Synopsis of Clinical cancer

SECOND EDITION

Condict Moore

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To

Virginia, Martha, and Michael

Preface

This summary of clinical cancer information originates from twenty years of learning, teaching, and practice in the field of oncology. It results from the study of cancer in many aspects: cancer in the patient at first diagnosis, cancer at the operating table, cancer under radiotherapy treatment, cancer in the gross and microscopic pathology laboratory, cancer in the follow-up clinic or office, cancer in laboratory animals and in statistical follow-up analyses, cancer in the family and social setting, and the cancer patient undergoing rehabilitation. Notes for lectures, talks, and seminars for medical students and practitioners, generally well received, have been expanded and updated. The wide scope of training given at the Memorial Hospital in New York City enabled me to begin work in cancer some years ago from an unusually broad base of knowledge about many types of cancer, and with an enthusiasm for the diagnosis and treatment of cancer considered naive by many. In retrospect the sum total of advances made in cancer during the past two decades justifies much of this enthusiasm.

In spite of undoubted advances a defeatist mythology persists about cancer in the minds of most doctors. I hope to help dispel this myth by the broad scope of the book, inclusion of very recent data, clear expression, condensation, separation of basic from trivial information, and emphasis on similarities among the various cancers, and by placing cancer in better perspective within the field of medicine.

Medicine seems to advance by steps. One consists of discoveries by superspecialist investigators; another step is the communication of newly discovered knowledge so that all may understand and use it. Physicians who feel responsible for communicating cancer information work, as a rule, in isolated specialties and in large institutions where they see only complicated or advanced cancers. The busy practicing physician who recognizes and controls localized cancers has little time to report his experience; he passes on quickly to more pressing problems. Communications that encompass the whole field from experience are, therefore, rarely achieved.

This volume is an attempt to perform a communications task that seems to need doing. Most of this material has already proved its appeal and usefulness

for medical students, house staff, and practitioners in our local area. I hope it serves as an introduction to cancer, a first reference, or a handy review for students and physicians in all specialties. I also hope it will prepare the reader to use recent and future discoveries in the emerging area of cancer prevention, an area destined to become an increasingly productive part of medical practice.

No one individual can be an expert in all fields of clinical cancer. I gratefully acknowledge the willing cooperation and careful, detailed criticism given by colleagues on the faculty of the University of Louisville School of Medicine during the preparation of this volume. Mention of these individuals does not necessarily mean that they approve all the ideas expressed herein. There are many controversial areas in clinical medicine, particularly in the field of cancer, where few individuals exactly agree. Nevertheless, without the unselfish cooperation of the following physicians this work would not have been possible: Drs. Marion F. Beard, William M. Christopherson, Marcine Davies, Ellis A. Fuller, Laman A. Gray, Douglas M. Haynes, James W. Harkess, William W. Johnson, Donald R. Kmetz, Roderick Macdonald, Fitzhugh Mullins, Rudolf J. Noer, Herbert T. Ransdell, Ralph M. Scott, Donn L. Smith, and Beverly T. Towery.

The excellent volume on cancer by Drs. Lauren V. Ackerman and Jual A. del Regato, edition 3, has been used extensively as a reference in nearly every chapter.

Mrs. Catherine Bauscher, medical artist, has brought unusual skill and experience to the preparation of the illustrations. A considerable debt is due the reference librarians, Mrs. Ruth Atwood and Miss Nancy Lorenzi, of the Kornhauser Health Sciences Library, University of Louisville. Dr. H. R. Pascoe of St. Louis contributed to an extensive revision of the chapters on lymphoma and leukemia. Dr. Lawrence W. O'Neal, also from St. Louis, gave valuable criticism of the chapter on the adrenal gland. The preparation of the manuscript has been most ably handled by Miss Edna Henderson, Miss Jean Fortwengler, and Mrs. Patricia McWilliams.

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Chapter 1

Introduction

Most physicians realize the fundamental changes taking place today in our approach to cancer; we are beginning to study causes rather than being content to describe effects. Next to pathologists, treatment specialists have led in the development of oncology; but surgery and radiation today have nearly reached their limit of effectiveness. We need surgeons and therapists more than ever, but other groups are now able to participate at the forefront. Chemotherapy has entered the picture and, although generally unsuccessful, it is a modality that all can use and one that compels us to undertake the biologic study of basic growth phenomena. We might reasonably predict that, as in other fields, the control of cancer will come from those who study basic mechanisms.

For these reasons, and because molecular biology and chemistry have given us new conceptual tools and new laboratory methods, the field of neoplasia is finding a firm foundation and a unification. Unifying trends appear in several areas: (1) we now accept neoplasia as a single field of study; (2) we can now recognize the outline of similar types of phenomena that precede many anatomically different tumors; for example, the same chemical carcinogen may produce different tumors in different organs and species at different times, but probably by the same basic process; (3) we can easily visualize the mechanisms of metastasis common to many diverse tumors; (4) we can apply a single method of early tumor detection, cytology, to different tissues of the body; (5) we find similar "precancerous" changes in different tissues when we seek them intently; (6) we often find that one drug inhibits growth in different types of tumors, whereas a single type of tumor responds to several different drugs. Until these and other ideas coincided, cancer reports treated each type of tumor as an isolated syndrome rather than as an example of a common growth disorder.

James Ewing drew all tumors together into a single field for study in 1919 by his monumental book, *Neoplastic Diseases*. However hard he sought a unifying thread, Ewing actually featured the differences among cancers, so painstakingly did he review all publications and so carefully did he eschew irresponsible speculation. Recent fairly reliable data, both clinical and laboratory, now make some responsible speculation possible. Neoplasia begins to take form in our minds as a *universal tissue response*. The peculiar combinations of cancer's antecedent cir-

cumstances (environmental, genetic, and metabolic) are as multiple and variable as are the morphologic growth patterns that result; but the fact remains that nearly all tissues develop tumors.

Traditional "mechanistic" concepts of tumor growth, with emphasis on gross and microscopic morphology, size, and anatomic relationships, although fundamental to a complete picture of neoplasia, now run second in importance to our growing understanding of cell and tissue growth processes, cell differentiation, and growth control mechanisms. The anatomic relations of a tumor, so vital to the therapist, soon fail the modern diagnostician as a basis for progress. Seeing the success of cervical cytology, the practitioner realizes that tomorrow's cancer control depends on recognition of minor tissue changes long before gross anatomic alteration takes place.

The strong need exists to emphasize neoplasia as a unique field of study, just as one studies infectious diseases, metabolic diseases, and trauma. No longer does the traditional assignment of tumors to traditional departments satisfy fundamental concepts of neoplasia. In the past some tumors were considered medical, others were considered surgical, and still others radiologic. Other tumors were parcelled out to various anatomically oriented specialties. Today all specialties must deal with cancer. Cancer is a truly multidisciplinary, interdepartmental disease complex. Only its consideration as a single, although complicated, pathologic process can give the beginning clinician a proper platform upon which to build future knowledge integrated with future experience.

RATIONALE FOR A SYNOPSIS

Comprehensive textbooks on cancer must necessarily be bulky because of the many volumes of publications they attempt to cover. Increasingly difficult revisions due to the rapid pace of new discoveries, make each new edition larger and less up-to-date. Few students will purchase such expensive texts as collateral or unrequired reading without a scheduled, required course on tumors in the medical school curriculum. Few of these courses, texts, or students exist. The student will pick up spotty information on tumors in medical and surgical tomes while hoping to get his turn at a cancer text in the library. If he writes a paper, he will rely on highly detailed journal reviews, abstracts, indexes, and library retrieval systems. The comprehensive text is the best starting point for a study of a particular tumor, but where does each beginner get enough reliable, basic information about neoplasia in general, related to each tumor in particular, to prepare for a meaningful clinical experience? He needs an accurate clinical sketch at the start and always at hand for check and review. He needs a basic orientation about tumors in general, a fundamental pattern into which he can fit each tumor patient to supplant memorization of a hundred or so isolated tumor syndromes.

A synopsis of clinical cancer information may be one answer to this problem. It can supplement any clinical departmental teaching program, can serve as a "starter" in courses with heavy tumor content, and can act as a "refresher" for practitioners. The reader of such a synopsis will have contact with data carefully selected by physicians who have had wide clinical experience with many types of neoplasia. Most clinicians have a limited experience with a variety of cancers

and perhaps an in-depth experience with only one. It is natural to view the world through one's own glass.

A recent remark by a family physician who had practiced for 40 years in a rural town illustrates the extreme of this situation. When a woman with breast cancer whom he had referred for treatment was returned with a good prognosis for 5-year survival (80%), he stated that if she were alive and well in 5 years he would be very much surprised because she would be the first such person he had seen in his entire medical practice. He had seen a great deal of advanced breast cancer and believed that he knew about cancer in general—it was invariably fatal.

On the other hand, most basic laboratory scientists have little clinical orientation. Although they contribute much to our basic concepts, they are unable to bring these to the bedside. Thus bridging the gap between the burgeoning biologic sciences and highly specialized and departmentalized clinical medicine to produce an integration of clinical and laboratory knowledge is necessarily slow. Beginning clinicians need to know how to make a start in such an integrative process and to realize their responsibility for carrying the process ever further during their professional lives.

A synopsis may mislead by oversimplifying, thus demeaning the importance of a field of study; it may select data poorly; or it may prevent the student from developing deep interest by seeming to sanction the adequacy of superficial review. However, the advantages of a carefully prepared condensation seem to us to outweigh these possible drawbacks. In addition to what we have said above, all of us are only too aware of the confusion and profusion of journal reports that flood us and threaten to inundate us every month. Any reasonable attempt to select and condense this material pays dividends to the student or physician beginning to review. In considering medical school curricula the new "core" curriculum nearly abolishes the lecture type of presentation of material to a large group of students. No effective opportunity remains for imparting the heart of cancer information to an entire group, but it must be done. Furthermore, with the advent of audiovisual aids and programed teaching to the learning process, codification of data in each discipline will eventually be required. A synopsis could constitute the first step toward programed teaching.

We do not suffer the delusion that we can present for clinicians the best possible synthesis of laboratory and clinical information about cancer. We merely present an effort at such a synthesis at this time. We urge the clinician to examine it and, after careful study and reflection, to improve upon it.

SPECIAL EMPHASES

In this résumé we aim at the student, resident, or young practicing general clinician, not the training specialists expert in one technique of therapy. We will not give lengthy descriptions of treatment. Several treatment modalities and the principles of treatment for each particular regional cancer are mentioned in each section, but detailed discussions of therapy will merely distract from our purpose —understanding cancer. We will try to emphasize the similarities of the neoplastic process wherever possible. Mechanisms of origin will be mentioned wherever they seem well founded. An attempt will also be made to reflect the more recent

realistic attitudes toward clinical cancer that have arisen because we have gained greater experience with this disease.

Now that the increasing possibilities of cancer control with our present knowledge of therapy become apparent, a general attitude of cautious optimism begins to replace an older, uncritical pessimistic approach. The concept of control rather than cure stands today as the real aim of cancer treatment. Prompt and vigorous rehabilitation of cancer patients is becoming more widespread. Wider appreciation of the importance of environmental agents in cancer causation promises real benefit in terms of cancer prevention and control; thus the growing wish of the medical profession to accept its responsibilities for the practice of preventive medicine is becoming possible in an increasing number of cancers.

When a point of information is controversial, simple mention of this will have to suffice without lengthy justification. The largest amount of space has been allotted to those cancers of which knowledge of etiology, diagnosis, and treatment has advanced enough to reward clinicians' efforts in terms of numbers of patients salvaged. Cancers that kill most patients, such as those in the esophagus, are not accorded extra space merely because of high mortality. In the résumé we seek to give a balanced importance to the three disciplines primarily involved in cancer —pathology, surgery, and radiology—without showing bias for one or the other. Such an even balance is seldom attainable, but our intention is to treat them equally.

CLASSIFICATION

Much as we are devoted to unifying the various clinical cancers, we have not tried to impose unity by attempting a new classification of cancers; far wiser men have tried and failed. Traditional classification by gross anatomic site gives us little information about tumor behavior. On the other hand, grouping of tumors by the function of the tissue of origin, although basic and enlightening, becomes confusing when followed to its logical conclusion. For example, small bowel mucosa acts like a lining tissue and produces a garden variety of gastrointestinal adenocarcinomas; it also acts like a secreting, absorbing, glandular tissue and produces carcinoid tumors of most unusual behavior.

Two fundamental points about tumor classifications bear emphasis: (1) structure and function (they always go together) of the tissue of origin exert great influence on the behavior of the cancer that develops from that tissue; and (2) tissues of basically similar structure and function occur in widely separate organs all over the body, whereas quite different tissues occur side by side in the same organ. Cancers of the mouth and anus behave in basically similar ways according to the similarity of the squamous epithelium in the two locations. However, the kidney produces two cancers that behave in dissimilar ways—the parenchymal cells of the collecting tubules and the lining cells of the kidney pelvis have considerably different structure and function. If we expect gross anatomy to correlate with tumor behavior, we court confusion. But if we study the tissues and cells of origin from the viewpoint of microscopic structure and detailed physiology and embryology, a picture begins to form of basically consistent tumor types arising from similar tissues.

Throughout we will endeavor to emphasize "early" cancer. However, under sections on natural history of the various cancers, descriptions of "late" disease will be included for contrast and background. We have included a section on "precancerous" lesions in many chapters. The term is properly in disrepute among pathologists and other experts on neoplasia because proof is lacking of the inevitable advancement of any of these lesions to invasive cancer. But we badly need some term to convey the idea that in most cancers there are tissue changes indicating preparation for invasive cancer, changes that mean a predisposed tissue. The more we look for these changes, the more we find them. We do not imply that a "precancerous" condition inevitably becomes cancer, but only that the *strong probability* exists.

Benign tumors will be given attention equally with the malignant tumors in some chapters; in other chapters they will only be mentioned among the differential diagnoses. Because benign tumors play a large role in diagnostic thinking at some sites and a small role in others, they will be treated somewhat irregularly. Emphasis throughout the synopsis will be on malignant neoplasms.

The volume is designed to be useful clinically, not as a reference book. A few references appear at the end of each chapter so that the reader may begin to compose a bibliography by consulting these references.

STATISTICS

We include a short chapter on end result reporting. Numerical data, necessarily part of the clinical lore of each regional cancer, appear in the text as approximate percentages only to confer a general idea of their value. Exact percentages of patients salvaged, for example, are of limited accuracy and of limited clinical value despite the extreme emphasis accorded them in cancer publications. Data on the incidence of each regional cancer are expressed as relative proportions of the total number of cancers. Absolute rates on incidence, prevalence, and mortality do not appear because imperfect reporting systems make the majority of such figures too suspect to be worth a student's concentrated effort at the beginning of the study of cancer. There is no section on the increasingly contributive field of cancer epidemiology; the sections on incidence, distribution, and etiology will note important epidemiologic data. When interesting geographic variations in the incidence of some cancers are mentioned, this does not necessarily imply hereditary, genetic, or racial basis for such distribution.

THE GOOD PHYSICIAN

The good physician is a rare human being. The most difficult activity of the human mind is a good physician's job—to analyze the multiple biologic variables of illness and to correlate basic scientific data with the individual needs of an ailing human being. It is a rare mind indeed that optimally responds to the emotional and physical illness of a patient with a fruitful mixing of his own scientific knowledge, sympathy, and logical deductive powers. Each physician aims for this optimum. Cancer offers him a special challenge—absolute cure is often possible, the disease is frequent, and it is inevitably devastating if nothing is done.

The good physician begins to develop when he first enters the physician-

patient relationship. He must realize the value of this relationship from the start. Here he first has a chance to practice the analysis of the multiple biologic variables in solving the problem of illness, an analysis requiring a more intimate blending of rigidly critical judgment and intuition than perhaps any other human activity. For this valuable analytical situation an outline, at least, of clinical background information about disease is essential. Without a minimum fund of clinical information to begin with, the clinician cannot take the first step toward understanding the process and component types of activity involved in the complex doctor-patient interaction. The learning doctor, who is an "applied" scientist, must have some guide to reliable clinical correlations as a background to apply before he can get the feel of the new vital role he is beginning to explore. In this regard, carefully prepared synopses of clinical information may be of help.

The qualities of a good physician are probably inherent and cannot be instilled at the graduate student level. Most aspiring clinicians possess these qualities and need only to have them stimulated. Some of the basic qualities, such as intellectual curiosity, intellectual honesty, deep concern for the individual human and his physical and mental health, and a real desire to be of service, can be fertilized by observing what facets and facts of human disease an older teacher selects as important and which ones he rejects. Here, again, some indications of this process may be evident from a synopsis.

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Chapter 2

Glossary of terms

Physicians dealing with neoplasia have evolved special meanings and usages for common words to describe more easily the material in their field. We will attempt a simple definition of some of these terms.

anaplastic Similar to the term undifferentiated, describes a tumor whose cells uniformly lack special cell characteristics.

benign tumor Neoplasm of partially controlled growth character that will not metastasize and will rarely cause death.

biopsy Strictly defined, the whole diagnostic process of securing a tissue specimen *plus* the interpretation by the pathologist; commonly used more loosely, the technical maneuver of taking the tissue specimen from the patient.

excision biopsy Narrow removal of a whole lesion for diagnosis, not for treatment.

negative biopsy Biopsy showing no cancer.

positive biopsy Biopsy showing cancer.

wedge biopsy Excision of a portion of a lesion for diagnosis.

cancer Any malignant neoplasm, regardless of histogenesis.

capsule Condensation or thin layer of compressed tissue at a growing tumor edge or the wall of cystic neoplasms, sometimes found with benign and malignant tumors. It was formerly considered a barrier to cancer spread. A better term for a cancer capsule is pseudocapsule, which implies a lack of any real function as a barrier to spread.

carcinoma Malignant neoplasm of epithelial origin.

chemotherapy Usually means treatment with a nonhormonal, cytotoxic drug.

cobalt 60 Radioactive source emitting the same general types of rays as x-ray machines and thus used for treatment of neoplasms.

cocarcinogen Agent that enhances the cancer-producing action of another agent.

cure Complete arrest of growth of cancer cells, primary and metastatic. It is, of course, the ultimate aim of treatment. This word must be used with circumspection because recurrences sometimes develop after many years. If a patient's survival is such that his calculated life expectancy equals that of the general population of the same age and sex, then this amounts to clinical cure. "Five-year cure" merely means 5-year survival without evidence of cancer.

differentiated Cells with characteristic features that correlate with specialized function.

direct extension Spread of cancer by continuous, invasive growth in contrast to spread by metastasis.

five-year survival Appropriate yardstick of successful management in many cancers, implying the probability of cure, while admitting the possibility of later recurrence. (In some other cancers, 10-year survivals may be more appropriate—breast melanoma, and lymphoma.)

gland Organ of internal or external secretion, as distinct from a lymph node.

grade Histopathologic class (usually I through IV) sometimes assigned to tumors by pathologists to help determine prognosis.

growth rate An imprecise expression dependent on clinical impressions. Precise measurements and comparisons of growth rates in human tumors have seldom been made. True growth rate depends upon concepts of cell population kinetics (Chapter 3).

initiator Agent that can start the first essential phase of the carcinogenic sequence.

irradiation Maneuver of using special rays, such as x-ray, to treat tissues and cancers.

latent period (latency) Time between the application of a carcinogenic agent and the clinical appearance of cancer.

leukemia Malignant overgrowth of blood cells.

local recurrence Reappearance of tumor at the primary site in the area of tissue treated or operated on.

local surgery Removal of all tissue around, and including, the primary tumor.

lymphoma Malignant neoplasm of lymphogenous origin.

malignant tumor Neoplasm with uncontrolled growth behavior, usually with the capability of metastasizing and the potential of killing the host.

margin Width of cancer-free tissue at the edges of a specimen.

megavoltage Very high energy x-rays (1000 kilovolts or more).

metastasis Established, spontaneous graft of malignant cells that takes place by embolization of cells in lymph or blood or by free-floating transport in a cavity.

- **distant metastasis** Any metastasis beyond the tumor region at a more remote site in the body.

neoplasm New growth, lacking normal growth controls.

node Lymph node.

- **negative node** Lymph node *without* metastasis on histologic examination.
- **positive node** Lymph node *with* metastasis on histologic examination.
- **regional nodes** Collection of lymph nodes nearest to the primary tumor.

orthovoltage X-rays of medium energy (200 to 400 kilovolts).

palliation Treatment aimed at symptomatic relief or prolongation of useful life only, without expectation of cure.

precancerous Tissue and cell changes that *probably,* but not necessarily, will progress to cancer if given enough time.

primary Original cancer at its original site.

promoter Agent that cannot initiate but can push forward the carcinogenic sequence once it has begun. (Sometimes we cannot distinguish between promoter and cocarcinogen.)

rad Commonly used unit of x-ray dosage, expressed as the amount of radiant energy (100 ergs) absorbed per gram of tissue.

radiation General phenomenon of x-ray production from natural and man-made x-ray sources. Used improperly sometimes to mean treatment by x-rays.

radical surgery Usually a complete removal, in more or less one block, of all local tissue and regional nodes that might contain cancer; usually done with intent to cure.

recurrence Clinical reappearance of cancer after its disapperance under treatment. It represents microscopic *residual* cancer that finally grows to a grossly detectable size.

regional node dissection One of the standardized operations for removal of nodes in the largest collection nearest the primary tumor (neck, axilla, groin, pelvis, retroperitoneum, or mediastinum).

sarcoma Malignant neoplasm of mesodermal origin.

second primary New, distinctly separate cancer developing from a new, separate carcinogenic process.

stage Degree of clinical spread of a cancer in the body (Chapter 31).

survival rate

- **crude survival rate** Simply the proportion of all patients seen who were alive at a given time interval after the last patient was admitted to the study.
- **relative survival rate** More accurate; the effect of cancer on longevity by adjusting for age and for the "natural" attrition of deaths from other causes.