as opposed to amputation. These approaches involve therapeutic decision-making for primary (local) or regional tumors.

The question of therapy for patients with advanced metastatic disease is often more difficult. The primary reasons for introducing therapy for patients with advanced disease are indicated in Table 1.2. If an established form of therapy is considered "standard," it must be associated with a reasonable degree of effectiveness as measured by tumor regression and improved survival. For example, the use of 5-fluorouracil for colon cancer and dacarbazine (DTIC) for melanoma have been considered "standard therapy" because they are associated with a 20-percent response rate. These drugs do not, however, have a significant impact on the disease because the tumor regressions are invariably partial, and survival is not affected. Tumors for which chemotherapy is associated with a 40- to 50-percent response rate and a substantial incidence of complete regression include lymphomas and cancers of the testicles, ovary, breast, and prostate. For these tumors, the effectiveness of the treatment is a primary indication for therapy even in the absence of symptoms or measurable disease.

Because an improvement in the quality of life is sometimes achieved, symptoms secondary to metastatic disease always justify therapy, even when such therapy is known to have only a marginal effect on the tumor. The presence of measurable disease that may be reasonably monitored to determine the impact of treatment on the tumor is another important component of therapeutic decision-making. Effectiveness of treatment can often be determined within one or two courses of the drug

Table 1.2 Therapeutic decision-making for patients with advanced metastatic cancer

Indications for therapy
1. Standard therapy with known effectiveness
2. Secondary symptoms
3. Measurable lesions
4. Limited prognosis