

SEVENTH EDITION

Cancer and its Management

Jeffrey Tobias and Daniel Hochhauser

WILEY Blackwell

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Fluorescence microscopy of human endothelium highlighting cadherin (green) between cells. Image courtesy of Wikimedia Commons under the GNU Free Documentation License.

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To Susan and Jo, with love and thanks

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Preface

In the 4 years that have elapsed since the previous edition of this book was published, we have been astonished by the number of changes made necessary by the introduction of newer treatments for cancer. Once again we can say without fear of contradiction that both our understanding of the biology, causation and natural history of many malignant tumours has continued to move forward. Equally and perhaps even more important, the outlook at least for some types of cancer has improved, in a number of cases, quite dramatically. Patients now have access to a far more integrated and seamless service, with multidisciplinary teams meeting regularly to discuss all aspects of patient management, resulting in a more balanced and expert approach to decision-making. They are increasingly managed by well-informed specialists with particular experience and expertise in their field of practice, and communication between general practitioners, hospital specialist and community services have continued to improve. Palliative care teams, which only 10 years ago were unevenly distributed even in economically developed parts of the world, have now become more fully accepted and much more widely available.

New chemotherapeutic agents and targeted therapies have appeared at a remarkably rapid rate, and in many cases have become fully established as part of standard treatment regimens – breast, lymphoma, colorectal cancer and melanoma are good examples. We noted this development in the Preface to this book when it last appeared in 2010, and these innovations have progressed still further since then. It seems hard to believe that targeted therapies, so widely used today, have been available for less than 20 years, the first of these, the monoclonal antibody rituximab, appearing and achieving licence for use as recently as 1997. As we have previously remarked, it remains an exciting time to be in cancer medicine, though it is profoundly important to remember that the human, pastoral and technical lessons of the past do not change. We have tried to stress this in the specific site-related chapters, particularly since increasing levels

of specialization carry the real danger that tomorrow's specialists will so to speak 'know more and more about less and less'. Broadly speaking, we accept as so many others do that the benefits of site specialization clearly outweigh the disadvantages, but nonetheless it is as well to remember that most patients look to their specialist oncologist for far more than simply his or her technical expertise.

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 can be presented. We have had to synthesize and abbreviate a variety of expert 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 in areas that are nonetheless of crucial importance in their professional lives. 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 – in a fair degree of detail – about what the radiotherapist and medical oncologist can offer.

In many medical schools, the students' knowledge of the management of malignant disease is acquired from specialists whose main interest may not be related to cancer. Medical students should know more about the disease that, in many countries, is now both the largest cause of mortality and 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 radiotherapy 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, management and terminal care, will find this book helpful. If specialists in cancer medicine feel that 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. Once again, the references that we have included in the text or for further reading have been chosen because they are either clear and authoritative reviews, historical landmarks or perhaps, most excitingly, represent the cutting edge of recent research.

Finally, a brief word about prevalence and mortality trends. In England alone, it is estimated that around 1.8 million people are currently living with and beyond a diagnosis of cancer, a figure that is increasing by over 3% annually giving a projected total figure of over 3 million by 2030. Despite the continuing fall in mortality from heart attacks and stroke, which has resulted in cancer now being the largest cause of death in the twenty-first

century, we can be sure that cancer deaths have certainly fallen over this same period. Recent figures from Cancer Research, UK, show that cancer deaths in middle-aged people have fallen in recent years to a record low – a remarkable reduction of 40% from 1971, when over 21,300 people aged between 50 and 59 years died, compared with under 14,000 people in the latest survey. The improvement in children's cancers has continued as well, with overall 5-year survival improving from 67% in 1990 to 81% last year.

However, we now need to redouble our efforts in diseases such as lung cancer, which have stubbornly remained resistant to major improvements in mortality, a particularly tragic example of course, since this disease could very largely be prevented by a further fall in the number of smokers. In 2012, lung cancer alone was responsible for over 30,000 deaths (England and Wales) compared, for example, with ischaemic heart disease just over 40,000, breast cancer around 10,500 and prostate cancer approximately 9,500. In many parts of the developing world, with increasing rates of smoking fuelled by increasing affluence and the cynical efforts of tobacco manufacturers and companies, the problem becomes still more acute and death rates will inevitably rise still further. In more affluent parts of the world, obesity is becoming not only an increasingly important cause of ill-health from non-malignant condition that is also now well recognized as a causative factor for cancer. A recent UK-based survey showed that each year some 12,000 of the commonest cancer can be attributed to obesity and that if average BMI in the population continues to increase, there could be over 3500 extra cancers every year as a result.

Although acknowledging the enormous advances made in cancer treatment over the past 25 years, we must recognize that there is no room for complacency – we still have a very long way to go. Making the best of today's treatments available to *all* patients, by improving the quality of care across the board to the high standards set by centres of excellence, would at least be a pretty good start.

*Jeffrey Tobias and Daniel Hochhauser
London 2014*

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*Jeffrey Tobias and Daniel Hochhauser
London 2014*

Abbreviations

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

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

TBI	total-body irradiation	UV	ultraviolet
TCC	transitional cell carcinoma	VAIN	vaginal intraepithelial neoplasia
Tdt	terminal deoxynucleotidyltransferase	VAP	vincristine, doxorubicin and prednisone
TGF	transforming growth factor	VEGF	vascular endothelial growth factor
TIBC	total iron-binding capacity	VEGFR	vascular endothelial growth factor receptor
TNF	tumour necrosis factor	VIN	vulval intraepithelial neoplasia
TNI	total nodal irradiation	VIP	vasoactive intestinal polypeptide
TNM	tumour, node, metastasis	VMA	vanillylmandelic acid
TS	thymidylate synthase	WBC	white blood cell count
TSH	thyroid-stimulating hormone	WHO	World Health Organization
UICC	<i>Union Internationale Contre le Cancer</i>		

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 leads to 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

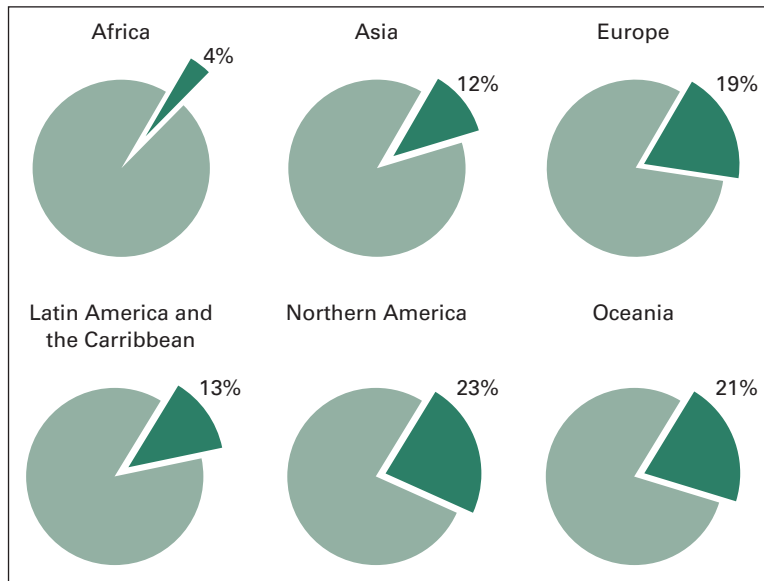


Figure 1.1 Percentage of all deaths due to cancer in the different regions of the world. Available at <http://info.cancerresearchuk.org/cancerstats/geographic/world/mortality/?a=5441>, accessed 10 September 2008. (© Cancer Research UK).

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 speciality 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 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 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 come only 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.

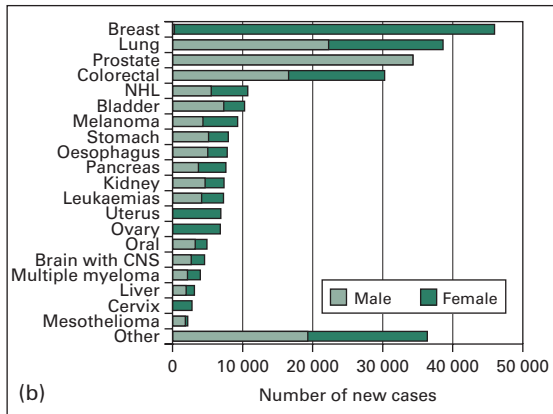
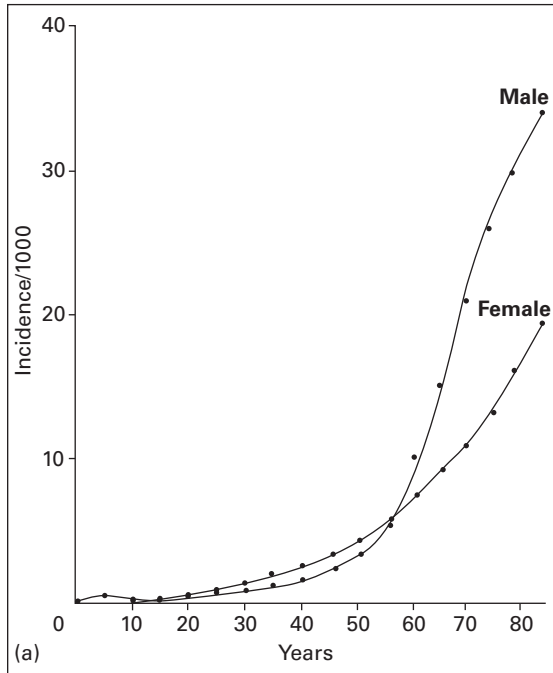


Figure 1.2 (a) Age-specific cancer incidence in England and Wales. (b) The 20 most commonly diagnosed cancers (excluding non-melanoma skin cancer) in the UK, 2005. NHL, non-Hodgkin’s lymphoma. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/commoncancers/>, accessed 10 September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

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

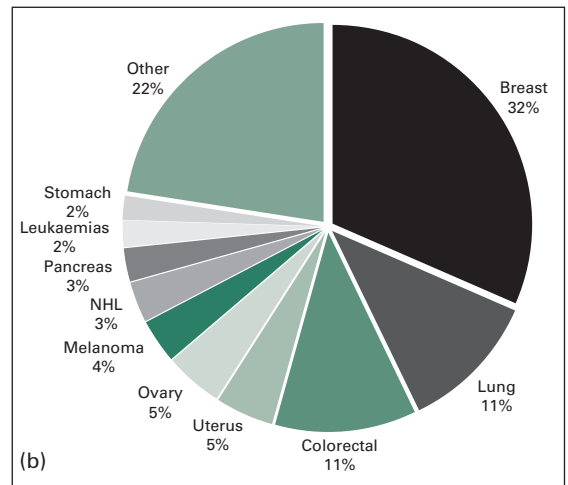
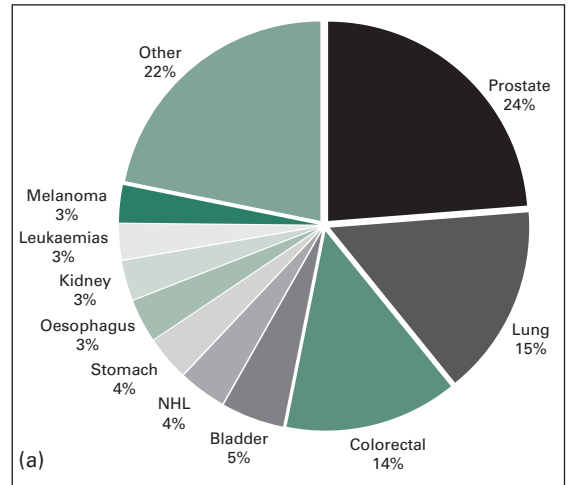


Figure 1.3 (a) The 10 most common cancers (excluding non-melanoma skin cancer) in the UK, 2005. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/males/>, accessed 10 September 2008. (b) The 10 most common cancers in females (excluding non-melanoma skin cancer) in the UK, 2005. Available at <http://info.cancerresearchuk.org/cancerstats/incidence/females/?a=5441>, accessed 10 September 2008. NHL, non-Hodgkin’s lymphoma. (© Cancer Research UK).

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 prevention of central nervous system relapse of leukaemia by prophylactic treatment. However, such clear-cut advances are seldom made (see,

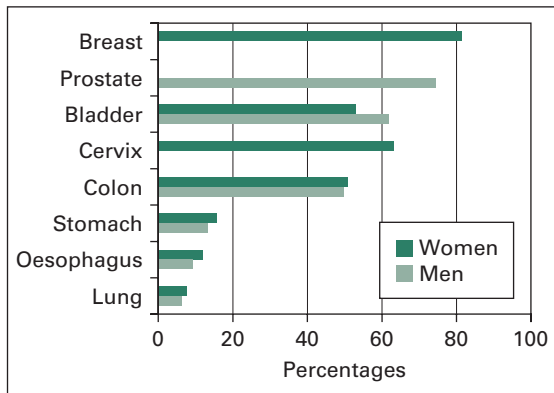


Figure 1.4 Cancer survival rates improved between 1999 and 2004. Available at <http://www.statistics.gov.uk/ci/nugget.asp?id=861>. (Reproduced under the terms of the Click-Use Licence).

Table 1.1 The 5-year relative survival percentage 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
Colon	Men	49.4	49.6
	Women	50.2	50.8
Lung	Men	6.3	6.5
	Women	7.5	7.6*
Prostate	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/pdfdir/can0807.pdf>. (Reproduced under the terms of the Click-Use Licence.)

e.g. 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 be justified only 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 to specialize in the oncological aspects of their speciality. 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 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, are often referred to oncologists. 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 come only 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