



International Union Against Cancer
Union Internationale Contre le Cancer

Manual of Clinical Oncology

Third Edition
Fully revised



Springer-Verlag Berlin Heidelberg New York

Manual of Clinical Oncology

Edited under the auspices of the
International Union Against Cancer

Third Edition
Fully revised

With 44 Figures

Springer-Verlag
Berlin Heidelberg New York 1982

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ISBN 3-540-11746-6 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-11746-6 Springer-Verlag New York Heidelberg Berlin

ISBN 3-540-08868-7 2. Auflage Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-08868-7 2nd Edition Springer-Verlag New York Heidelberg Berlin

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Typesetting, printing and bookbinding: Oscar Brandstetter Druckerei GmbH & Co. KG,
Wiesbaden.
2121/3140-543210

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E49

Preface to the Third Edition

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The continuing success of the UICC's "Clinical Oncology" and the continuing refinement of our educational objectives in cancer designed for graduating medical students and young practitioners, coupled with significant additional knowledge in the cancer field have all led to the decision to publish a Third Edition. The collaboration of the World Health Organization (WHO) and the Pan-American Health Organization (PAHO) in our international and regional conferences in cancer education and the development of courses using the Manual as a basic resource have aided further definition of the UICC's role in cancer education throughout the world.

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Our Revision Committee believes that we have incorporated in this small volume most of the knowledge about cancer which it is essential for all students and practioners to know and that we have done so in a clear and concise manner.

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A large proportion of the material presented herein is devoted to basic aspects, yet presented so that the clinical implications are clear. Although we do not feel that general physicians need to know minor details about all cancers, we feel it particularly important to be somewhat thorough in our discussions of the more common cancers. We have omitted discussion of the rare cancers, and limited ourselves to the major concepts and principles of the less common cancers. Although there is no intention to cover oncological research in this Manual, it was felt important for young physicians to have some understanding of the role basic research contributes to the care of patients. Therefore a brief overview of selected areas in which research is about to impact on clinical work has been prepared under the auspices of the US National Cancer Institute.

The table of contents, then, serves as an outline of our "educational objectives". We feel the Manual is concise, clear, not encyclopædic, and that it should be read and understood in its entirety. The whole of Part I is especially important and should be read carefully prior to taking up Part II.

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The Manual has been translated into many languages and our central UICC Committee continues to work with those who are translating and adapting the book for local use in different parts of the world. Although the most common cancers in one part of the world may be quite different from those in another part, the basic concepts and principles are much the same.

As one aspect of its Professional Education Programme, the International Union Against Cancer has laid particular stress on the need for “improved organization” of cancer education in the world’s medical schools. One method suggested to attain this objective is the establishment of a separate department (chair) of oncology which has, as one of its responsibilities the co-ordination and integration of cancer education both in the preclinical and clinical years; an alternative is an interdepartmental committee of basic and clinical faculty.

More than any other area of medicine, oncology “demands” the integration of basic and clinical sciences, since the clinical oncologist of today must know and use a great deal of basic science – carcinogenesis, epidemiology, screening principles, cell biology and metabolism, cytokinetics, pharmacology of cancer chemotherapy, basic principles of surgery and radiation therapy, etc. In order to avoid gaps, fragmentation and unnecessary duplication, and also to develop appropriate teaching materials and experiences, it is essential to prepare a broad-based educational plan. With good planning and careful execution, an integrated cancer programme can “reduce” the curriculum time necessary to accomplish this objective and yet do a better job. Indeed, the integrated cancer committee can be a driving force in improving the medical school’s educational programme and also serve as a stimulus and example to other departments. It is hoped that this Manual will be an important resource in every medical school.

The Manual Revision Committee
of the UICC

1982

Preface to the First Edition

There can be no doubt that a knowledge of cancer is becoming of increasing importance to doctors throughout the world. The changing patterns of disease incidence, following changes in living standards and public health services and in medical diagnosis and treatment, reveal the importance of neoplastic disorders as causes of morbidity and mortality. If doctors are to recognize these conditions at the earliest opportunity and advise on the treatment, they must be familiar not only with clinical appearances but with the scientific principles on which the management is based. These are so important that they must be assimilated during undergraduate medical education and become an integral part of the doctor's professional equipment.

The clinical study of a neoplastic disorder has usually been related to its site of appearance in the body, and its treatment has been the concern of organ- or system-specialists. This has tended to obscure the fundamental principles of growth disorder which are common to many varieties of tumours. A unified approach of clinical oncology can recognize common features and highlight diversity as a stimulus to further investigation. It is at the same time becoming increasingly recognized that neoplasia is a multidisciplinary problem, requiring the collaboration of many specialists: physicians, surgeons, radiotherapists, chemotherapists, pathologists, immunologists, epidemiologists, and many varieties of research workers. But the fate of the individual patient with cancer is often determined by the first doctor he consults, and this further emphasizes the importance of sufficient education in oncology at all stages of medical training.

The Committee on Professional Education of the International Union Against Cancer has therefore prepared a Manual incorporating accounts of those aspects of neoplastic disorders which are likely to be important to a practising physician in any part of the world. The incidence of various tumours varies considerably with geography and other factors; but in this volume an account will be found firstly of the general principles which underlie the processes of growth disorder, and later the principles of treatment of the commoner tumours. This conspectus of neoplastic disorders is commended for the use of undergraduate medical students during their clinical period, and for doctors during their general professional training. It is hoped that it will also be of value to family physicians as an initial and rapid reference source.

While principles remain, rapid advances are occurring in the methods of treatment of cancer, and it is intended that the Manual shall be revised regularly in an attempt to conform with the best of current methods of treatment. The Committee on Professional Education would be glad to have comments of readers, both medical students and specialist teachers, on how these aims can best be achieved.

1972

The Committee on Professional
Education of the UICC

Acknowledgements

This Manual could not have been written without the unselfish help of many friends and colleagues whose work deserves great credit. In particular, thanks should be given to: Dr. N. DAY, Dr. C. MUIR, Dr. A. LINSELL and Dr. R. SARACCI of the International Agency for Research on Cancer, who revised the various sections on epidemiology, ætiology, occupational factors in carcinogenesis, pathology, natural history of cancer, and mass screening and early detection; Dr. R. HUTCHINS; Dr. W. KARSHIN, Dr. R. KEATING and Dr. E. McKELVEY, who were responsible for developing Part III; Dr. R. QAZI, who revised the section on the principles of chemotherapy; Dr. R. KENNEDY, who revised the section dealing with the eye; Dr. M. MOTT, who revised the section on childhood cancers; and Dr. W. LEHMANN, who contributed to the chapter on head and neck cancers.

Thanks should also be given to those who contributed to the First and Second Editions of this Manual and especially those who gave advice and assistance in the revision work.

The Committee would like to express its appreciation to Mr. D. W. REED, who acted as Committee Secretary and provided editorial assistance and to Ms. C. SCHMIDT and Ms. C. MORAND for their help in manuscript preparation.

Finally, gratitude is extended to the publishers for their patience in meeting exacting demands.

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Part I. General aspects

Introduction and overview

In the past, most clinicians have focused their interest on the end stage of human cancer, i.e. diagnosis and treatment of the patient with an established cancer, usually (in over 50% of cases) progressing fairly rapidly to a terminal situation. With new knowledge, clinical oncologists will need to have a much broader and more comprehensive view of cancer as an extremely long-term process usually lasting many years (see Fig. 1). In particular, clinicians will have to have a better understanding of "preventive oncology".

Fig. 1. Modern viewpoint of cancer as a long-term process.

Induction phase	<i>In-situ</i> phase	Invasion phase	Dissemination phase
Up to 15–30 years	5–10 years	1–5 years	1–5 years

This long-range concept of cancer represents a synthesis of many concepts with important clinical implications (see text).

Induction phase

Looking at all the causes of cancer in man that have so far been identified with certainty, the induction phase usually lasts 15–30 years (see Fig. 1). Currently, we still cannot identify with certainty the causes of most cancers, but epidemiologists today feel that environmental factors probably account for about 70–80% of human cancers. It usually takes many years of exposure to a carcinogen before the progressively severe dysplasia becomes a definite cancer. The exceptions to this are: (a) radiation-induced leukæmias (where the induction phase may be as short as 2 years); and (b) the genetically determined cancers of infancy (in which cancer is present at birth or shortly thereafter).

Obviously, not everyone who is exposed to a carcinogen gets cancer. Among the factors which help to determine who *does* get cancer are the following: the nature, amount and concentration of the carcinogen; the site or sites at which it acts; the duration of exposure; the presence of other carcinogens or co-carcinogens; and individual or tissue susceptibility.

In-situ phase

During the past 25 years, much has been learned about precancerous and *in-situ* changes in *epithelial* tissues by means of cytological and pathological examinations of the cervix, oral cavity, lung, upper and lower gastrointestinal tract, bladder, skin, and recently of the breast. Yet opportunities for examination of precancerous lesions of *mesenchymal* origin have been negligible. Because of the tremendous worldwide interest in cervical cytology, we have learned most about lesions of the uterine cervix. It seems that progressively severe dysplasia results in carcinoma *in situ* in a high percentage of cases. Furthermore, after a number of years (up to 10), most *in-situ* cancers become invasive. Although there are fewer data about organs other than the cervix, it seems almost certain that the process leading from progressively severe dysplasia to *in-situ* cancer and finally to invasive cancer, is a continuous one proceeding over many years.

Invasion phase

During this phase, the cells that are now malignant multiply and invade through the basement membrane into the deeper tissues and thus gain access to lymphatic channels and blood vessels. Although there are few data about this process of invasion in humans, a great deal of animal research has been done, and the following factors are among those considered to have some importance:

1. increased pressure within the tumour caused by active multiplication of cells;
2. increased amœboid motivity of cells;
3. decreased cohesiveness between cells, perhaps related to a decreased calcium ion content or to altered cell-membrane electric charges;
4. elaboration, by the cancer cell, of lytic substances; and
5. the lack of intercellular "bridges" found in all normal cells.

As the tumour grows and invades further, its direct spread is resisted more by some tissues (such as fascia, bone, cartilage, arteries, nerves) than by others; cancer often spreads for several centimetres in the submucosa beyond its apparent limits in the œsophagus and colon, and sarcomas notoriously spread along fascial planes. An understanding of such situations has clinical significance.

Eventually, tumour cells (or clumps of cells) spread to the regional lymph nodes and/or to distant sites and grow to form metastases, and thus the cancer becomes disseminated. The elapsed time between the start of invasion and the existence of established metastases may vary from a few weeks to several years.

Dissemination phase

As the cancer grows and invades more and more tissue locally, the chances of metastases increase. In the very first stages of dissemination, when the metastases are still microscopic in size ("micrometastases"), the clinician's ability to detect them is very poor. In the 1950s, when surgical excision was the main hope for cure of most patients with solid tumours, nearly half of all patients operated on "for cure" (i. e. where there was no evidence of distant metastases) eventually developed metastases. Although our abilities to detect cancers early have improved somewhat, about 50% of all patients will, even today, have unrecognized distant micrometastases at the time of diagnosis and treatment. In some situations, the likelihood of subclinical disseminated disease being present is much higher than 50% and in others it is lower; however, the concept of treating the local (or regionalized) cancer with surgery (and/or X-ray therapy) and using appropriate chemotherapy for the presumed disseminated disease (and/or residual local microscopic-sized foci) form the basis for today's multi-modal therapy. Some of the experimental and clinical evidence regarding mechanisms of the development of metastases and factors promoting or inhibiting metastases are discussed in the section on Tumour spread (p. 48). Again, the elapsed time between the beginning of dissemination and death may be only a few weeks or it may be several years.

Conclusion

This integrated concept of a four-phase evolution of cancer emphasizes the chronicity and continuity of the process and ties together the work of basic researchers and that of clinical oncologists. In the pages that follow, some aspects related to these four phases will be discussed in more detail.

Further reading

Bertino, J. R., Farber, E., Kaplan, H. S., Klein, G., Upton, A. C.: *Cancer – a Comprehensive Treatise*. New York: Plenum Press 1977 (6 Vol.).

Vol. 1: Etiology: chemical and physical carcinogenesis.

Vol. 2: Etiology: viral carcinogenesis.

Vol. 3: Biology of tumours : cellular biology and growth.

Vol. 4: Biology of tumours : surfaces, immunology and comparative pathology.

Vol. 5: Chemotherapy.