

Cancer Survivors: A Physician's Perspective

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During the past three decades since the declaration of a war on cancer with the National Cancer Act of 1971, we have been exposed to a very public display of both the challenges and triumphs in this war. As a young medical oncologist, I anxiously awaited each annual meeting of the American Society of Clinical Oncology (ASCO), expecting to hear the latest small advances in the treatment of leukemia, lymphoma, Hodgkin's disease, and then breast cancer (the first solid tumor that seemed to respond to multiagent chemotherapy), gradually seeing plateaus in the survival curves suggesting cure. With the phase II trials of cisplatin, there were rumors of young men with advanced testicular cancer rising from their deathbeds after a single course of treatment. Soon thereafter, the Einhorn regimen¹ of vinblastine, bleomycin and cisplatin, brought about high cure rates in this rare but devastating cancer of young men. And of course, three decades later we all know the story of Lance Armstrong, one of the world's most famous testicular cancer survivors. However, as the breast cancer activists reminded us in the early 1990s, there were still more American women dying each year from breast cancer than U.S. deaths during the entire Vietnam War.^{2*} Fortunately, in 2006, with new targeted therapies, we may now be modifying the course of disease for many other solid tumors.

So without revealing my specific age, I have told you about how I have personally observed advances that have led to the growth in the absolute numbers and relative proportion of cancer survivors, who now in the U.S. are more than 10 million strong and growing.³ In the past two decades, the 5-year survival rate for the top 15 cancers (as identified in SEER data from 1975 to 1979 and then from 1995 to 2000) has increased from 42.7% for men and 56.6% for women, to 64% for men and to 64.3% for women.⁴ Figures 1.1 to 1.4 provide the most recent statistics available on cancer survivors from the National Cancer Institute (NCI) Office of Cancer Survivorship (OCS),⁵ and set the stage for why this book has been written, and the rationale for the specific chapters that are included. In this volume we focus on disease sites or patient groups who have most benefited from treatments during the past three decades.

However, the purpose of this chapter is to provide a physician's perspective on issues related to cancer survivorship,

and the chapters that immediately follow present the perspectives of my colleagues in nursing and social work. In this way, we hope to make this topic relevant to various health care providers involved in the ongoing and follow-up care of cancer survivors.

In this chapter, I will discuss the following:

- the role of the physician in the care of the cancer survivor;
- strategies to address the positive and negative consequences of cancer treatments;
- how to help patients and families heal;
- managing long-term relationships and caring for multiple generations; and
- addressing the critical role of prevention among survivors.

The reader must understand that this reflects only one physician's perspective and that the content is strongly influenced by the author's most recent clinical work and research focused on breast cancer patients and survivors. However, it is clear that these observations can be generalized to other cancer sites and settings.

How Did We Get Here and What Is the Role of the Physician?

In parallel with the expansion of research associated with the National Cancer Act of 1971, there was an enormous investment of federal funds in cancer centers and training programs, fostering the expanded development of a large number of specialists to diagnose, treat, and rehabilitate cancer patients. We now have mature oncology subspecialty training programs in general surgery, thoracic oncology, urologic oncology, gynecological oncology, otolaryngology and so forth, in addition to pediatrics, internal medicine, and radiology. Subsequently, there was growing interest in early detection, screening and prevention, which were also fostered through central programs at the NCI as well as funding of the extramural research program. The NCI Cooperative Group Program, first established in the 1950s to evaluate new anticancer agents from NCI's drug development program, gradually shifted to studies of combined modality therapy approaches in cancer treatment characterized by the large phase III clinical trials that are in place today, many of which are supported by the pharmaceutical industry.

The NCI designated cancer centers and their affiliated hospitals are the setting in which most clinical oncologists

*Forty-four thousand women were dying each year from breast cancer. While subsequent estimates of death in Vietnam were 759,000, breast cancer activists often used this for a point (Patricia A. Ganz, personal recollection).

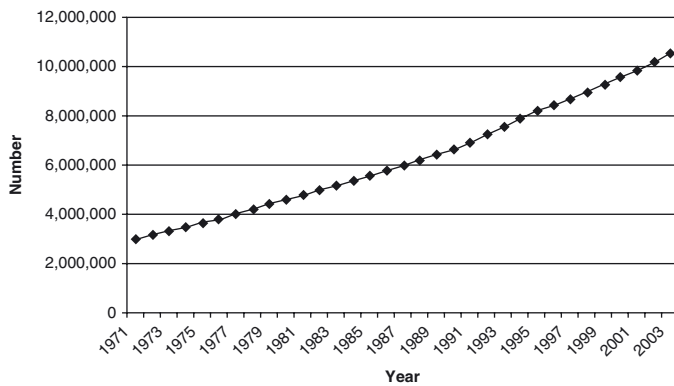


FIGURE 1.1. Estimated number of cancer survivors in the United States from 1971 to 2003. U.S. estimated prevalence counts were estimated by applying U.S. populations to SEER 9 and to historical Connecticut Limited Duration Prevalence proportions, and adjusted to represent complete prevalence. Populations from January 2003 were based on the average of the July 2002 and July 2003 population estimates from the U.S. Bureau of Census. (Source: 2005 submission.)

in practice today have been trained. This is especially true for medical oncologists, but also includes specialists trained in surgery and radiation oncology. Most trainees were introduced to clinical research through participation in cooperative group trials, investigator initiated studies, and pharmaceutical industry studies. The systematic development of cancer treatments through clinical investigation has contributed to an extensive published literature which is often summarized in evidence based reviews or guidelines that can facilitate best practices and treatment decision making. Cancer care is viewed today as multidisciplinary, requiring the input of several clinicians, including nurses, social workers and others. The gains in survival described earlier reflect the systematic approach to treatment, which benefits from the advances in clinical research as well as the diffusion of well-trained oncology specialists into the community away from specialized NCI designated cancer centers.

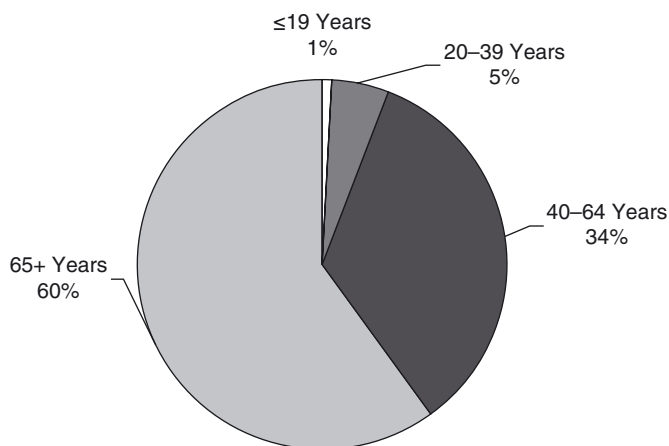


FIGURE 1.2. Estimated number of persons alive in the United States diagnosed with cancer by current age (invasive/first primary cases only, $n = 10.5$ million survivors). U.S. estimated prevalence counts were estimated by applying U.S. populations to SEER 9 and to historical Connecticut Limited Duration Prevalence proportions, and adjusted to represent complete prevalence. Populations from January 2003 were based on the average of the July 2002 and July 2003 population estimates from the U.S. Bureau of Census. (Source: 2005 submission.)

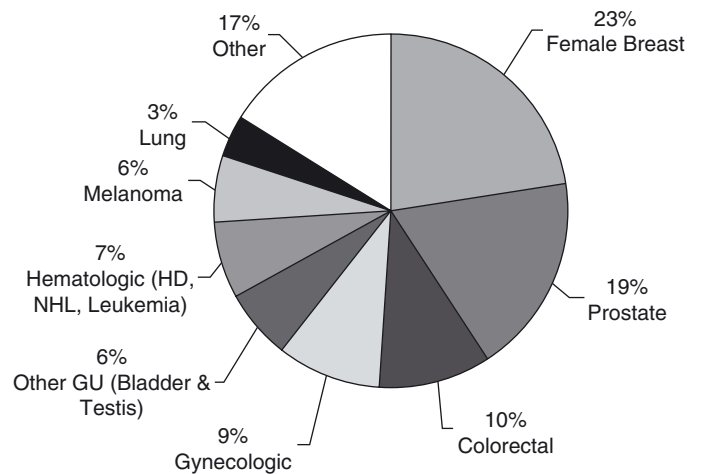


FIGURE 1.3. Estimated number of persons alive in the United States diagnosed with cancer by site ($n = 10.5$ million survivors). U.S. estimated prevalence counts were estimated by applying U.S. populations to SEER 9 and to historical Connecticut Limited Duration Prevalence proportions, and adjusted to represent complete prevalence. Populations from January 2003 were based on the average of the July 2002 and July 2003 population estimates from the U.S. Bureau of Census. (Source: 2005 submission.)

Unfortunately, in spite of excellent training in the curative approach to cancer treatment, most oncology specialists have had little formal training in the follow-up care of cancer survivors. However, during the past 10 to 15 years, the number of articles on the late effects of cancer treatment has grown substantially, spearheaded first by those interested in childhood cancer survivors,^{6–10} and more recently by those investigating adult cancer survivors.^{11–19} A recent IOM report focused on the needs of childhood cancer survivors²⁰ with a parallel report on adult cancer survivors in 2005.²¹ For children, the price of cure is detailed extensively in Chapter 7 in this volume. It is important to note that most children with cancer in the United States are treated in specialized centers and are enrolled in cooperative group trials. This has facilitated the linkage of specific treatments to untoward late effects (e.g., second malignancies, neuropsychological impair-

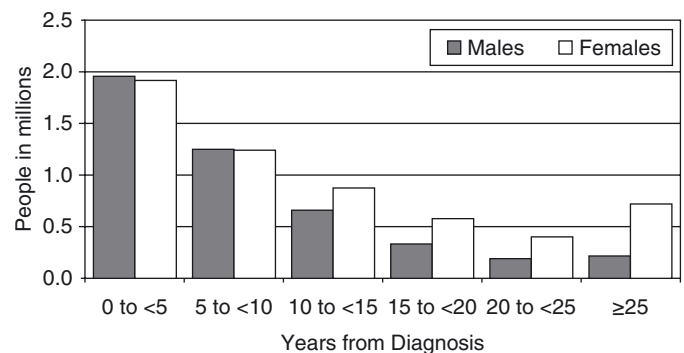


FIGURE 1.4. Estimated number of persons alive in the United States diagnosed with cancer on January 1, 2003, by time from diagnosis and gender (invasive/first primary cases only, $n = 10.5$ million survivors). U.S. estimated prevalence counts were estimated by applying U.S. populations to SEER 9 and to historical Connecticut Limited Duration Prevalence proportions, and adjusted to represent complete prevalence. Populations from January 2003 were based on the average of the July 2002 and July 2003 population estimates from the U.S. Bureau of Census. (Source: 2005 submission.)

ment, cardiac complications). These observations have influenced the conduct of subsequent clinical trials.

In adult oncology, where participation in clinical trials is more limited, there is less precision in understanding the incidence of late effects, whether serious or minimal. Nevertheless, there is a growing body of information, especially for survivors of breast cancer, prostate cancer, leukemia, lymphoma, Hodgkin's disease, and testes cancers, as described later in this volume. More important, as delineated in the IOM report on adult cancer survivors,²¹ there is growing awareness of a distinct phase in the cancer trajectory where acute treatment is completed and the patient/survivor transitions into a period of less intensive medical follow-up that necessitates a new model for care. There is a need for coordinated care between cancer specialists and primary care physicians at this juncture, with a focus on paying attention to the short-term and late effects of cancer treatment, prevention of late sequelae (e.g., osteoporosis) and/or recurrence, surveillance for new cancers, and monitoring of adjuvant therapy (e.g., extended hormonal or maintenance treatments). In addition, someone must make sure that routine preventive health care (e.g., smoking cessation, obesity prevention, cardiovascular disease prevention) is addressed. To this end, the recent IOM report suggests that an *end-of-treatment summary and survivorship care plan* be completed, which is forward looking and anticipates these aspects of care.²¹ Such a summary is currently lacking, but if used it can be the means of providing explicit communication of this information by the treating oncologist to the patient/survivor, as well as to the primary care physician and other health care professionals. It is expected that this process will influence better coordination of care during the posttreatment phase of cancer survivorship. In addition, such documentation in the medical record can be a source of information for evaluation of quality of care, as well as systematic evaluation of the linkage between treatment exposures and outcomes.

Currently, care during this phase of treatment is often shared in a nonexplicit way between oncology specialists and primary care physicians.^{22,23} This leads to both under and overutilization of surveillance testing for cancer recurrence,^{24,25} and lack of attention to prevention and rehabilitation services (see more detailed discussion in Chapter 5 in this volume). It is hoped that this proposed IOM recommendation will serve to better coordinate the care for survivors by defining the role(s) of each of these groups of physicians in the long-term follow-up of cancer survivors. In addition, there is likely an important potential role for other allied health-care providers (nurse practitioners, physician assistants) in providing the ongoing care for cancer survivors within the oncology care setting. Oncology specialists and primary care physicians each have their role, and just as we recommend shared decision making in cancer treatment planning, there is also a critical role for shared care in the follow-up of cancer survivors. This proposed strategy is designed to facilitate a dialogue among all of these stakeholders so that the care and follow-up of the cancer survivors can be optimized.

Another group of medical specialists who have largely been left out of this dialogue are physical medicine and rehabilitation specialists. While rehabilitation medicine demonstration projects were a key component of the early years of the National Cancer Act,²⁶⁻²⁸ in recent years there has been much less involvement of this group of physicians in cancer

care. Possible exceptions to this have been in lymphedema management, neurological rehabilitation (e.g., brain tumor patients), postlaryngectomy patients, and for patients with stomas. However, an active and preventive role for rehabilitative medicine services across a wide variety of cancer sites needs to be considered early in the cancer treatment process, and is largely neglected in current practice.²⁹ The IOM adult cancer survivor report calls attention to this issue²¹ and perhaps we will see more involvement of this physician community working with survivors in the future.

Facing the Positive and Negative Consequences of Therapy

Oncology physicians clearly appreciate seeing long-term survivors for return office visits, as this reminds them of the value of their efforts in managing the complexities of initial treatment. However, these physicians are often ill-equipped to identify and manage some of the lingering effects of cancer therapy. Furthermore, they may experience guilt as well as distress, at seeing patients they have treated develop serious health problems that are a result of cancer treatments (e.g., second malignancies, infertility, cognitive changes, congestive heart failure). The oncology specialist whose practice is focused on one particular cancer site (e.g., breast, prostate, lymphoma, or colorectal) can become quite expert in managing some of the common problems in these survivors. For example, most urologists are able to address the problems of erectile dysfunction and urinary incontinence in prostate cancer survivors, and they may have access to support groups for these patients and their partners. However, for the busy oncologist who sees patients with a wider variety of diagnoses and cares for only a limited number of survivors, these types of problems might be quite vexing. Oncologists might never ask questions about sexual functioning nor offer specific treatments. As a result, cancer survivors are often disappointed that no one is paying attention to the late effects they experience as a result of their cancer treatment, and that no one has a systematic approach to monitoring them after initial treatment.

How can we address this challenge? Among the best things we can do is to try to prepare our patients for the possibility of some common late effects of treatment from the outset. That means addressing the likelihood of infertility, early menopause, cardiac dysfunction, chronic side effects from treatment, and even second malignancies. This is sometimes challenging to do, given the rapidity with which cancer treatment decisions are made and the complexity of preventive interventions (e.g., sperm banking).^{30,31} Nevertheless, survivors appreciate that they were at least told about the possibilities of these difficulties, even though we may not be able to predict who will develop specific side effects or long-term sequelae from treatment. (This is where more research is absolutely needed.) How much individual patients recall from these early discussions is unclear, but as part of informed consent for treatment, known risks for late effects should be disclosed.

Even though no formalized system of care exists for cancer survivors, it appears that a substantial number of oncologists are regularly caring for them. As part of a recent survey performed by ASCO's Cancer Prevention Committee,³² a random sample of ASCO members (surgeons, medical oncologists, radiation oncologists) were asked three questions

related to the care of cancer survivors. The survey respondents were asked "To what extent do you provide ongoing general medical care, including health maintenance, screening, and preventive services, to the cancer survivors in your practice?" Thirty-one percent reported "always," 48% "sometimes," 15% "rarely," and 5% "not at all or do not care for survivors." When asked whether or not it was the role of the oncology specialist to provide this type of continuing care to cancer survivors, the overwhelming majority (74%) responded "yes." Finally, they were asked whether or not they were comfortable providing ongoing general medical care to cancer survivors and 66% responded "yes."³² So although it appears that many of ASCO's members are providing some form of care to cancer survivors, we do not know how focused that care is on surveillance for cancer recurrence *versus* health promotion, disease prevention, and monitoring/prevention of late effects.

A major focus, however, is likely to be surveillance for recurrence and/or detection of new cancers that may be independent of the original primary or related to the original cancer (e.g., new breast or colorectal cancers in patients with a first primary). New cancers may also occur because of a past exposure history (tobacco, sunlight, infection) or as a secondary effect of past cancer treatments. The oncologist is probably the best physician member of the team to follow survivors who may have these risks, and often second cancers are detected earlier in cancer survivors. In my own practice, I have had three breast cancer survivors in whom stage I lung cancers were detected early (chest x-rays taken for minimal pulmonary symptoms). All three of these women had remote and limited histories of tobacco exposure, and had quit smoking many years earlier. There are also some cancer survivors who are just unlucky, and they may be prone to multiple primary cancers, either related to their age, past treatments, or rarely, hereditary predisposition genes. Increasingly, oncologists have taken on the responsibility for providing genetic counseling to their patients and their families.^{33,34} Being proactive in addressing the risk for future cancers is often reassuring to cancer survivors, and physicians play an important role in this activity.

Helping Patients and Families Heal

Just as physicians play a critical role at the time of cancer diagnosis, describing the etiology of the specific cancer and why the patient may have developed the disease, as well as explaining the rationale for staging, diagnostic procedures, and the treatment plan, so must the physician guide the patient and family making the transition from the acute phase of survivorship to the phase that Mullan calls "extended survival."³⁵ This is often a difficult time psychologically, as all of life's activities that might have been put on hold during treatment (e.g., work, school, marriage, child-bearing) must now be addressed and often the patient/survivor is a changed person as a result of the cancer treatment experience. This may include the enhancement of some personal relationships and the abandonment of others; a decision to change jobs; a reinvigoration of life goals and plans; separation or divorce related to longstanding marital difficulties; adoption of a healthier lifestyle; increased spirituality and focus on existential issues. The changes invoked by the

cancer experience affect patients and their families, and this is often a time when patients are most interested in obtaining psychosocial support. Patients may find that their family members and co-workers think that everything is over when the treatment ends, but in fact, the patient must continue dealing with the uncertainties of survival and the necessity of maintaining their health through regular check-ups and ongoing maintenance therapies. In the case of childhood cancer, the patient's family may require special attention, with strong evidence of posttraumatic stress in parents and aftereffects on siblings.^{36,37}

Couples and families may find it useful to seek counseling or join support groups if relationship issues become apparent. Physicians can provide expert guidance at this time, being available to address the specific concerns about important life plans (e.g., pregnancy, life insurance, job discrimination). They also can provide assistance with rehabilitative issues such as diet, lifestyle, sexuality and body image concerns. For the patient entering this phase of the survivorship trajectory, there is much greater uncertainty, and reassurance and structured psychosocial and educational intervention may facilitate the patient's recovery and return of energy.

Also at this time family members may become much more concerned about their own vulnerability with regard to a cancer diagnosis. Especially concerning diseases such as breast and colorectal cancer, where hereditary predisposition genes have been identified, or in which familial risk of cancer may be heightened. Physicians are often called upon to counsel these individuals about their risk for cancer and what might be done to prevent it. Having just seen a close relative experience cancer treatment can be a catalyst for these family members to come forward and seek help and advice. Being prepared to care for the extended family of a survivor in this way is an important part of the physician's role. Increasingly, I have found myself serving as a family physician in this setting, albeit cancer focused. Helping these family members obtain an accurate estimate of their cancer risk, as well as educating them about preventive interventions, often allows them to provide better ongoing emotional support to their loved one.

As wisely stated two decades ago by physician and cancer survivor, Fitzhugh Mullan,

Since this phase is not predominantly a medical one, doctors and nurses tend to have a diminishing role in providing support and counseling. The result is a void that leaves many cancer patients and their families fending awkwardly for themselves in the "healthy world." . . . Treatment plans for patients in this postacute phase rarely address the psychosocial problems of reentering the active world. Systematic referrals by oncologists, primary care physicians, and nurses to support services for patients at this point in their recovery would do a tremendous amount to aid adjustment, relieve suffering, and stimulate the further development of these scarce resources.³⁵

Long-Term Relationships and Caring for Multiple Generations

There is a unique bond that is established between cancer patients and the physicians who treat them. The close calls of cancer treatment (e.g., febrile neutropenia) and the ups and downs of surgery, radiation or toxic therapies delivered and received for the benefit of the patient/long-term survivor,

engenders the development of a strong dyadic relationship. Many years later, cancer survivors will often reminisce with fondness and/or gallows humor about their treatment experience, and they frequently maintain contact with these physicians for many years thereafter, even with relocation to another community. The cancer treatment physician is often seen as a trusted source of information, for issues related to late effects of treatment, as well as for referrals to other physicians. The intensity of the relationship may vary, but under most circumstances, that physician is a key authority figure for the cancer survivor.

As long-term survival has increased, especially with common diseases such as breast, colorectal and prostate cancers, it is not uncommon for the cancer specialist to become professionally involved with family members of the cancer patient. These new medical relationships may focus on prevention and genetic testing in close family members (e.g., daughters, sisters, brothers, children),³³ or actual treatment of cancer in close family members. In my practice, I have cared for mothers and daughters, sisters, as well as husbands and wives. Sometimes it is easier on everyone concerned to have the same familiar oncologist take on the new cancer patient in the family due to the levels of trust and personal relationship, although it may be challenging for the physician to have to go through cancer treatment once again with another member of the family. As our knowledge of risk factors (exposure and genetics) for cancer increases, physicians will need to consider the extended family as well as the patient/survivor.

Critical Role of Prevention

A cancer diagnosis can teach something to both patients and their physicians.^{38,39} Faced with a life-threatening illness, survivors often want to do the best they can to reduce their risk of having another cancer episode. This may take the form of smoking cessation, dietary modifications, weight loss, exercise, use of mind-body techniques (meditation, relaxation), and exploration of various complementary and alternative medicine strategies.¹⁹ To the extent possible, physicians must be prepared to support these survivors in making lifestyle changes, which means we need to be prepared to offer smoking cessation treatment and counseling, diet and exercise counseling, as well as access to mind-body treatments to help manage stress and enhance psychological well-being. These types of services may be part of routine care within primary care practices, but may need to be adapted to the special needs of cancer survivors. Frequently, these types of services are available at community and comprehensive cancer centers. They might also be available through some community organizations such as the American Cancer Society and American Lung Association (e.g., smoking cessation).

At the same time, physicians may be called upon by their patients to weigh in on the latest media reports of cancer cures or prevention strategies, including diet and lifestyle products that are heavily marketed to the public. We live in a health and youth oriented culture, and it is impossible to escape having to deal with these issues in medical practice. The big challenge occurs when scientific reports conflict (e.g., vitamin E prevents cancer in one study, but increases heart disease in another). Under these circumstances, it is essential

to communicate to patients and survivors the incremental nature of scientific discovery, and the need for patience in sorting out conflicting results. Ultimately, it is usually large randomized clinical trials that settle many of these questions. A good example was the issue of whether or not it was safe to give hormone therapy to women after a breast cancer diagnosis. Breast cancer survivors who were either very symptomatic with vasomotor symptoms or were concerned about prevention of heart disease and dementia felt deprived of the potentially disease preventing effects of postmenopausal hormone therapy. This question for breast cancer survivors was largely resolved with the negative results from the Women's Health Initiative trial in healthy women,⁴⁰⁻⁴³ and then in breast cancer patients in the HABITS trial.⁴⁴ Having randomized controlled trial data provide the strongest arguments for or against a health promoting strategy, and we may need to reinforce that with our patients and survivors.

There also has been an expanding role for chemoprevention in this target population, with many large phase III clinical trials demonstrating cancer risk reduction benefit in high risk patient groups that include cancer survivors.^{45,46} Increasingly, those who care for cancer survivors will need to address the potential use of chemopreventive agents in survivors. This is now a standard of care in the management of breast cancer survivors with estrogen receptor positive tumors, where long-term endocrine therapies are used for reduction in the risk of second primaries.⁴⁷⁻⁴⁹ Trials of chemoprevention also have been conducted in survivors of early stage colorectal cancer,⁵⁰ however, standardized approaches to chemoprevention in this setting have not taken hold. Rather surveillance with colonoscopy is the primary strategy in use for prevention.

Childhood cancer survivors are probably the group in greatest need of preventive interventions, as the risks for second cancers are so much greater in this population (see Chapters 6, 7, 15, and 17). Research suggests that these high-risk individuals do not undergo cancer screening at a frequency generally recommended in the population, and certainly not at the rate expected given their high-risk status.⁵¹ Some work has already been done to target childhood cancer survivors who use tobacco, as they are at a substantially higher risk of developing smoking related neoplasms.^{52,53} Other important interventions in this target group are sun protection, dietary and physical activity interventions. These interventions are necessary due to the high rates of basal cell carcinoma, as well as the metabolic syndrome.³⁸ Finally, adolescent and young adult women who receive chest irradiation as part of their cancer treatments are at high risk for breast cancer⁵⁴ and should receive high-risk screening and potentially endocrine directed chemopreventive treatments. Other detailed recommendations regarding cancer screening for childhood cancer survivors can be found in the "Children's Oncology Group Long Term Follow-up Guidelines" that are briefly reviewed in the *Journal of Clinical Oncology*⁵⁵ and can be found online at www.survivorshipguidelines.org.

Conclusions

During the past 4 decades, cancer has been transformed from a highly stigmatized condition that was often acutely fatal, to one in which the vast majority of individuals can expect

cure. Today, few public figures can hide that they have been diagnosed with cancer and the concept of cancer survivorship has been widely popularized. We are on the brink of the widespread use of more personalized and targeted forms of cancer therapies that are likely to enhance the likelihood of cure and lead to avoidance of unnecessary toxicities in many patients. Nevertheless, there is an entire generation of cancer survivors who are living with the sequelae of our more traditional treatments (see Chapters 7, 9, 15, and 17). Just as physicians must keep abreast of the latest developments in detection and treatment, now they will be expected to be able to provide comprehensive and coordinated care for the growing number of cancer survivors. The challenge for us will be to develop systems of long-term follow-up and care for these survivors, and most importantly, expand our knowledge base regarding the most frequent late effects they might experience. In parallel, we must develop preventive interventions and comprehensive rehabilitation programs to maximize recovery and quality of life after cancer treatment ends.^{54,55} This all must be done in collaboration with our patients and other members of the healthcare team.

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