

Cancer Chemotherapeutic Agents:

Handbook of
Clinical Data

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**Martinus Nijhoff Medical Division
The Hague — Boston — London
1979**

Published by G.K. Hall & Co.
70 Lincoln Street
Boston, Massachusetts 02111

Sole distributor outside the USA, its dependencies,
the Philippine Islands, and Canada:

Martinus Nijhoff Publishers
P.O.B. 566
2501 CN The Hague, The Netherlands

ISBN 90 247 2170 9

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This publication is intended to serve merely as an outline guide for those skilled in chemotherapy. Care has been taken in compiling and checking the information; however, in NO circumstance should the information and protocols be used as a substitute for current medically accepted diagnostic and treatment procedures. The information is abbreviated and serves only to improve recall and assist in the normal diagnostic and therapeutic processes. Therapeutic decisions, including doses, intervals, and routes of administration, should be based on information contained in more comprehensive references. Neither the authors nor the publisher will be responsible for the continued currency of the information, for any inaccuracies, or any consequences of the clinical use of this material.

The authors wish to express their appreciation to Ms. Mary D. Allman and Miss Loretta A. Borah for their painstaking efforts in typing and proofreading the manuscript.

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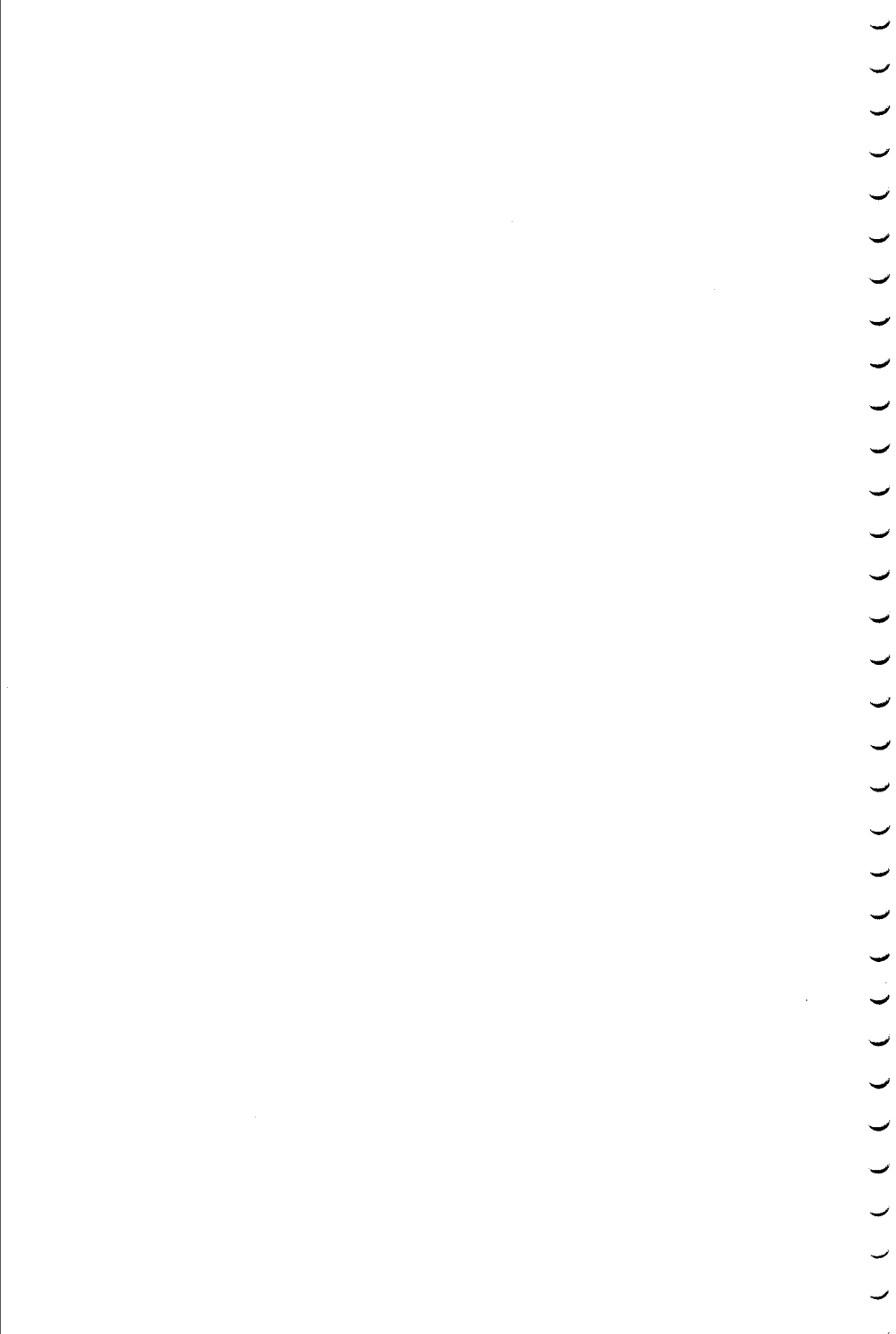
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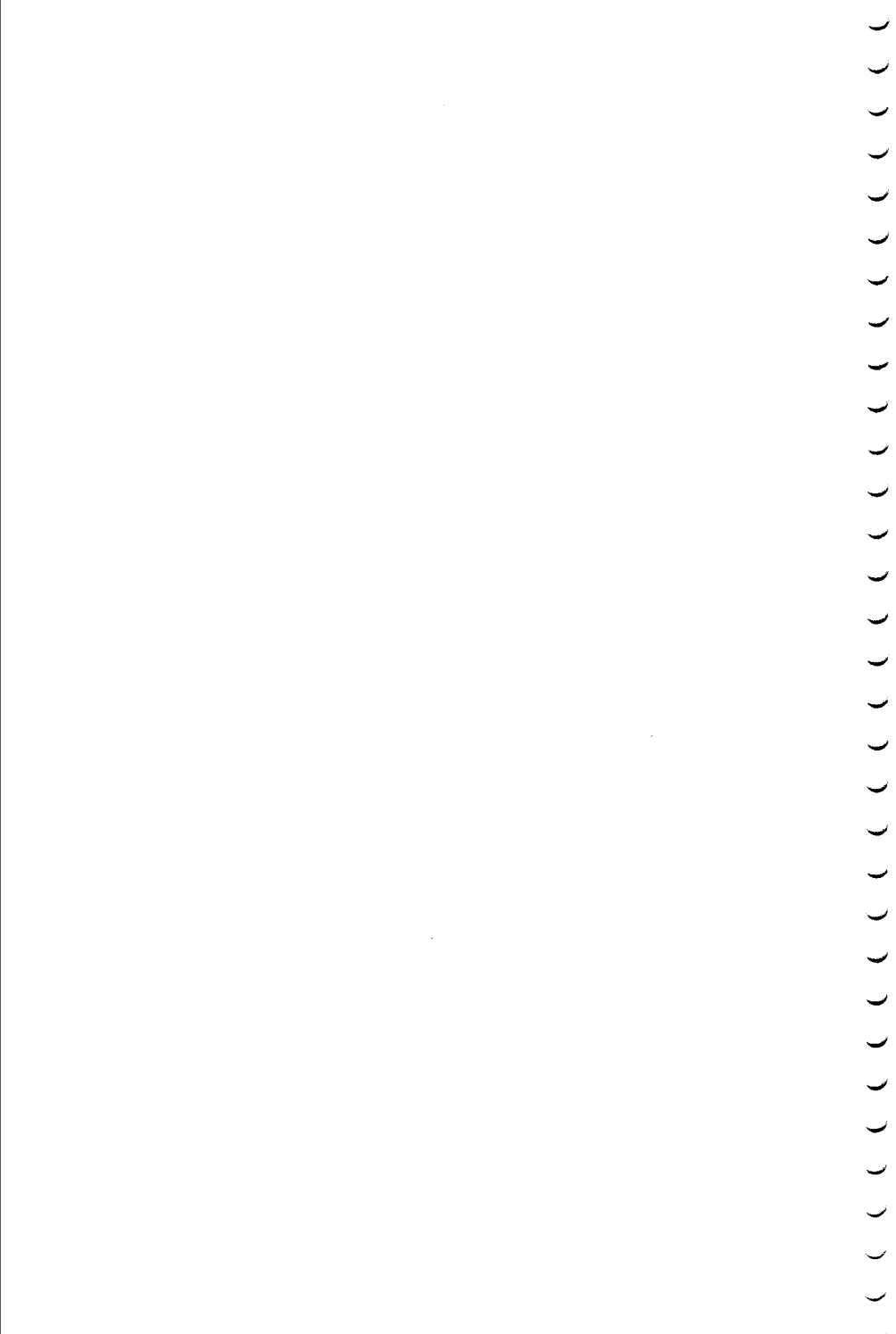
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Cancer Chemotherapeutic Agents



Introduction

Cancer Chemotherapeutic Agents brings together from many diverse sources information relevant to the preparation and administration of drugs used in cancer chemotherapy. Drugs are listed alphabetically by nonproprietary name, and many of their trade names are identified. This is not, however, a comprehensive listing and should not be considered an endorsement of any product or manufacturer. This handbook has been prepared for use by physicians, pharmacists, and nurses involved in oncology. It should also prove to be particularly helpful to those health professionals who find themselves newly involved with cancer treatment in wards and clinics of health-care facilities. As cancer care rapidly expands throughout this country, more and more individuals find themselves at least peripherally involved. The authors sincerely hope this text will make that involvement easier.



1

Principles of Tumor Cell Biology

1. In preparation for division, all renewing cells go through a series of stages (the cell cycle) that includes G_1 (protein and RNA synthesis), S (DNA synthesis), G_2 (protein and RNA synthesis), and M (mitosis, cell division).
2. The *growth fraction* is the percentage of cells in a tumor that are in the cell cycle (proliferating pool).
3. Large differences in tumor doubling times in man cannot be explained on the basis of small differences in cell cycle times. Cells in the resting phase (G_0), tumor-cell death, and tumor-cell differentiation must be considered.
4. Normal cell growth is limited by certain genetic and epigenetic factors, such as various growth factors, nutritional needs, and cell-cell interactions.
5. Cells may lose all capacity to grow (static cells), resume growth on stimulation (expanding cells), or continuously replace effete elements (renewing cells).
6. The basic oncologic problem is the partial loss of control that would normally regulate expansion of a proliferating pool of cells.
7. Tumor size is directly proportional to the number of tumor cells, which is inversely proportional to the growth fraction.

8. A single unchallenged tumor cell can proliferate in an exponential fashion to kill the host. As the tumor size increases, cell proliferation slows, at a rate approximating a Gompertzian growth curve.
9. There is a normal host mechanism based on tumor-specific membrane antigens, which serves to initiate an immune response and eradicate small numbers of tumor cells.
10. Malignant disease becomes clinically manifest only when a large tumor burden is present (e.g., 10^8 cells or more).
11. Some, or perhaps most, tumors produce biochemical markers or fetal proteins, which may be detectable when other clinical evidence of tumor cells is absent.

Current incidence figures for carcinoma in the United States by site and sex are presented in Table 1.

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2

Principles of Cancer Chemotherapy

1. Chemotherapeutic agents act through first-order kinetics (fixed percentage of cell-kill), with subsequent survival inversely correlated with the initial tumor-cell mass.
2. All chemotherapeutic agents affect normal tissues as well as malignant cells. Renewing populations of cells, including bone marrow, gastrointestinal mucosa, and skin, are most severely affected.
3. Phases of chemotherapeutic management
 - a. Supportive care only
 - b. Palliation/symptom control
 - c. Remission/induction
 - d. Remission/consolidation
 - e. Remission/maintenance
 - f. Cure (adjuvant therapy)
4. Factors influencing chemotherapeutic responsiveness
 - a. Type of malignancy
 - b. Proliferative state of malignant cells
 - (1) Growth fraction (percentage of cells in cycle)