

02 - 73 Approach to the Patient with Cancer

73 Approach to the Patient with Cancer

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Approach to the Patient

with Cancer The application of current treatment techniques (surgery, radiation therapy, chemotherapy, and biologic therapy) results in the cure of nearly two of three patients diagnosed with cancer. Nevertheless, patients experience the diagnosis of cancer as one of the most traumatic and revolutionary events that has ever happened to them. Independent of prognosis, the diagnosis brings with it a change in a person's self-image and in their role in the home and workplace. The prognosis of a person who has just been found to have pancreatic cancer is the same as the prognosis of the person with aortic stenosis who develops the first symptoms of congestive heart failure (median survival, ~8 months). However, the patient with heart disease may remain functional and maintain a self-image as a fully intact person with just a malfunctioning part, a diseased organ ("a bum ticker"). By contrast, the patient with pancreatic cancer has a completely altered self-image and is viewed differently by family and anyone who knows the diagnosis. The patient is being attacked and invaded by a disease that could be anywhere in the body. Every ache or pain takes on

TABLE 73-1 Distribution of Cancer Incidence and Deaths for 2021

MALE	FEMALE	SITES	%	NUMBER	SITES	%	NUMBER
Cancer Incidence	Prostate						
299,010	Breast						
310,720	Lung						
116,310	Lung						
118,270	Colorectal						
81,540	Colorectal						
71,270	Bladder						
63,070	Endometrial						
67,880	Melanoma						

59,170 Melanoma

41,470 Kidney

52,380 Lymphoma

36,030 Lymphoma

44,590 Pancreas

31,910 Oral cavity

41,510 Thyroid

31,520 Leukemia

36,450 Kidney

29,230 Pancreas

34,530 Leukemia

26,320 All others

200,520 All others

207,440 All sites

1,029,080 All sites

972,060 Cancer Deaths Lung

65,790 Lung

59,280 Prostate

35,250 Breast

42,250 Colorectal

28,700 Pancreas

24,480 Pancreas

25,270 Colorectal

24,310 Liver

19,120 Endometrial

13,250 Leukemia

13,640 Ovary

12,740 Esophagus

12,880 Liver

10,720 Bladder

12,290 Leukemia

10,030 Lymphoma

11,780 Lymphoma

8,360 CNS

10,690 CNS

8,070 All others

87,390 All others

75,4330 All sites

322,800 All sites

288,920 Source: From RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:12, 2024.
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Oncology and Hematology PART 4 desperate significance. Cancer is an exception to the coordinated interaction among cells and organs. In general, the cells of a multicellular organism are programmed for collaboration. Many diseases occur because the specialized cells fail to perform their assigned task. Cancer takes this malfunction one step further. Not only is there a failure of the cancer cell to maintain its specialized function, but it also strikes out on its own; the cancer cell competes to survive using natural mutability and natural selection to seek advantage over normal cells in a recapitulation of evolution. One consequence of the traitorous behavior of cancer cells is that the patient feels betrayed by their body. The cancer patient feels that they, and not just a body part, are diseased. THE MAGNITUDE OF THE PROBLEM No nationwide cancer registry exists; therefore, the incidence of cancer is estimated on the basis of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, which tabulates cancer incidence and death figures from 13 sites, accounting for about 10% of the U.S. population, and from population data from the U.S. Census Bureau. In 2024, 2.001 million new cases of invasive cancer (1,029,080 men and 927,060 women) were diagnosed, and 611,720 persons (322,800 men

and 288,920 women) died from cancer. The percent distribution of new cancer cases and cancer deaths by site for men and women is shown in Table 73-1. Cancer mortality continues to decline; however, 6 of the 10 most common cancers have increased in incidence by 1–3% in recent years, and troubling disparities among different racial/ethnic groups persist. Mortality is twice as high in black people than white people for cancers of the prostate, stomach, and uterine corpus. Cancer is the cause of one in four deaths in the United States.

Male

Prostate

Rate per 100,000 population

Lung & bronchus

Colorectum

Urinary bladder PART 4 Oncology and Hematology

Thyroid Livera Melanoma of the skin 1975 1980 1985 1990 1995 2000 Year of diagnosis 2005 2010 2015 2020

FIGURE 73-1 Trends in cancer incidence for men and women, 1975–2020. Incidence data for 2020 are indicated by color dots separate from the trend lines. (Reproduced with permission from RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:1, 2024.) The most significant risk factor for cancer overall is age; 58% of all cases were in those aged >65 years, down from 61% in 1995, despite an increase in this age group from 13% to 17% of the population. Cancer incidence increases as the third, fourth, or fifth power of age in different sites. For the interval between birth and age 49 years, 1 in 29 men and 1 in 19 women will develop cancer; for the interval between ages 50 and 59 years, 1 in 15 men and 1 in 17 women will develop cancer; for the interval between ages 60 and 69 years, 1 in 6 men and 1 in 10 women will develop cancer; and for people aged ≥70, 1 in 3 men and 1 in 4 women will develop cancer. Overall, men have a 40.5% risk of developing cancer at some time during their lives; women have a 38.9% lifetime risk. Cancer is the second leading cause of death behind heart disease. Deaths from heart disease have declined 45% in the United States since 1950 and continue to decline. Cancer has overtaken heart disease as the number one cause of death in persons aged <85 years. Incidence trends over time are shown in Fig. 73-1. After a 70-year period of increase, cancer deaths began to decline in 1990–1991 (Fig. 73-2). Between 1990 and 2010, cancer deaths decreased by 21% among men and 12.3% among women. The incidence has been steady since 2013. The magnitude of the decline is illustrated in Fig. 73-3. The five leading causes of cancer deaths are shown for various populations in Table 73-2. The 5-year survival for white patients was 39% in 1960–1963 and 68% in 2010–2016. Cancers are more often deadly in blacks; the 5-year survival was 63% for the 2010–2016 interval; however, the racial differences are narrowing over time. Incidence and mortality vary among racial and ethnic groups (Table 73-3). The basis for these differences is unclear. Advances in cancer prevention, diagnosis, and treatment since the early 1990s have averted millions of cancer deaths based on projections from the slopes of the mortality curves leading up to the 1990s (Fig. 73-4). ■

■CANCER AROUND THE WORLD In 2022, nearly 20 million new cancer cases and 9.7 million can

cer deaths were estimated worldwide, according to estimates of GLOBOCAN 2022, developed by the International Agency for Research on Cancer (IARC). Rates are increasing worldwide. When

Female

Breast

Lung & bronchus Colorectum

Uterine corpus

Thyroid Livera Melanoma of the skin 1975 1980 1985 1990 1995 2000 Year of diagnosis 2005 2010 2015 2020

broken down by region of the world, almost half of cases were in Asia (which has 59.2% of the world's population), 26% in Europe (9.6% of the world's population), 13.1% in North America, 7.1% in Central/ South America (the Americas, North and South, account for 13.3% of the world's population), 6% in Africa (16.6% of the world's population), and 1% in Australia/New Zealand (0.5% of the world's population) (Fig. 73-5). Lung cancer is the most common cancer and the most common cause of cancer death in the world. Its incidence is highly variable, affecting only 2 per 100,000 African women but as many as 61 per 100,000 North American men. Breast cancer is the second most common cancer worldwide; however, it ranks fourth as a cause of death behind lung, stomach, and liver cancer. Among the eight most common forms of cancer, lung (2-fold), breast (3-fold), prostate (2.5-fold), and colorectal (3-fold) cancers are more common in more developed countries than in less developed countries. By contrast, liver (2-fold), cervical (2-fold), and esophageal (2- to 3-fold) cancers are more common in less developed countries. Stomach cancer incidence is similar in more and less developed countries but is much more common in Asia than North America or Africa. The most common cancers in Africa are cervical, breast, and liver cancers. It has been estimated that nine modifiable risk factors are responsible for more than one-third of cancers worldwide. These include smoking, alcohol consumption, obesity, physical inactivity, low fruit and vegetable consumption, unsafe sex, air pollution, indoor smoke from household fuels, and contaminated injections. PATIENT MANAGEMENT Important information is obtained from every portion of the routine history and physical examination. The duration of symptoms may reveal the chronicity of disease. The past medical history may alert the physician to the presence of underlying diseases that may affect the choice of therapy or the side effects of treatment. The social history may reveal occupational exposure to carcinogens or habits, such as smoking or alcohol consumption, that may influence the course of disease and its treatment. The family history may suggest an underlying familial cancer predisposition and point out the need to begin surveillance or other preventive therapy for unaffected siblings of the patient. The review of systems may suggest early symptoms of metastatic disease or a paraneoplastic syndrome.

All sites combined

Deaths per 100,000 population

Males, by site

Stomach Colorectum Liver & intrahepatic bile duct Pancreas Lung & bronchus Prostate Leukemia
Deaths per 100,000 males

Females, by site

Stomach Colorectum Liver & intrahepatic bile duct Pancreas Lung & bronchus Breast Uterus
(corpus and cervix combined) Deaths per 100,000 females

Year of death

FIGURE 73-2 Trends in cancer mortality rates in men and women, 1930–2021. (Reproduced with permission from RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:1, 2024.) ■

■ **DIAGNOSIS** The diagnosis of cancer relies most heavily on invasive tissue biopsy and should never be made without obtaining tissue; no noninvasive diagnostic test is sufficient to define a disease process such as cancer (one exception to this rule may be hepatocellular carcinoma, which may be reliably diagnosed based on computed tomography [CT] or magnetic resonance imaging [MRI] showing the characteristic dynamic perfusion pattern of arterial hyperenhancement and venous or delayed phase washout). Although in rare clinical settings (e.g., thyroid nodules), fine-needle aspiration is an acceptable diagnostic procedure, the diagnosis generally depends on obtaining adequate tissue to permit careful evaluation of the histology of the tumor, its grade, and its invasiveness and to yield further molecular diagnostic information, such as the expression of cell-surface markers or intracellular proteins that typify a particular cancer, or the presence of a molecular marker, such as the t(8;14) translocation of Burkitt's lymphoma. Increasing evidence links the expression of certain genes with the prognosis and response to therapy (Chaps. 76 and 77). Occasionally, a patient will present with a metastatic disease process that is defined as cancer on biopsy but has no apparent primary site of

disease. Efforts should be made to define the primary site based on age, sex, sites of involvement, histology and tumor markers, and personal and family history. Particular attention should be focused on ruling out the most treatable causes (Chap. 97).

Male Once the diagnosis of cancer is made, the management of the patient is best undertaken as a multidisciplinary collaboration among the primary care physician, medical oncologists, surgical oncologists, radiation oncologists, oncology nurse specialists, pharmacists, social workers, rehabilitation medicine specialists, and a number of other consulting professionals working closely with each other and with the patient and family. **Female** ■ ■ **DEFINING THE EXTENT OF DISEASE AND THE PROGNOSIS** The first priority in patient management after the diagnosis of cancer is established and shared with the patient is to determine the extent of disease. The curability of a tumor usually is inversely proportional to the tumor burden. Ideally, the tumor will be diagnosed before symptoms develop or as a consequence of screening efforts (Chap. 75). A very high proportion of such patients can be cured. However, most patients with cancer present with symptoms related to the cancer, caused either by mass effects of the tumor or by alterations associated with the production of cytokines or hormones by the tumor. **CHAPTER 73 Approach to the Patient with Cancer** For most cancers, the extent of disease is evaluated by a variety of noninvasive and invasive diagnostic tests and procedures. This process is called staging. There are two types. Clinical staging is based on physical examination, radio graphs, isotopic scans, CT scans,

and other imaging procedures; pathologic staging takes into account information obtained during a surgical procedure, which might include intraoperative palpation, resection of regional lymph nodes and/or tissue adjacent to the tumor, and inspection and biopsy of organs commonly involved in disease spread. Pathologic staging includes histologic examination of all tissues removed during the surgical procedure. Surgical procedures performed may include a simple lymph node biopsy or more extensive procedures such as thoracotomy, mediastinoscopy, or laparotomy. Surgical staging may occur in a separate procedure or may be done at the time of definitive surgical resection of the primary tumor. A subset of pathologic staging is the examination of tissue obtained at initial surgery that occurs after the delivery of some treatment, which is called neoadjuvant therapy. Stage of disease determined after neoadjuvant therapy is designated with the prefix y. Knowledge of the predilection of particular tumors for spreading to adjacent or distant organs helps direct the staging evaluation. Information obtained from staging is used to define the extent of disease as localized, as exhibiting spread outside of the organ of origin to regional but not distant sites, or as metastatic to distant sites. The most widely used system of staging is the tumor, node, metastasis (TNM) system codified by the International Union Against Cancer and the American Joint Committee on Cancer. The TNM classification is an anatomically based system that categorizes the tumor on the basis of the size of the primary tumor lesion (T1–4, where a higher number indicates a tumor of larger size), the presence of nodal involvement (usually N0 and N1 for the absence and presence, respectively, of involved nodes, although some tumors have more elaborate systems of nodal grading), and the presence of metastatic disease (M0 and M1).

Male

Rate per 100,000

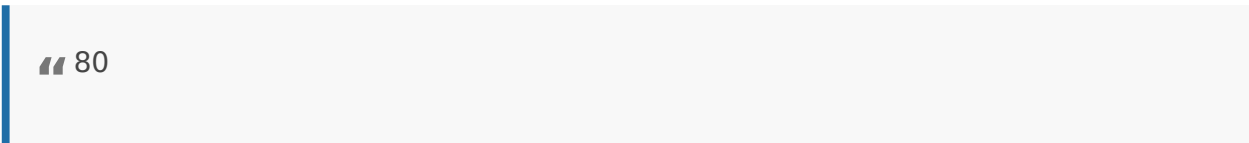
Lung & bronchus

Colorectum Leukemia

Brain & other nervous system 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020

7,000 PART 4 Oncology and Hematology 6,000 5,000 Lung & bronchus Number of deaths 4,000
3,000 Colorectum Leukemia 2,000 1,000 Brain & other nervous system 1975 1980 1985 1990 1995
2000 Year of death 2005 2010 2015 2020

FIGURE 73-3 Trends in cancer incidence and death rates. (Reproduced with permission from RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:1, 2024.) TABLE 73-2 The Five Leading Primary Tumor Sites for Patients Dying of Cancer Based on Age and Sex in 2018 RANK SEX ALL AGES UNDER 20 20-39 40-49 50-64 65-79



M Lung CNS Colorectal Colorectal Lung Lung Lung F Lung CNS Breast Breast Lung Lung Lung

M Prostate Leukemia CNS Lung Colorectal Prostate Prostate F Breast Leukemia Cervix Colorectal Breast Breast Breast

M Colorectal Bone sarcoma Leukemia CNS Pancreas Liver Colorectal F Colorectal Soft tissue sarcoma Colorectal Lung Colorectal Pancreas Colorectal

M Pancreas Soft tissue sarcoma Testis Pancreas Liver Colorectal Bladder F Pancreas Bone sarcoma CNS Cervix Pancreas Colorectal Pancreas

M Liver Lymphoma Lymphoma Esophagus Esophagus Liver Pancreas F Ovary Kidney Leukemia Ovary Ovary Ovary Leukemia Abbreviations: CNS, central nervous system; F, female; M, male. Source: From RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:12, 2024.

Female Breast Lung & bronchus Colorectum Uterine cervix 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020 Breast Lung & bronchus Colorectum Uterine cervix 1975 1980 1985 1990 1995 2000 Year of death 2005 2010 2015 2020 AGE, YEARS

TABLE 73-3 Cancer Incidence and Mortality in Racial and Ethnic Groups, United States, 2016–2020

SITE	SEX	WHITE	BLACK	Incidence per 100,000 Population	All	M	511.2	533.9	299.0	504.1	377.2	F	499.3	409.9	307.3	465.5	351.3																																																																																					
Breast	M	134.9	129.6	104.6	115.5	100.7	Colorectal	M	40.4	48.8	33.4	57.8	38.2	F	30.5	35.0	23.7	43.7	27.2	Kidney	M	24.3	26.4	11.6	43.9	23.5	F	12.1	13.7	5.5	23.9	13.3																																																																						
Liver	M	11.2	17.0	18.4	27.3	20.4	F	4.2	5.5	6.7	12.3	8.4	Lung	M	765.7	72.4	40.8	67.2	34.3	F	54.8	45.8	28.1	58.6	24.0	Prostate	110.7	186.1	60.9	91.9	90.9	Stomach	M	7.1	13.0	11.8	13.1	11.4	F	3.4	7.4	6.9	7.8	7.7	Cervix	7.2	8.6	6.0	11.4	9.7	Endometrial	27.9	28.9	21.7	30.4	25.8																																														
Deaths per 100,000 Population	All	M	183.3	217.4	111.6	221.6	130.2	F	133.6	150.2	83.7	157.9	93.5	Breast	19.7	27.8	11.8	21.1	13.7	Colorectal	M	15.5	22.4	11.0	23.1	13.6	F	11.1	14.4	7.8	16.0	8.5	Kidney	M	5.3	5.2	2.4	9.9	4.8	F	2.3	2.2	1.0	4.2	2.1	Liver	M	8.5	13.0	12.6	19.9	13.1	F	3.7	4.8	5.2	8.8	6.0	Lung	M	44.9	51.3	25.9	52.3	21.-	F	32.9	28.0	15.6	37.0	11.4	Prostate	17.9	37.9	8.7	22.5	15.4	Stomach	M	2.9	7.2	6.0	7.7	5.9	F	1.5	3.5	3.7	4.1	3.9	Cervix	2.0	3.3	1.7	2.3	2.5	Endometrial	4.6	9.1	3.5	4.9	4.3

aBased on Indian Health Service delivery areas. Abbreviations: F, female; M, male. Source: From RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:12, 2024. Reproduced of John Wiley & Sons Ltd. for the absence and presence, respectively, of metastases). The various permutations of T, N, and M scores (sometimes including tumor histo logic grade [G]) are then broken into stages, usually designated by the roman numerals I through IV. Tumor burden increases and curability decreases with increasing stage. Other anatomic staging systems are used for some tumors, e.g., the Dukes classification for colorectal can cers, the International Federation of Gynecologists and Obstetricians classification for gynecologic cancers, and the Ann Arbor classification for Hodgkin’s lymphoma. Certain tumors cannot be grouped on the basis of anatomic con siderations. For example, hematopoietic tumors such as leukemia, myeloma, and lymphoma are often disseminated at presentation and do not spread like solid tumors. For these tumors, other prognostic factors have been identified (Chaps. 109–116). In addition to tumor burden, a second major determinant of treatment outcome is the physiologic reserve of the patient. Patients who are bedridden before developing cancer are likely to fare worse, stage for stage, than fully active patients. Physiologic reserve is a determinant of how a patient is likely to cope with the physiologic stresses imposed by the cancer and its treatment. This factor is dif ficult to assess directly. Instead, surrogate markers for physiologic

ASIAN/PACIFIC ISLANDER AMERICAN INDIANa HISPANIC CHAPTER 73 Approach to the Patient with Cancer reserve are used, such as the patient's age or Karnofsky performance status (Table 73-4) or Eastern Cooperative Oncology Group (ECOG) performance status (Table 73-5). Older patients and those with a Karnofsky performance status <70 or ECOG performance status ≥3 have a poor prognosis unless the poor performance is a reversible consequence of the tumor. Some have advocated for using one of the geriatric assessment tools to gauge physiologic reserve. See ASCO's video for an example of a geriatric assessment tool (<https://www.youtube.com/watch?v=jnaQljOz2Dw>). Increasingly, biologic features of the tumor are being related to prognosis. The expression of particular oncogenes, drug-resistance genes, apoptosis-related genes, and genes involved in metastasis is being found to influence response to therapy and prognosis. The presence of selected cytogenetic abnormalities may influence survival. Tumors with higher growth fractions, as assessed by expression of proliferation-related markers such as proliferating cell nuclear antigen (detectable by staining with Ki67 antibody), behave more aggressively than tumors with lower growth fractions. Information obtained from studying the tumor itself will increasingly be used to influence treatment decisions. Host genes involved in drug metabolism can influence the safety and efficacy of particular treatments.

	Male	Female
550,000	500,000	450,000
400,000	350,000	300,000
250,000	200,000	150,000
100,000	50,000	

Number of deaths 300,000 2,794,900
cancer deaths averted 250,000 200,000 150,000 PART 4 Oncology and Hematology 100,000 50,000

Year of death FIGURE 73-4 Cancer deaths averted in men and women since the early 1990s. Projections based on death continuing on the established trajectory. (Reproduced with permission from RL Siegel et al: Cancer statistics, 2024. CA Cancer J Clin 74:1, 2024.) Enormous heterogeneity has been noted by studying tumors; we have learned that morphology is not capable of discerning certain distinct subsets of patients whose tumors have different sets of abnormalities. Tumors that look the same by light microscopy can be very different. Similarly, tumors that look quite different from one another histologically can share genetic lesions that predict responses to treatments. Furthermore, tumor cells vary enormously within a single patient even though the cells share a common origin. ■ ■MAKING A TREATMENT PLAN From information on the extent of disease and the prognosis and in conjunction with the patient's wishes, it is determined whether the treatment approach should be curative or palliative in intent. Cooperation among the various professionals involved in cancer treatment is of the utmost importance in treatment planning. For some cancers, chemotherapy or chemotherapy plus radiation therapy delivered before the use of definitive surgical treatment (so-called neoadjuvant therapy) may improve the outcome, as seems to be the case for locally advanced breast cancer, head and neck cancers, and lung cancers, among others. In certain settings in which combined-modality therapy is intended, coordination among the medical oncologist, radiation oncologist, and surgeon is crucial to achieving optimal results. Sometimes the chemotherapy and radiation therapy need to be delivered sequentially and other times concurrently. Surgical procedures may precede or follow other treatment approaches. It is best for the treatment plan either to follow a standard protocol precisely or else to be part of an ongoing clinical research protocol evaluating new treatments. Ad hoc modifications of standard protocols are likely to compromise treatment results. The choice of treatment approaches was formerly dominated by the local culture in both the university and the practice settings. However, it is now possible to gain access electronically to standard treatment

550,000 500,000 450,000 400,000 350,000 300,000 250,000 1,344,600 cancer deaths averted
200,000 150,000 100,000 50,000

Year of death protocols and to every approved clinical research study in North America through a personal computer interface with the Internet.¹ The skilled physician also has much to offer the patient for whom curative therapy is no longer an option. Often a combination of guilt and frustration over the inability to cure the patient and the pressure of a busy schedule greatly limit the time a physician spends with a patient who is receiving only palliative care. Resist these forces. In addition to the medicines administered to alleviate symptoms (see below), it is important to remember the comfort that is provided by holding the patient’s hand, continuing regular examinations, and taking time to talk. ■ ■MANAGEMENT OF DISEASE AND

TREATMENT COMPLICATIONS Although medicine has been guided through centuries by the aphorism “primum non nocere,” first do no harm, it fits modern medicine poorly. As a practical matter, nearly everything we do in patient care has risk of doing harm; diagnostic tests, therapeutic interventions, and even physical diagnosis can lead to patient harm. A more relevant guide to modern medicine is “primum succerrere”; first hasten to help. Because cancer therapies are toxic (Chap. 78), patient management involves addressing complications of both the disease and its treatment as well as the complex psychosocial problems associated with cancer. In the short term during a course of curative therapy, the patient’s functional 1The National Cancer Institute maintains a database called PDQ (Physician Data Query) that is accessible on the Internet under the name CancerNet at <https://www.cancer.gov/publications/pdq>. Information can be obtained through a facsimile machine using CancerFax by dialing 301-402-5874. Patient information is also provided by the National Cancer Institute in at least three formats: on the Internet via CancerNet at www.cancer.gov, through the CancerFax number listed above, or by calling 1-800-4-CANCER. The quality control for the information provided through these services is rigorous.

Mortality, males Colorectum (5) Esophagus (3) Kaposi sarcoma (2) Lip, oral cavity (2) Lung (89) Prostate (52) Liver (24) Stomach (8) A Mortality, females Colorectum (4) Stomach (2) Esophagus (1) Breast (112) Cervix uteri (37) Lung (23) Liver (6) B FIGURE 73-5 Global maps showing most common cause of cancer mortality by country in 2022 among (A) men and (B) women. (Reproduced with permission from F Bray et al: Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74:229, 2024.) TABLE 73-4 Karnofsky Performance Index PERFORMANCE STATUS FUNCTIONAL CAPABILITY OF THE PATIENT

- Normal; no complaints; no evidence of disease
- Able to carry on normal activity; minor signs or symptoms of disease
- Normal activity with effort; some signs or symptoms of disease
- Cares for self; unable to carry on normal activity or do active work
- Requires occasional assistance but is able to care for most needs

Requires considerable assistance and frequent medical

care

Disabled; requires special care and assistance

Severely disabled; hospitalization is indicated, although death is not imminent

Very sick; hospitalization is necessary; active supportive treatment is necessary

Moribund, fatal processes progressing rapidly

Dead

CHAPTER 73 Approach to the Patient with Cancer status may decline. Treatment-induced toxicity is less acceptable if the goal of therapy is palliation. The most common side effects of treatment are nausea and vomiting (see below), febrile neutropenia (Chap. 79), and myelosuppression (Chap. 78). Tools are now available to minimize the acute toxicity of cancer treatment. TABLE 73-5 The Eastern Cooperative Oncology Group (ECOG) Performance Scale ECOG grade 0: Fully active, able to carry on all predisease performance without restriction ECOG grade 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work ECOG grade 2: Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about >50% of waking hours ECOG grade 3: Capable of only limited self-care, confined to bed or chair >50% of waking hours ECOG grade 4: Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair ECOG grade 5: Dead Source: Reproduced with permission from MM Oken et al: Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649, 1982.

New symptoms developing in the course of cancer treatment should always be assumed to be reversible until proven otherwise. The fatalistic attribution of anorexia, weight loss, and jaundice to recurrent or progressive tumor could result in a patient dying from a reversible intercurrent cholecystitis. Intestinal obstruction may be due to reversible adhesions rather than progressive tumor. Systemic infections, sometimes with unusual pathogens, may be a consequence of the immunosuppression associated with cancer therapy. Some drugs used to treat cancer or its complications (e.g., nausea) may produce central nervous system symptoms that look like metastatic disease or may mimic paraneoplastic syndromes such as the syndrome of inappropriate antidiuretic hormone. A definitive diagnosis should be pursued and may even require a repeat biopsy.

A critical component of cancer management is assessing the response to treatment. In addition to a careful physical examination in which all sites of disease are physically measured and recorded in a flow chart by date, response assessment usually requires periodic repeating of imaging tests that were abnormal at the time of staging. If imaging tests have become normal, repeat biopsy of previously involved tissue is performed to document complete response by pathologic criteria. Biopsies are not usually required if there is macroscopic residual disease. A complete response is defined as disappearance of all evidence of disease, and a partial response as >50% reduction in the sum of the products of the perpendicular diameters of all measurable lesions. The

determination of partial response may also be based on a 30% decrease in the sums of the longest diameters of lesions (Response Evaluation Criteria in Solid Tumors [RECIST]). Progressive disease is defined as the appearance of any new lesion or an increase of >25% in the sum of the products of the perpendicular diameters of all measurable lesions (or an increase of 20% in the sums of the longest diameters by RECIST). Tumor shrinkage or growth that does not meet any of these criteria is considered stable disease. Some sites of involvement (e.g., bone) or patterns of involvement (e.g., lymphangitic lung or diffuse pulmonary infiltrates) are considered unmeasurable. No response is complete without biopsy documentation of their resolution, but partial responses may exclude their assessment unless clear objective progression has occurred.

PART 4 Oncology and Hematology For some hematologic neoplasms, flow cytometric and genetic assays may determine the presence of residual tumor cells that escape microscopic detection. In general, these techniques can reliably detect as few as 1 tumor cell among 10,000 cells. If such tests do not detect tumor cells, the patient is said to have minimal residual disease negativity, a finding generally associated with more durable remissions. Accumulating data are defining interventions in patients with minimal residual disease positivity that can extend remission duration and survival. Tumor markers may be useful in patient management in certain tumors. Response to therapy may be difficult to gauge with certainty. However, some tumors produce or elicit the production of markers that can be measured in the serum or urine, and in a particular patient, rising and falling levels of the marker are usually associated with increasing or decreasing tumor burden, respectively. Some clinically useful tumor markers are shown in Table 73-6. Tumor markers are not in themselves specific enough to permit a diagnosis of malignancy to be made, but once a malignancy has been diagnosed and shown to be associated with elevated levels of a tumor marker, the marker can be used to assess response to treatment. The recognition and treatment of depression are important components of management. The incidence of depression in cancer patients is ~25% overall and may be greater in patients with greater debility. This diagnosis is likely in a patient with a depressed mood (dysphoria) and/or a loss of interest in pleasure (anhedonia) for at least 2 weeks. In addition, three or more of the following symptoms are usually present: appetite change, sleep problems, psychomotor retardation or agitation, fatigue, feelings of guilt or worthlessness, inability to concentrate, and suicidal ideation. Patients with these symptoms should receive therapy. Medical therapy with a serotonin reuptake inhibitor such as fluoxetine (10–20 mg/d), sertraline (50–150 mg/d), or paroxetine (10–20 mg/d) or a tricyclic antidepressant such as amitriptyline (50–100 mg/d) or desipramine (75–150 mg/d) should be tried, allowing 4–6 weeks

TABLE 73-6 Tumor Markers	
TUMOR MARKERS	CANCER
Hormones	Nonneoplastic conditions
Human chorionic gonadotropin	Gestational trophoblastic disease, gonadal germ cell tumor
Pregnancy	Calcitonin
Medullary cancer of the thyroid	Catecholamines
Pheochromocytoma	Oncofetal Antigens
α Fetoprotein	Hepatocellular carcinoma, gonadal germ cell tumor
Cirrhosis, hepatitis	Carcinoembryonic antigen
Adenocarcinomas of the colon, pancreas, lung, breast, ovary	Pancreatitis, hepatitis, inflammatory bowel disease, smoking
Enzymes	Prostatic acid phosphatase
Prostate cancer	Prostatitis, prostatic hypertrophy
Neuron-specific enolase	Small-cell cancer of the lung, neuroblastoma
Lactate dehydrogenase	Lymphoma, Ewing's sarcoma
Hepatitis, hemolytic anemia, many others	Tumor-Associated Proteins
Prostate-specific antigen	Prostate cancer
Prostatitis, prostatic hypertrophy	Monoclonal immunoglobulin
Myeloma	Infection, MGUS
CA-125	Ovarian cancer, some lymphomas
Menstruation, peritonitis, pregnancy	CA 19-9
Colon, pancreatic, breast cancer	Pancreatitis, ulcerative colitis
CD30	Hodgkin's disease, anaplastic large-cell

lymphoma — CD25 Hairy cell leukemia, adult T-cell leukemia/lymphoma Hemophagocytic lymphohistiocytosis Abbreviation: MGUS, monoclonal gammopathy of uncertain significance. for response. Effective therapy should be continued at least 6 months after resolution of symptoms. If therapy is unsuccessful, other classes of antidepressants may be used. In addition to medication, psychosocial interventions such as support groups, psychotherapy, and guided imagery may be of benefit. Many patients opt for unproven or unsound approaches to treatment when it appears that conventional medicine is unlikely to be curative. Those seeking such alternatives are often well educated and may be early in the course of their disease. Unsound approaches are usually hawked on the basis of unsubstantiated anecdotes and not only cannot help the patient but may be harmful. Physicians should strive to keep communications open and nonjudgmental, so that patients are more likely to discuss with the physician what they are actually doing. The appearance of unexpected toxicity may be an indication that a supplemental therapy is being taken.² LONG-TERM FOLLOW-UP/LATE COMPLICATIONS At the completion of treatment, sites originally involved with tumor are reassessed, usually by radiography or imaging techniques, and any persistent abnormality is biopsied. If disease persists, the multidisciplinary team discusses a new salvage treatment plan. If the patient has been rendered disease-free by the original treatment, the patient

²Information about unsound methods may be obtained from the National Council Against Health Fraud, Box 1276, Loma Linda, CA 92354, or from the Center for Medical Consumers and Health Care Information, 237 Thompson Street, New York, NY 10012.

is followed regularly for disease recurrence. The optimal guidelines for follow-up care are not known. For many years, a routine practice has been to follow the patient monthly for 6–12 months, then every other month for a year, every 3 months for a year, every 4 months for a year, every 6 months for a year, and then annually. At each visit, a battery of laboratory and radiographic and imaging tests was obtained on the assumption that it is best to detect recurrent disease before it becomes symptomatic. However, where follow-up procedures have been examined, this assumption has been found to be untrue. Studies of breast cancer, melanoma, lung cancer, colon cancer, and lymphoma have all failed to support the notion that asymptomatic relapses are more readily cured by salvage therapy than symptomatic relapses. In view of the enormous cost of a full battery of diagnostic tests and their manifest lack of impact on survival, new guidelines are emerging for less frequent follow-up visits, during which the history and physical examination are the major investigations performed. As time passes, the likelihood of recurrence of the primary cancer diminishes. For many types of cancer, survival for 5 years without recurrence is tantamount to cure. However, important medical problems can occur in patients treated for cancer and must be examined (Chap. 100). Some problems emerge as a consequence of the disease and some as a consequence of the treatment. An understanding of these disease- and treatment-related problems may help in their detection and management. Despite these concerns, most patients who are cured of cancer return to normal lives. ■ ■ SUPPORTIVE CARE In many ways, the success of cancer therapy depends on the success of the supportive care. Failure to control the symptoms of cancer and its treatment may lead patients to abandon curative therapy. Of equal importance, supportive care is a major determinant of quality of life. Even when life cannot be prolonged, the physician must strive to preserve its quality. Quality-of-life measurements have become common endpoints of clinical research studies. Furthermore, palliative care has been shown to be cost-effective when approached in an organized fashion. A credo for oncology could be to cure sometimes, to extend life often, and to comfort always. Management strategies for cancer pain, nausea, and other common side effects of cancer and its treatment are outlined in Chap. 74. An approach to end-of-

life care is provided in Chap. 13. Psychosocial Support The psychosocial needs of patients vary with their situation. Patients undergoing treatment experience fear, anxiety, and depression. Self-image is often seriously compromised by deforming surgery and loss of hair. Women who receive cosmetic advice that enables them to look better also feel better. Loss of control over how one spends time can contribute to the sense of vulnerability. Juggling the demands of work and family with the demands of treatment may create enormous stresses. Sexual dysfunction is highly prevalent and needs to be discussed openly with the patient. An empathetic health care team is sensitive to the individual patient's needs and permits negotiation where such flexibility will not adversely affect the course of treatment. Cancer survivors have other sets of difficulties. Patients may have fears associated with the termination of a treatment they associate with their continued survival. Adjustments are required to physical losses and handicaps, real and perceived. Patients may be preoccupied with minor physical problems. They perceive a decline in their job mobility and view themselves as less desirable workers. They may be victims of job and/or insurance discrimination. Patients may experience difficulty reentering their normal past life. They may feel guilty for having survived and may carry a sense of vulnerability to colds and other illnesses. Perhaps the most pervasive and threatening concern is the ever-present fear of relapse (the Damocles syndrome). Patients in whom therapy has been unsuccessful have other problems related to the end of life. Death and Dying The most common causes of death in patients with cancer are infection (leading to circulatory failure), respiratory

failure, hepatic failure, and renal failure. Intestinal blockage may lead to inanition and starvation. Central nervous system disease may lead to seizures, coma, and central hypoventilation. About 70% of patients develop dyspnea preterminally. However, many months usually pass between the diagnosis of cancer and the occurrence of these complications, and during this period, the patient is severely affected by the possibility of death. The path of unsuccessful cancer treatment usually occurs in three phases. First, there is optimism at the hope of cure; when the tumor recurs, there is the acknowledgment of an incurable disease, and the goal of palliative therapy is embraced in the hope of being able to live with disease; finally, at the disclosure of imminent death, another adjustment in outlook takes place. The patient imagines the worst in preparation for the end of life and may go through stages of adjustment to the diagnosis. These stages include denial, isolation, anger, bargaining, depression, acceptance, and hope. Of course, patients do not all progress through all the stages or proceed through them in the same order or at the same rate. Nevertheless, developing an understanding of how the patient has been affected by the diagnosis and is coping with it is an important goal of patient management.

It is best to speak frankly with the patient and the family regarding the likely course of disease. These discussions can be difficult for the physician as well as for the patient and family. The critical features of the interaction are to reassure the patient and family that everything that can be done to provide comfort will be done. They will not be abandoned. Many patients prefer to be cared for in their homes or in a hospice setting rather than a hospital. The American College of Physicians has published a book called Home Care Guide for Cancer: How to Care for Family and Friends at Home that teaches an approach to successful problem-solving in home care. With appropriate planning, it should be possible to provide the patient with the necessary medical care as well as the psychological and spiritual support that will prevent the isolation and depersonalization that can attend in-hospital death. CHAPTER 73 Approach to the Patient with Cancer The care of dying patients may take a toll on the physician. A "burn out" syndrome has been described that is characterized by fatigue, disengagement from patients and colleagues, and a loss of self-

fulfillment. Efforts at stress reduction, maintenance of a balanced life, and setting realistic goals may combat this disorder. End-of-Life Decisions Unfortunately, a smooth transition in treatment goals from curative to palliative may not be possible in all cases because of the occurrence of serious treatment-related complications or rapid disease progression. Vigorous and invasive medical support for a reversible disease or treatment complication is assumed to be justified. However, if the reversibility of the condition is in doubt, the patient's wishes determine the level of medical care. These wishes should be elicited before the terminal phase of illness and reviewed periodically. Information about advance directives can be obtained from the American Association of Retired Persons, 601 E Street, NW, Washington, DC 20049, 202-434-2277, or Choice in Dying, 250 West 57th Street, New York, NY 10107, 212-366-5540. Some states allow physicians to assist patients who choose to end their lives. This subject is challenging from an ethical and a medical point of view. Discussions of end-of-life decisions should be candid and involve clear informed consent, waiting periods, second opinions, and documentation. A full discussion of end-of-life management is provided in Chap. 13. ■ ■FURTHER READING Bray F et al: Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74:229, 2024. Hesketh PJ et al: Antiemetics: ASCO guideline update. J Clin Oncol 38:2782, 2020. Kelley AS, Morrison RS: Palliative care for the seriously ill. N Engl J Med 373:747, 2015. Martini RS et al: Integrative approaches for cancer pain management. Curr Oncol Rep 26:691, 2024. Samala RV et al: Frequently asked questions about managing cancer pain: An update. Cleve Clin Med J 88:183, 2021. Siegel RL et al: Cancer statistics, 2024. CA Cancer J Clin 74:12, 2024.

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