

SIXTH EDITION

Cancer and its Management

Jeffrey Tobias and Daniel Hochhauser

 WILEY-BLACKWELL

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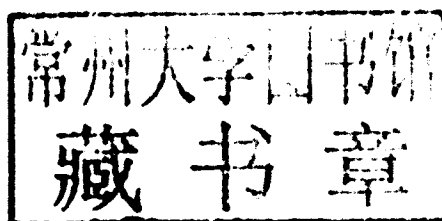
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Foreword

Few medical textbooks that are entirely written by two people are alive and well almost 25 years after the first edition. They, and their authors, are usually submerged by changes in the subject and the difficulty and effort required in keeping up to date. This book, however, has the advantage of its primary purpose, which is to provide a balanced, readable, synthesis of the practice of cancer medicine: one that is accessible and of value to students and medical professionals, in all disciplines, who encounter cancer in daily practice but who are not themselves specialists in the field.

It is relatively straightforward to identify new treatments and principles that are in the process of becoming, or have become, part of everyday practice. It is more difficult to be sure of what is becoming redundant as a result of change and which should therefore be reduced in content or

excluded. Yet without these judgements the book would grow to become yet another indigestible tome that rests on the shelf and is seldom read.

Jeffrey Tobias and Daniel Hochhauser are among the relatively few oncologists capable of providing, over the entire field, the balance, authority and judgement necessary. To be publishing the sixth edition is a great achievement. In their hands the book will surely continue to prosper and will introduce new readers to the human and technical challenges that are at the heart of the care of patients who have cancer.

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London 2010*

Preface

Professor Robert Souhami and I began work on this book almost 30 years ago, and after a 5-year gestation the first edition appeared in 1986. Naturally we are delighted that it remains so popular. In the past, each time we settled down to start work on the new edition we always felt that this time, surely, the changes would be relatively minor. We were always wrong, and on this occasion, following Bob Souhami's retirement and joined for the first time by my close colleague Professor Daniel Hochhauser, I now discover that the necessary amendments, alterations and updates are greater than ever before.

It was a great pleasure working with Robert for so long, and from my own point of view, our book remains a lasting reminder of an exceptionally close working relationship over so many years. I am delighted that Daniel has agreed to join me in the challenging task of producing this sixth edition of *Cancer and its management*. As on all the previous occasions, we have been astonished by the scale of the innovations and changes in management that have rapidly become an essential part of the gold-standard care of cancer patients. Perhaps it is only by writing a book covering all aspects of malignant disease that these developments can be fully appreciated, though this is not an approach to what is now called continued professional development that we recommend to others!

Bidding a professional farewell to a highly respected close friend and colleague, and warmly welcoming a new one, set me to thinking about some of the changes that have occurred over the past 30 years, though they are far too numerous, of course, to list separately. Without question, the outlook has changed dramatically, and for the better. Patients now have access to a far more integrated and seamless service, with multidisciplinary teams regularly meeting to discuss all aspects of a patient's management, resulting in a more balanced and expert approach to decision-making. Patients are increasingly managed by well-informed specialists with particular experience and expertise in their field of practice. Communication between general practitioners, hospital specialists and community

services, including those for continuing and palliative care, have improved enormously.

New chemotherapeutic agents have appeared at a remarkably rapid rate. Most notable of all, even since the last (fifth) edition of this book appeared in 2005, we have seen the increasing and now routine use of biologically targeted therapies in a wide variety of malignant conditions, though it seems hard to believe that these agents, so ubiquitous today, have been available for only a decade or less. The very first of these, the monoclonal antibody rituximab, was approved in the USA by the Food and Drug Administration (FDA) for the treatment of relapsed low-grade CD20-positive non-Hodgkin's lymphoma as recently as the latter part of 1997. This relatively recent discovery has in turn led to the introduction of a huge spectrum of new targeted agents and monoclonal antibodies against the many cellular targets known to be involved in cancer cell growth. An even greater number are in development and we can further predict that microarray diagnostic techniques will lead to far more precise identification of patients who will gain the greatest benefit from the multitude of these newer treatments. It is an exciting time to be in cancer medicine, but it is profoundly important to remember that the human, pastoral and technical lessons of the past do not change. Our book is based largely on these. Virtually all other areas of cancer medicine have seen dramatic improvements as well, whether it be early detection and referral, improved diagnosis, surgical techniques or other major areas of clinical management.

As we pointed out in the preface to previous editions, a textbook limited to this size and designed to be widely comprehensible demands that only essential information be presented. We have had to synthesize and abbreviate a variety of differing, sometimes conflicting, opinions, and summarize interesting or unresolved controversies which, in a larger text, would have been the subject of more detailed discussion. Nonetheless, we hope the result is an accessible text that avoids being too didactic in tone or

synoptic in style. The aim of the book has not altered: it is to provide an introductory text for medical staff, nurses and other allied professionals, students and scientists interested in and challenged by the problems of cancer care.

Initially we wrote this book because we were aware that many busy physicians, surgeons and gynaecologists, who are not themselves cancer specialists, may find it difficult to keep abreast of areas of considerable importance to them. General surgeons, for example, spend a substantial portion of their time dealing with gastrointestinal and abdominal tumours, yet have little working knowledge of the non-surgical treatment of these conditions. Similarly, gynaecological surgeons need to know more about what the radiotherapist (nowadays more frequently termed 'clinical oncologist') and medical oncologist can offer.

In many medical schools, a student's knowledge of the basics and management of malignant disease is acquired from specialists whose main interest may not be related to cancer. Medical students should surely know more about the disease that in many countries is now the largest cause of mortality as well as being regularly recognized by the public at large as the most feared of all diseases. Needless to say, we hope that postgraduate trainees in medicine, surgery and gynaecology will find the book of value, and that it will also be of help to those beginning a career in clinical or medical oncology. Finally, we would like to think that general practitioners, all of whom look after cancer patients and who have such an important role in diagnosis, early referral of patients with suspicious symptoms, shared management, follow-up and terminal care, will find this book helpful. If specialists in cancer medicine feel it is a useful digest of current thought in cancer management, so much the better. However, this book is not intended primarily for them. There are several very large texts that give specialist advice. Although some of these details necessarily appear in our book, we do not regard it as a handbook of chemotherapy or radiotherapy. To some extent it is a personal view of cancer and its management today and, as such, it will differ in some details from the attitudes and approaches of our colleagues.

We have attempted to give a thorough working knowledge of the principles of diagnosis, staging and treatment of tumours and to do so at a level that brings the reader up to date. We have tried to indicate where the subject is

growing, where controversies lie, and from which direction future advances might come. In the first nine chapters we have attempted to outline the essential mechanisms of tumour development, cancer treatment and supportive care. In the remaining chapters we have given an account of the principles of management of the major cancers. For each tumour we have provided details of the pathology, mode of spread, clinical presentation, staging and treatment with radiotherapy and chemotherapy. The role of surgery is of course outlined, but details of surgical procedure are beyond the scope of this book. The references which we have included in the text or for further reading have been chosen because they are clear and authoritative reviews, historical landmarks or, perhaps most excitingly, represent the cutting edge of recent research.

For me personally, the gestation, writing and production of this new edition has been a wonderfully challenging task, enormously enhanced by the arrival of my co-author Professor Daniel Hochhauser, a medical oncologist as passionate and committed as his distinguished predecessor. We both hope that this edition of *Cancer and its management* will live up to the high standards that Robert Souhami always imposed, and that it will be of help to those of you struggling like ourselves to offer the highest standards of care for our cancer patients in a rapidly changing clinical world.

This edition is dedicated to the memory of my late wife Dr Gabriela Tobias (1950–2008), an outstanding general medical practitioner and champion of patient welfare, who died from metastatic cancer of the colon during the preparation of the manuscript. Gaby qualified from University College London and University College Hospital in 1973, and devoted virtually the whole of her professional life to the care of patients in the deprived East End of London. Words cannot sufficiently express my profound sense of gratitude to Professor Hochhauser and his team at University College Hospital, London, who supervised her care with such tireless devotion and expertise. The concept of 'patient-centred care', so widely discussed yet so often poorly understood, takes on profound significance from the other side of the consulting-room desk.

Jeffrey Tobias
London 2010

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My personal thanks also go to my long-suffering secretary Jayshree Kara, who dealt with many alterations, reverses and inconsistencies with unfailing good cheer. Any inaccuracies or shortcomings are of course entirely the responsibility of the authors.

Cover image: Fluorescent *in situ* hybridization image of cells recovered from a Her-2-positive breast cancer. Used with permission from Baylor College of Medicine, Lester & Sue Smith Breast Center's Pathology Core, Houston, TX.

Although every effort has been made to ensure the accuracy of the drug dosages and side-effects described in this book, the authors and publisher make no representation, expressed or implied, that they are correct. Readers are advised to refer to published information from the pharmaceutical companies and other reference works to check accuracy.

Abbreviations

5-FU	5-fluorouracil	CSF	cerebrospinal fluid
5-HIAA	5-hydroxyindoleacetic acid	CT	computed tomography
5-HT	5-hydroxytryptamine	CTV	clinical target volume
6-MP	6-mercaptopurine	DCIS	ductus carcinoma <i>in situ</i>
6-MPRP	6-mercaptopurine ribose phosphate	DHFR	dihydrofolate reductase
6-TG	6-thioguanine	DIC	disseminated intravascular coagulation
ACTH	adrenocorticotrophic hormone	DPD	dihydropyrimidine dehydrogenase
ADH	antidiuretic hormone	EBV	Epstein–Barr virus
AFP	α -fetoprotein	ECOG	Eastern Cooperative Oncology Group
AJCC	American Joint Committee on Cancer	EF	extended field
ALL	acute lymphoblastic leukaemia	EGF	epidermal growth factor
AML	acute myeloid leukaemia; acute myeloblastic leukaemia	EGFR	epidermal growth factor receptor
AMML	acute myelomonocytic leukaemia	EORTC	European Organization for Research and Treatment of Cancer
ANL	acute non-lymphocytic leukaemia	EpCAM	epithelial cell adhesion molecule
APL	acute promyelocytic leukaemia	EPO	erythropoietin
APUD	amine precursor uptake and decarboxylation	ER	estrogen receptor
ASCO	American Society for Clinical Oncology	ERCP	endoscopic retrograde cholangiopancreatography
ATRA	all- <i>trans</i> -retinoic acid	ESR	erythrocyte sedimentation rate
BCG	bacille Calmette–Guérin	FAP	familial adenomatous polyposis
BCNU	bis-chloroethyl nitrosourea	FDA	Food and Drug Administration
BMI	body mass index	FdUMP	5-fluoro-2-deoxyuridine monophosphate
BMT	bone-marrow transplantation	FIGO	International Federation of Gynecology and Obstetrics
BrdU	bromodeoxyuridine	FISH	fluorescence <i>in situ</i> hybridization
BTV	biological target volume	FIT	faecal immunochemical test
CALLA	common acute lymphoblastic leukaemia antigen	FOBT	faecal occult blood test
CCNU	<i>cis</i> -chloroethyl nitrosourea	FSH	follicle-stimulating hormone
CEA	carcinoembryonic antigen	G6PD	glucose 6-phosphate dehydrogenase
CGL	chronic granulocytic leukaemia	G-CSF	granulocyte colony-stimulating factor
CHART	continuous hyperfractionated accelerated radiotherapy	GFR	glomerular filtration rate
CI	confidence interval	GH	growth hormone
CIN	cervical intraepithelial neoplasia	GIST	gastrointestinal stromal tumour
CLL	chronic lymphocytic leukaemia	GM-CSF	granulocyte/macrophage colony-stimulating factor
CMF	cyclophosphamide, methotrexate and 5-fluorouracil	GSH	glutathione
CMI	cell-mediated immunity	GTV	gross tumour volume
CML	chronic myeloid leukaemia	HAART	highly active antiretroviral therapy
CNS	central nervous system	HBI	hemibody irradiation

HBV	hepatitis B virus	MTT	malignant teratoma trophoblastic
HCC	hepatocellular carcinoma	MTU	malignant teratoma undifferentiated
HCG	human chorionic gonadotrophin	NCAM	neural-cell adhesion molecule
HCL	hairy cell leukaemia	NCRI	National Cancer Research Institute
HCV	hepatitis C virus	NF	neurofibromatosis
HDI	HER dimerization inhibitor	NHL	non-Hodgkin's lymphoma
HGPRT	hypoxanthine-guanine phosphoribosyltransferase	NICE	National Institute for Health and Clinical Excellence
HHV	human herpesvirus	NK	natural killer (cell)
HIV	human immunodeficiency virus	NLCN	North London Cancer Network
HLA	human leucocyte antigen	NSABP	National Surgical Adjuvant Breast Project
HNPCC	hereditary non-polyposis colon cancer	NSAID	non-steroidal anti-inflammatory drug
HPV	human papillomavirus	NSCLC	non-small-cell lung cancer
HR	hazard ratio	NWF	New Working Formulation
HRT	hormone-replacement therapy	PAS	periodic acid-Schiff (stain)
HTLV	human T-cell leukaemia/lymphotropic virus	PCI	prophylactic cranial irradiation
HVA	homovanillic acid	PCR	polymerase chain reaction
IF	involved field	PDGF	platelet-derived growth factor
IGF	insulin-like growth factor	PDGFR	platelet-derived growth factor receptor
IL	interleukin	PEL	primary effusion lymphoma
IMRT	intensity-modulated radiation therapy	PET	positron emission tomography
INRG	International Neuroblastoma Risk Group	PKC	protein kinase C
INSS	International Neuroblastoma Staging System	PLAP	placental alkaline phosphatase
IPSID	immune proliferative small-intestine disease	PMBL	primary mediastinal B-cell lymphoma
IVU	intravenous urography	PNET	primitive neuroectodermal tumour
KGF	keratinocyte growth factor	PR	progesterone receptor
KSHV	Kaposi's sarcoma herpesvirus	PSA	prostate-specific antigen
LAK	lymphokine-activated killer (cell)	PTH	parathyroid hormone
LDH	lactate dehydrogenase	PTHrP	parathyroid hormone-related protein
LET	linear energy transfer	PTV	planning target volume
LH	luteinizing hormone	REAL	revised European-American lymphoma (classification)
LHRH	luteinizing hormone releasing hormone	RPA	recursive partitioning analysis
LOH	loss of heterozygosity	RS	Reed-Sternberg (cell)
LVEF	left ventricular ejection fraction	RSV	Rous sarcoma virus
M-CSF	macrophage colony-stimulating factor	RTOG	Radiation Therapy Oncology Group
MDR	multidrug resistance	RT-PCR	reverse-transcriptase polymerase chain reaction
MDS	myelodysplastic syndrome	SCLC	small-cell lung cancer
MEN	multiple endocrine neoplasia	SEER	Surveillance, Epidemiology and End Results (program)
MGMT	O ⁶ -methylguanine-DNA methyltransferase	SNCC	small non-cleaved cell (lymphoma)
MGUS	monoclonal gammopathy of unknown significance	SVCO	superior vena caval obstruction
MHC	major histocompatibility complex	TBI	total-body irradiation
MIBG	meta-iodobenzylguanidine	TCC	transitional cell carcinoma
MMP	matrix metalloproteinase	Tdt	terminal deoxynucleotidyltransferase
MRC	Medical Research Council	TGF	transforming growth factor
MRCP	magnetic resonance cholangiopancreatography	TIBC	total iron-binding capacity
MRI	magnetic resonance imaging	TNF	tumour necrosis factor
MTI	malignant teratoma intermediate	TNI	total nodal irradiation
mTOR	mammalian target of rapamycin		

TNM	tumour, node, metastasis	VEGF	vascular endothelial growth factor
TS	thymidylate synthase	VEGFR	vascular endothelial growth factor receptor
TSH	thyroid-stimulating hormone	VIN	vulval intraepithelial neoplasia
UICC	<i>Union Internationale Contre le Cancer</i>	VIP	vasoactive intestinal polypeptide
UV	ultraviolet	VMA	vanillylmandelic acid
VAIN	vaginal intraepithelial neoplasia	WBC	white blood cell count
VAP	vincristine, doxorubicin and prednisone	WHO	World Health Organization

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1

The modern management of cancer: an introductory note

Cancer is a vast medical problem. It is now the major cause of mortality, both in the UK and elsewhere in the Western world [1] (Figure 1.1), diagnosed each year in one in every 250 men and one in every 300 women. The incidence rises steeply with age so that, over the age of 60, three in every 100 men develop the disease each year (Figure 1.2a). It is a costly disease to diagnose and investigate, and treatment is time-consuming, labour-intensive and usually requires hospital care. In the Western world the commonest cancers are of the lung, breast, skin, gut and prostate gland [2,3] (Figures 1.2b and 1.3). The lifetime risk of developing a cancer is likely to alter sharply over the next decade because the number of cancer cases has risen by nearly one-third over the past 30 years. An ageing population, successes from screening and earlier diagnosis have all contributed to the rise. Present estimates suggest that the number of cases is still rising at a rate of almost 1.5% per annum. The percentage of the population over the age of 65 will grow from 16% in 2004 to 23% by 2030, further increasing the overall incidence [4].

For many years the main methods of treating cancer were surgery and radiotherapy. Control of the primary tumour is indeed a concern, since this is usually responsible for the patient's symptoms. There may be unpleasant symptoms due to local spread, and failure to control the disease locally means certain death. For many tumours, breast cancer for example, the energies of those treating the disease have been directed towards defining the optimum methods of eradication of the primary tumour. It is perhaps not surprising that these efforts, while improving management, have not greatly improved the prognosis because the most important cause of mortality is metastatic spread. Although prompt and effective treatment of the primary cancer diminishes the likelihood of recurrence,

metastases have often developed before diagnosis and treatment have begun. The prognosis is not then altered by treatment of the primary cancer, even though the presenting symptoms may be alleviated. Progress in treatment has been slow but steady. Worldwide, between 1990 and 2001, the mortality rates from all cancers fell by 17% in patients aged 30–69 years, but rose by 0.4% in those aged 70 years or older [1,5]. This may sound impressive at first reading, but the fall was lower than the decline in mortality rates from cardiovascular disease, which decreased by 9% in the 30–69 year age group (men) and by 14% in the 70 year (or older) age group. In the UK there has been a steady fall in mortality from cancer of about 1% a year since the 1990s (Figure 1.4), but with a widening gap in the differing socioeconomic groups. As the authors forcefully state [2]: 'Increases in cancer survival in England and Wales during the 1990s are shown to be significantly associated with a widening deprivation gap in survival.' In the USA, the number of cancer deaths has now fallen over the past 5 years, chiefly due to a decline in deaths from colorectal cancer, itself thought to be largely due to an increase in screening programmes. Interestingly, the fall in mortality has also been paralleled by a reduction in incidence rates in the USA – for men since 1990 and for women since 1991 [6]. Nonetheless, cancer continues as the leading cause of death in the USA, under the age of 85 years [3].

Every medical specialty has its own types of cancer which are the concern of the specialist in that area. Cancer is a diagnosis to which all clinicians are alerted whatever their field and, because malignant disease is common, specialists acquire great expertise in diagnosis, often with the aid of techniques such as bronchoscopy and other forms of endoscopy. Conversely, the management of cancer once the diagnosis has been made, especially the non-surgical management, is not part of the training or interest of many specialists. This has meant that radiotherapists ('clinical oncologists') and medical oncologists are often asked to see patients who have had a laparotomy at which a tumour such as an ovarian cancer or a lymphoma

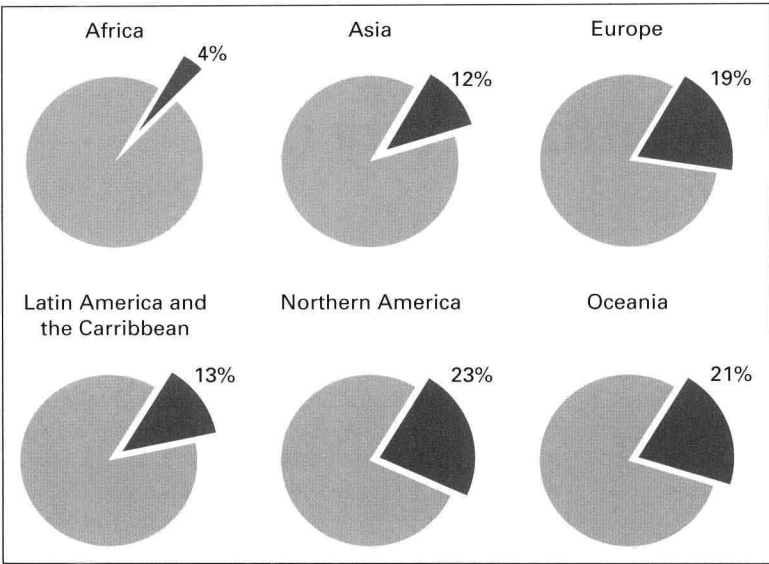


Figure 1.1 Percentage of all deaths due to cancer in the different regions of the world. Available at <http://info.cancerresearchuk.org/cancerstats/geographic/world/mortality/?a=5441>, accessed 10 September 2008. (© Cancer Research UK.)

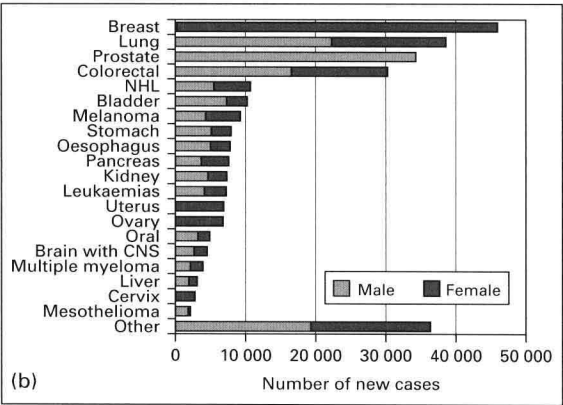
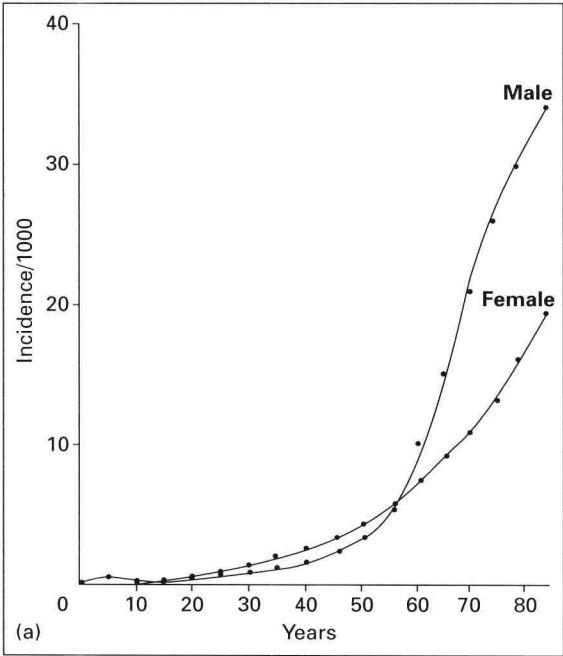


Figure 1.2 (a) Age-specific cancer incidence in England and Wales. (b) The 20 most commonly diagnosed cancers (excluding non-melanoma skin cancer) in the UK, 2005. NHL, non-Hodgkin's lymphoma. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/commoncancers/>, accessed 10 September 2008. (© Cancer Research UK.)

has been found, but the abdomen then closed without the surgeon having made an attempt to stage the disease properly or, where appropriate, to remove the main mass of tumour. This poses considerable problems for the further management of the patient. More generally, lack of

familiarity with the principles of cancer management, and of what treatment can achieve, may lead to inappropriate advice about outcome and a low level of recruitment into clinical trials. An understanding of the principles of investigation and treatment of cancer has become essential for

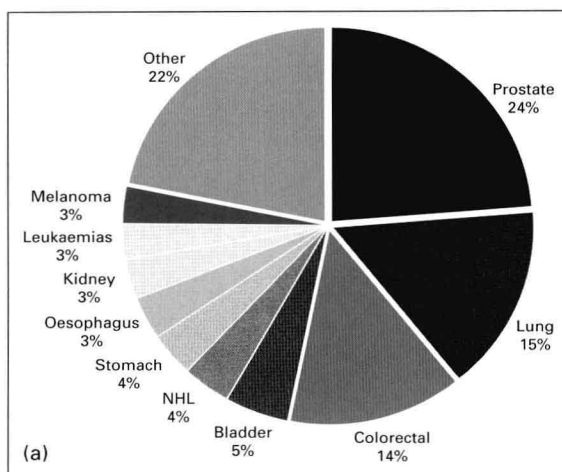
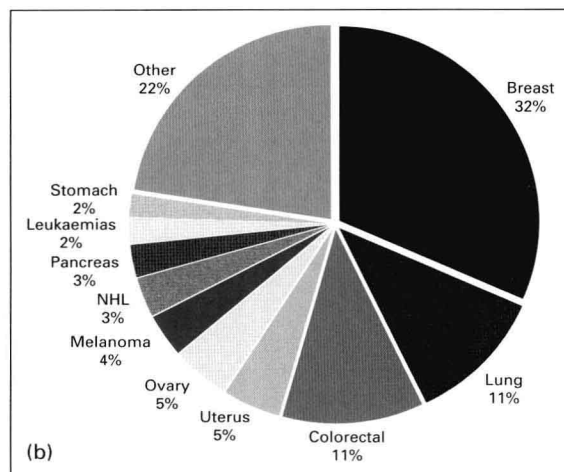


Figure 1.3 (a) The 10 most common cancers in males (excluding non-melanoma skin cancer) in the UK, 2005. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/males/>, accessed 10 September 2008. (b) The 10 most common cancers in females (excluding



non-melanoma skin cancer) in the UK, 2005. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/females/?a=5441>, accessed 10 September 2008. NHL, non-Hodgkin's lymphoma. (© Cancer Research UK.)

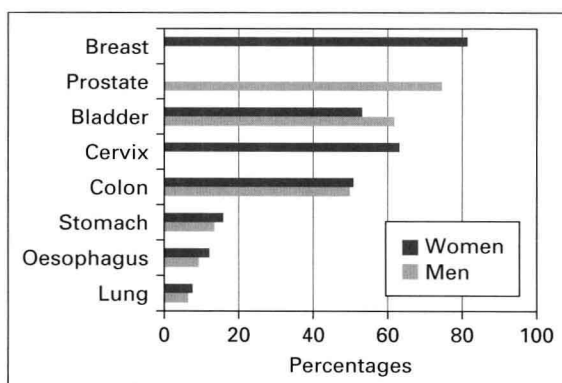


Figure 1.4 Cancer survival rates improved between 1999 and 2004. Available at <http://www.statistics.gov.uk/cci/nugget.asp?id=861>. (Reproduced under the terms of the Click-Use Licence.)

every physician and surgeon if the best results for their patients are to be achieved.

During the latter part of the last century, advances in the chemotherapy and radiotherapy of uncommon tumours such as Hodgkin's disease and germ-cell tumours of the testis, together with the increasing complexity of treatment decisions in more common tumours, led to a

greater awareness of the importance of a planned approach to clinical management. This applies not only for the problems in individual patients, but also in the planning of clinical trials. For each type of cancer, an understanding of which patients can be helped, or even cured, can only come by close attention to the details of disease stage and pathology. Patients in whom these details are unknown are at risk from inappropriate over-treatment or from inadequate treatment, resulting in the chance of cure being missed. Even though chemotherapy has not on the whole been of outstanding benefit to patients with diseases such as squamous lung cancer or adenocarcinoma of the pancreas, it is clearly essential that clinicians with a specialized knowledge of the risks and possible benefits of chemotherapy in these and other diseases are part of the staff of every oncology department. Knowing when not to treat is as important as knowing when to do so.

For many cancers, improvements in chemotherapy have greatly increased the complexity of management. Cancer specialists have a particular responsibility to validate the treatments they give, since the toxicity and dangers of many treatment regimens mean that the clinical indications have to be established precisely. In a few cases an imaginative step forward has dramatically improved results and the need for controlled comparison with previous treatment is scarcely necessary. Examples are the early studies leading to the introduction of combination chemotherapy in the management of advanced Hodgkin's disease, and the

Table 1.1 The 5-year relative survival for adults diagnosed with major cancers during 1998–2001 and 1999–2003, England.

Cancer		1998–2001 survival (%)	1999–2003 survival (%)
Breast	Women	79.9	81.0
	Men	49.4	49.6
Colon	Women	50.2	50.8
	Men	6.3	6.5
Lung	Women	7.5	7.6*
	Men	70.8	74.4

* It was not possible to produce an age-standardized 5-year survival figure for lung cancer in women; therefore this figure refers to the unstandardized estimate.

Source: Cancer survival increases in England. Available at <http://www.statistics.gov.uk/pdffdir/can0807.pdf>. (Reproduced under the terms of the Click-Use Licence.)

prevention of central nervous system relapse of leukaemia by prophylactic treatment. However, such clear-cut advances are seldom made (see, for example, Table 1.1, which outlines the modest improvement in survival for four major types of cancer between 1998 and 2003 in England). For the most part, improvements in treatment are made slowly in a piecemeal fashion and prospective trials of treatment must be undertaken in order to validate each step in management. Modest advances are numerically nonetheless important for such common diseases. Only large-scale trials can detect these small differences reliably. Collaboration on a national and international scale has become increasingly important, and the results of these studies have had a major impact on management, for example in operable breast cancer. There is always a tendency in dealing with cancer to want to believe good news and for early, uncontrolled, but promising results to be seized upon and over-interpreted. Although understandable, uncritical enthusiasm for a particular form of treatment is greatly to be deplored, since it leads to a clamour for the treatment and the establishment of patterns of treatment that are improperly validated. There have been many instances where treatments have been used before their place has been clearly established: adjuvant chemotherapy in non-small-cell lung cancer, limb perfusion in sarcomas and melanoma, radical surgical techniques for gastric cancer and adjuvant chemotherapy for bladder cancer are examples. The toxicity of cancer treatments is considerable and can only be justified if it is unequivocally shown that the end-results are worthwhile either by increasing survival or by improving the quality of life.

The increasing complexity of management has brought with it a recognition that in most areas it has become necessary to establish an effective working collaboration between specialists. Joint planning of management in specialized clinics is now widely practised for diseases such as lymphomas and head and neck and gynaecological cancer. Surgeons and gynaecologists are now being trained who specialize in the oncological aspects of their specialty. In this way patients can benefit from a coordinated and planned approach to their individual problems.

Before a patient can be treated, it must be established that he or she has cancer, the tumour pathology must be defined, and the extent of local and systemic disease determined. For each of these goals to be attained the oncologist must rely on colleagues in departments of histopathology, diagnostic imaging, haematology and chemical pathology. Patients are often referred in whom the diagnosis of cancer has not been definitely made pathologically but is based on a very strong clinical suspicion with suggestive pathological evidence, or where a pathological diagnosis of cancer has been made which, on review, proves to be incorrect. It is essential for the oncologist to be in close contact with histopathologists and cytologists so that diagnoses can be reviewed regularly. Many departments of oncology have regular pathology review meetings so that the clinician can learn of the difficulties which pathologists have with diagnosis and vice versa. Similarly, modern imaging techniques have led to a previously unattainable accuracy in preoperative and postoperative staging, although many of these techniques are only as reliable as the individuals using them (e.g. abdominal or pelvic ultrasound). The

cancer specialist must be fully conversant with the uses and limitations of imaging methods. The techniques are expensive and the results must be interpreted in the light of other clinical information. The practice of holding regular meetings to review cases with specialists from the imaging departments has much to commend it.

Modern cancer treatment often carries a substantial risk of toxicity. Complex and difficult treatments are best managed in a specialized unit with skilled personnel. The centralization of high-dependency care allows staff to become particularly aware of the physical and emotional problems of patients undergoing treatments of this kind. Additionally, colleagues from other departments such as haematology, biochemistry and bacteriology can more easily help in the investigation and management of some of the very difficult problems which occur, for example in the immunosuppressed patient.

The increasingly intensive investigative and treatment policies which have been adopted in the last 25 years impose on clinicians the additional responsibility of having to stand back from the treatment of their patients and decide on the aim of treatment at each stage. Radical and aggressive therapy may be essential if the patient is to have a reasonable chance of being cured. However, palliative treatment will be used if the situation is clearly beyond any prospect of cure. It is often difficult to decide when the intention of treatment should move from the radical to the palliative, with avoidance of toxicity as a major priority. For example, while many patients with advanced lymphomas will be cured by intensive combination chemotherapy, there is no prospect of cure in advanced breast cancer by these means, and chemotherapy must in this case be regarded as palliative therapy. In this situation it makes little sense to press treatment to the point of serious toxicity. The judgement of what is tolerable and acceptable is a major task in cancer management. Such judgements can only come from considerable experience of the treatments in question, of the natural history of individual tumours and an understanding of the patient's needs and wishes.

Modern cancer management often involves highly technological and intensive medical care. It is expensive, time-consuming and sometimes dangerous. Patients should seldom be in ignorance of what is wrong with them or what the treatment involves. The increasingly technical nature of cancer management, and the change in public and professional attitudes towards malignant disease, have altered the way in which doctors who are experienced in cancer treatment approach their patients. There has been a decisive swing towards honest and careful discussion

with patients about the disease and its treatment. This does not mean that a bald statement should be made to the patient about the diagnosis and its outcome, since doctors must sustain the patient with hope and encouragement through what is obviously a frightening and depressing period. Still less does it imply that the decisions about treatment are in some way left to the patient after the alternatives have been presented. Skilled and experienced oncologists advise and guide patients in their understanding of the disease and the necessary treatment decisions. One of the most difficult and rewarding aspects of the management of malignant disease lies in the judgement of how much information to give each particular patient, at what speed, and how to incorporate the patient's own wishes into a rational treatment plan.

The emotional impact of the diagnosis and treatment can be considerable for both patients and relatives. Above everything else, treating patients with cancer involves an awareness of how patients think and feel. All members of the medical team caring for cancer patients must be prepared to devote time to talking to patients and their families, to answer questions and explain what is happening and what can be achieved. Because many patients will die from their disease, they must learn to cope with the emotional and physical needs of dying patients and the effects of anxiety, grief and bereavement on their families.

In modern cancer units management is by a team of healthcare professionals, each of whom has their own contribution to make. They must work together, participating in management as colleagues commanding mutual respect. The care and support of patients with advanced malignant disease and the control of symptoms such as pain and nausea have greatly improved in the last 10 years. This aspect of cancer management has been improved by the collaboration of many medical workers. Nurses who specialize in the control of symptoms of malignancy are now attached to most cancer units, and social workers skilled in dealing with the problems of malignant disease and bereavement are an essential part of the team. The development of hospices has led to a much greater appreciation of the way in which symptoms might be controlled and to a considerable improvement in the standard of care of the dying in general hospitals. Many cancer departments now have a symptom support team based in the hospital but who are able to undertake the care of patients in their own homes, giving advice on control of symptoms such as pain and nausea and providing support to patients' families.

There have been dramatic advances in cell and molecular biology in the last 20 years, with the result that our