Ongoing Care of Patients After Primary Treatment for Their Cancer

Herman Kattlove, MD, MPH; Rodger J. Winn, MD

ABSTRACT   Nearly nine million people living in the United States have had a diagnosis of cancer. As the population ages, this number will increase. Most of these people will need follow-up care to deal with problems related to their cancer. Depending on the cancer, they may or may not benefit from surveillance to detect recurrence. Most will be more likely than average to develop a second primary cancer. Some will be genetically susceptible to another type of cancer. Many will have complications from their treatment that need attention. Also, their treatment may have altered certain physiologic functions. Finally, many will have suffered psychosocial difficulties either as a result of their cancer or its treatment. This article deals with these issues for the most commonly encountered cancers. Its major goal is to alert physicians to be aware of and help them to deal with these issues. Clearly, such an ambitious goal can only be partly achieved in a single journal article. Hopefully, the references included will allow physicians to proceed further if they wish. (CA Cancer J Clin 2003;54:172-196.) © American Cancer Society, 2003.

INTRODUCTION

In 2003, more than 1,300,000 Americans will be diagnosed with cancer.¹ As the population grows and ages, this number will likely increase. Most people will survive their cancer. The five-year survival from all cancers is almost 62 percent and excluding lung cancer, it is 69 percent.² Recent statistics from the National Cancer Institute Surveillance Epidemiology and End Results (SEER) database estimate that nearly nine million people who have had a diagnosis of cancer were alive at the end of 1999.³ Almost 3.5 million of these people have had their diagnosis within five years.

Cancer survivors have a spectrum of unique medical needs that require focused attention. All patients are at risk for recurrence of their primary tumor. Others may develop a second primary cancer because of genetic susceptibility or as a consequence of their treatment. Many will need psychosocial support or help in dealing with the physiologic consequences of their cancer treatment. The question that we will address in this article is: what measures should be taken to care for and follow cancer survivors? Our purpose is to provide information to physicians assuming the primary responsibility of caring for patients who are thought to be cured or at least free of their cancer.

During their follow-up, cancer survivors may require care for diverse needs that span a broad spectrum of medical areas. The physician providing follow-up services
should be prepared to evaluate the patient’s needs in each of these areas and initiate appropriate interventions or referrals when needed. The specific domains that make up the constellation of problems facing the cancer survivor include:

- Surveillance to detect recurrent cancer;
- Assessing genetic susceptibility to cancer of both the patient and the family;
- Detecting a second primary;
- Monitoring complications of treatment;
- Dealing with any altered physiologic status due to the cancer or its treatment;
- Support for psychosocial problems associated with the cancer.

Another important aspect of the management of cancer survivorship must be addressed: namely that the issues that arise for the cancer survivor are, for the most part, disease (tumor) specific. Thus, the follow-up of a breast cancer survivor compared with a colorectal cancer patient will involve different problems within each of these domains. The physician involved in long-term management of these patients must realize that a comprehensive set of knowledge and skills is required. In order to assist in this endeavor, we have undertaken to detail appropriate management that is tumor-specific (Table 1).

**General Comments on Benefits of Follow-up Care**

Any evaluation of the benefits of follow-up should take into account the major outcomes in oncology: survival, quality of life, patient satisfaction, and cost-effectiveness. To many observers, survival is the most important issue in evaluating the worth of follow-up visits and testing. Most studies of careful follow-up and routine testing have not demonstrated a survival advantage. With the exception of surgically resectable isolated recurrences or chemotherapy-sensitive or hormone-sensitive cancers, finding recurrent cancer early does not appear to improve patient survival. In a review of the value of follow-up testing, Edelman, et al. found that it seldom detected the vast majority of recurrences early nor did it seem to result in a higher chance of cure or prolonged survival.4

Very few studies have examined the benefits of follow-up care on quality of life. Anxiety associated with follow-up visits would be one concern. Visits may increase anxiety because of a patient’s fear of recurrence.5 Or they might lessen it when nothing is found. Most cancer patients welcome follow-up visits in spite of some psychological distress before the visit.6 In general, this distress is mild. In a study by Lampic, et al.7 only about one-fifth of patients who were in remission and receiving follow-up care for their cancer reported anxiety. This lessened as the time from diagnosis increased.

One reason often cited for follow-up exams is patient demand. This is probably not a valid reason. Gulliford, et al.8 have reported a randomized study in which women with breast cancer were followed up with routine quarterly visits or only an annual exam at the time of mammography. There was no difference in patient satisfaction between the two schedules, and perhaps of even greater interest, 16 percent in each group thought the follow-up schedule was excessive.

We have chosen for discussion those cancers that are likely to undergo long-term follow-up care and are seen most frequently and typically by primary care physicians as well as by specialists.

**BREAST CANCER**

Breast cancer may be said to be the paradigm for discussion of follow-up care. It is the most frequent cancer in women,9 and over 85 percent of patients are alive five years after diagnosis.5 For these reasons, over 700,000 breast cancer survivors in the United States are alive within five years of their diagnosis; their total prevalence is over two million.3 An excellent review of survivorship issues for women with breast cancer has been published.9
### Summary of the Most Prominent Issues in Each Domain

| Cancer                  | Surveillance | Genetic Counseling and Testing | Second Primary | Treatment Complications | Physiologic Alteration | Psychosocial Problems |
|-------------------------|--------------|--------------------------------|----------------|-------------------------|------------------------|-----------------------|
| **Breast cancer**       | Breast exams and mammography only | BRCA mutations Genetic counseling ( +/- testing) based on family history | High-risk – ipsilateral or contralateral breast, ovarian, and colorectal cancers | Arm edema | Menopausal symptoms, osteoporosis | Anxiety about cancer recurrence, sexuality, and body image |
| **Colorectal cancer**   | Carcinembryonic antigen test Consider CT scan, PET scan | FAP, HNPC mutations Genetic counseling ( +/- testing) based on family history | High-risk – colorectal, endometrial cancer with HNPC mutations | Radiation proctitis | Colostomy/anal incontinence, sexual dysfunction | Secondary to physiologic alterations |
| **Prostate cancer**     | Prostate specific antigen test | Genetic counseling if strong family history Testing not routinely available | Bladder | Sexual dysfunction, incontinence, radiation proctitis | Impotence, urinary incontinence and leakage, diarrhea | Secondary to physiologic alterations – support groups useful |
| **Testes cancer**       | HCG test, AFP test, chest x-ray | Some familial cases, no genetic testing available | High-risk – testes, leukemia, solid tumors | Infertility | No major problems | Related to sexual and fertility issues |
| **Hodgkin disease**     | CT/PET scans | None | High-risk – lung, breast, GI, leukemia, non-Hodgkin lymphoma | Hypothyroidism, heart failure, reduced lung function, neuropathy, infertility | Fatigue, sexual dysfunction | Marital difficulties, sexual problems |
| **Leukemias/ non-Hodgkin lymphomas** | CBCs, CT and PET scans for NHL | None | Increased risk for multiple sites – not high | Heart failure, hepatitis | Fatigue, sexual dysfunction | Marital difficulties, sexual and vocational problems |
| **Lung cancers**        | Chest x-rays only | No gene identified – counseling for familial occurrence | High-risk – lung, upper aerodigestive tract | Reduced lung function, renal damage, neuropathy | Dyspnea, cognitive loss | Dependence due to lung damage and cognitive loss |
| **Gynecologic cancers** | Pelvic exams, Pap tests, CA-125 test (for ovarian cancer). | BRCA, HNPC mutations Genetic counseling ( +/- testing) based on family history | Colorectal cancer risk increased with HNPC Risk of second HPV-related cancer | Urinary frequency, diarrhea, vaginal stenosis, neuropathy | Menopausal symptoms, sexual problems | Anxiety about cancer recurrence |
| **Bladder, kidney cancers** | Chest x-rays, CT scans, cystoscopy, and urinary cytology for bladder cancers | VHL gene mutations in RCC Genetic counseling ( +/- testing) based on family history | Second primary bladder tumors, upper urinary tract tumors | Sexual and urinary dysfunction in bladder cancer patients | Urinary leakage and impotence | Secondary to physiologic alterations |

**Key:**
- AFP = Alpha-fetoprotein.
- CBC = Complete blood count.
- CT = Computed tomography.
- FAP = Familial adenomatous polyposis.
- GI = Gastrointestinal.
- HCG = Human chorionic gonadotropin.
- HNPC = Hereditary nonpolyposis colon cancer.
- HPV = Human papilloma virus.
- NHL = Non-Hodgkin lymphoma.
- PET = Positron emission tomography.
- RCC = Renal cell carcinoma.
- VHL = von Hippel-Lindau.
Surveillance After Primary Treatment

Monitoring for recurrent breast cancer entails evaluation for local recurrences in patients who have undergone breast-conserving surgery and for disseminated recurrences in all patients. A large Italian study of 2,233 women treated with breast-conserving surgery followed by radiation therapy to the breast found a local recurrence rate of approximately one percent per year. The National Surgical Adjuvant Breast and Bowel Project (NSABP) found a cumulative rate of 14 percent 20 years after breast-conserving surgery and post-operative radiation therapy. The rate was 39 percent if radiation was not given. Follow-up after 20 years revealed a 39 percent recurrence rate for those receiving the adjuvant irradiation and 14 percent in those who did not.

In the Italian cohort, distant recurrences were found most frequently in the second year after treatment. This rate declined thereafter so that in the fifth year, only 1.5 percent developed distant recurrences, and in the tenth year, only one percent. These rates were affected by tumor stage and patient age. A review of the Eastern Cooperative Oncology Group data for 3,585 patients found recurrence rates twice that of the Italian study, but with the same pattern of greatest recurrence rate in the second year. The differing results in the two studies probably arose from the greater proportion of node-positive women in the American study. Other studies have reported similar local and distant recurrence rates.

What benefit, if any, is there for careful search for these recurrences? Two major randomized trials and a Cochrane Review have concluded that there is no survival benefit in routine laboratory and imaging testing as part of a follow-up regimen. In the Interdisciplinary Group for Cancer Care Evaluation (GIVIO) study of routine visits and mammograms versus routine bone scans, chest x-rays, and liver ultrasounds, the five-year survival was 82 percent and 80 percent for the two groups, respectively, demonstrating the lack of benefit for intensive routine testing. A recent study found that one-third of recurrences were manifested by history, one-third detected by physical exam, and one-sixth by mammogram.

Another study found that primary care physicians could successfully provide follow-up care. Patients were randomly assigned to follow-up by specialists or primary care physicians. Specialist care did not lead to earlier diagnosis of a recurrence, improved quality of life, or lower anxiety levels. These and other data led to follow-up/surveillance guidelines issued by the American Society of Clinical Oncology and the National Comprehensive Cancer Network (NCCN) that advised only routine histories and physicals at three to six month intervals, with lengthening of the interval to annually five years after treatment along with annual mammography. Annual pelvic exams were also recommended, particularly if the woman was taking tamoxifen. No laboratory testing or imaging studies were recommended.

Assessing Genetic Susceptibility

This is an important issue for women with breast cancer. About 5 to 10 percent of breast cancers are caused by an inherited mutation of either the BRCA1 or BRCA2 gene. Women with these mutations usually develop their cancer early in life and have a strong family history of breast cancer. Any women with these clinical features should undergo genetic counseling and possibly testing for these mutations. If they do carry the gene, they will be much more likely to develop recurrent ipsilateral as well as contralateral breast cancers. In addition, they have a high risk of developing ovarian cancer. Prophylactic oophorectomy should be considered, particularly after childbearing is complete, although some of these women will develop peritoneal or tubal
carcinomas. Oophorectomy in BRCA carriers decreases the incidence of breast cancer as well as ovarian cancer. Other strategies to reduce the breast cancer risk are prophylactic mastectomy, which is highly effective and treatment with tamoxifen for five years. Although these maneuvers have been mainly reported for women who have not developed cancer, they should still be valid for those who have. Women who have opted not to undergo prophylactic mastectomy are traditionally followed with mammography. Recent studies have shown that breast magnetic resonance imaging (MRI) may be more effective, particularly for younger women.

In addition to their responsibility for following the cancer patient if a genetic syndrome is present, the treating physician must also assume a public health role and provide information regarding the management of at-risk family members. Current recommendations call for the initiation of screening at age 25 or five years younger than the earliest reported cancer in the family.

Many women with a family history of breast cancer will not carry known specific gene mutations. Their risk of developing cancer may be higher than normal also. Other than consideration of the use of preventive tamoxifen, they are followed in the same way as women who have no family history.

Diagnosing a Second Primary

Women with one primary breast cancer are at greater risk for developing a second primary breast cancer than the normal population. The probability of a metachronous tumor developing within 20 years of the primary tumor has been reported to be in the range of 15 percent. Annual mammograms are therefore indicated for the remainder of the patient’s life. Women with ductal carcinoma in situ, lobular carcinoma in situ, and small invasive breast cancer may receive tamoxifen. There is evidence that tamoxifen will reduce their chance of ipsilateral breast cancer recurrence as well as reduce breast cancer incidence in the contralateral breast.

Women with BRCA mutations are not only at risk of ovarian cancer, they also have a higher risk of non-colonic gastrointestinal (GI) cancers. There are no specific guidelines for screening for these. Finally, there may be an increased risk of myelodysplasia and acute myelogenous leukemia in women who have had chemotherapy, particularly intensive-dose chemotherapy. There is no established value in frequent blood counts unless there are symptoms of anemia, thrombocytopenia, or frequent infections.

Monitoring and Treating Complications of Treatment

Complications can arise either from surgery, hormonal therapy, or chemotherapy. The major complication of the surgery is lymphedema secondary to the axillary dissection. This occurs about 20 to 30 percent of the time with numbers ranging from 10 percent to over 40 percent. Radiation to the axilla after dissection will lead to the highest incidence. With the increasing use of sentinel lymph node mapping this should decrease but will not disappear; women with positive sentinel nodes will inevitably undergo a complete axillary dissection. Treatment with arm elevation, elastic sleeves, and sometimes, special lymphedema massage therapy may be helpful. It is important that this be treated early since as the edema increases, it becomes harder to resolve.

In addition to its development after high-dose therapy, leukemia also occurs after treatment with alkylating agents such as cyclophosphamide or topoisomerase inhibitors, such as topotecan or etoposide. The latter are rarely used to treat breast cancer. The development of heart failure secondary to anthracycline therapy is a relatively uncommon side effect in breast cancer patients who have received these agents as part of their adjuvant chemotherapy regimens. This complication becomes more prevalent after doxorubicin
cumulative doses of 550 mg/m²; most adjuvant regimens stop below this dose. The combination of trastuzumab and anthracyclines has been found to lead to a particularly high incidence of congestive heart failure. Because trastuzumab is not recommended for adjuvant therapy outside a clinical trial, it should not be frequently encountered in the follow-up of the breast cancer survivor. Most physicians use echocardiography to assess cardiac function when there are symptoms.

Tamoxifen therapy causes symptoms of estrogen deprivation. Hot flashes and night sweats are two common complaints. Another is vaginal discharge. Sexual function is usually unaffected. Clinical trials have shown that some selective serotonin reuptake inhibitor (SSRI) antidepressants can partially alleviate the hot flashes. Soy products are not recommended because they contain estrogen-like substances that may interfere with tamoxifen. Adjuvant therapy with tamoxifen increases the risk of endometrial cancer. No screening test for endometrial cancer has proven useful in this context. Routine yearly pelvic exams and careful evaluation of any abnormal bleeding with ultrasound appear to be the best strategy.

Dealing With Altered Physiologic Status

The major physiologic problem that breast cancer survivors face is menopause. This will occur naturally, but may be hastened by chemotherapy. Osteoporosis is one concern, particularly in thin women. They should be assessed for osteoporosis. If it is found, they should be encouraged to take adequate amounts of calcium and exercise, but may require pharmacological treatment.

Weight gain after chemotherapy can be distressing for many women. This seems to be a consequence of the adjuvant therapy and menopause. Therapy is difficult, but important, since increasing weight seems to lead to poorer prognosis.

Particularly distressing to many women are the symptoms of menopause. They can occur quite abruptly with chemotherapy or, of course, oophorectomy. Although retrospective studies have not shown harm from hormone replacement therapy in breast cancer survivors, no randomized control studies have been performed that would allow physicians to confidently prescribe these drugs. Patients need to be completely involved in decision making if they wish to take these agents. The recent findings of increased risk of developing breast cancer while on hormone replacement therapy with estrogen and progesterone makes recommendations in this area even more difficult.

Weakness and inability to use the arm on the affected side after axillary dissection may plague some patients. Physical therapy can help alleviate this problem. The weakness often reverses by six months after surgery.

Finally, there is concern about what some have called “chemo brain.” Cognitive impairment has been found by specific testing two years after treatment in about one-third of women treated with high-dose chemotherapy. Patients themselves recognize this as trouble with memory, concentration, and thinking. No treatment has been proposed for this; it is not known if this eventually disappears. A recent study found persistent defects five years after treatment.

Psychosocial Problems of Breast Cancer Survivors

Although the diagnosis of breast cancer and its subsequent treatment has a major impact on a woman’s life, there is little residual psychological effect once treatment has been completed. A large prospective study of women five years after primary treatment for breast cancer found that their mental health functioning was better than at diagnosis and was slightly above the population norm for
healthy women.55 Other aspects of quality of life were not significantly different from baseline, but women who received chemotherapy did have somewhat lower values.

Fear of cancer recurrence is found in the majority of patients. Others are worried about their future, and some about finances.56 Discussion of these fears along with follow-up care has been recommended. Whether these fears become a problem generally reflects the underlying psychological health of the patient.57 After diagnosis, these fears decline with time.58

**COLORECTAL CANCER**

The Surveillance, Epidemiology, and End Results (SEER)³ review estimates that slightly over one million people were alive after a diagnosis of colorectal cancer. Nearly 380,000 had been diagnosed within the previous five years.

**Surveillance for Recurrence After Primary Treatment**

Probably no area has generated more controversy than the value of intensive surveillance after surgery for colorectal cancer. The potential benefits of intensive surveillance may be realized in two ways: the monitoring may identify patients with resectable metastases (usually hepatic) or the early chemotherapy treatment of disseminated disease may confer a survival advantage. Although the evidence is not conclusive and more information from randomized controlled trials is pending, the weight of evidence favors some form of surveillance.

An early study⁵⁹ using frequent carcino-embryonic antigen (CEA) measurements followed 400 patients and found 75 with recurrences that appeared curable by surgery. Of these, 22 were long-term survivors. A more recent study⁶⁰ of patients entered into a large National Cancer Institute adjuvant therapy trial (Intergroup 0035) found a similar benefit for intensive testing. Patients were followed with frequent visits, liver panels, and chest x-rays. CEA levels and detailed imaging, such as computed tomography (CT), magnetic resonance imaging, and ultrasound, were optional. These studies led to 109 patients undergoing curative-intent surgery; 25 lived over five years without recurrence and were probably cured.

In addition to these retrospective studies, several randomized controlled trials have also been conducted that compare intensive follow-up with less intensive follow-up. Five of these studies⁶¹-⁶⁵ that met the criteria for inclusion have been incorporated into a recently published meta-analysis.⁶⁶ All these studies used different surveillance strategies. Nevertheless, when the results for the 1,342 participants were combined, those who underwent intensive surveillance had an absolute survival advantage of seven percent (37% versus 30% five-year survival). This translated into a relative survival benefit of 21 percent.

These conclusions were strengthened when the results of the Danish study,⁶⁵ which avoided CT scans and CEA measurements, were excluded. The remaining four studies yielded an improvement in absolute five-year survival of 9 to 13 percent or a relative 27 percent increase. The four studies all used CT scans of the liver, CEA measurements, chest x-rays, and endoscopies. Most of the studies were done every three months except CT scans, which were done at intervals of 6 to 12 months. The intensity of the follow-up decreased after two years. The major benefit appeared to be the early detection of liver and lung metastases. No benefit accrued from frequent endoscopies.

It seems reasonable that follow-up CEA may be performed in patients who would be suitable candidates for surgery of isolated recurrences.⁶⁷ The performance of routine CT scanning is still controversial. These recommendations must still be viewed as
preliminary, since other randomized controlled studies are in progress. Also, the value of newer techniques, such as positron emission tomography (PET) scans, in assessing (for example) an elevated CEA may lead to the discovery of even more curable recurrences.

Assessing Genetic Susceptibility

Hereditary nonpolyposis colon cancer (HNPCC) is the major genetic disorder associated with colorectal cancer. Its prevalence among colorectal cancer patients has been estimated as anywhere between 0.5 percent and 13 percent, depending on the criteria used.68 The usual estimate is around five to ten percent.69 The major criteria for its diagnosis are the Amsterdam criteria.68 These include: (1) at least three relatives with HNPCC-associated cancer (see below); (2) one affected relative should be a first-degree relative of the other two; (3) at least two successive generations should be affected; (4) colon cancer should be diagnosed in one relative under 50 years of age; (5) familial adenomatous polyposis (FAP) should be excluded. Patients with HNPCC who develop colon cancer may be treated with a total colectomy70 or a limited resection.71 These patients should undergo intensive surveillance with colonoscopy every one to three years.

The other major, inherited colorectal cancer syndrome is FAP. This genetic disorder is much less common than HNPCC.69 This disease, resulting in multiple polyps throughout the colon, is usually managed by some form of prophylactic proctocolectomy.72 In some patients with a low-polyp burden in the rectum, the rectum is retained, in which case, frequent proctoscopy is indicated. For these patients, consideration can be given to the use of a cyclo-oxygenase-2 (COX-2) inhibitor to suppress polyp growth.73,74 Patients with this disorder are also at risk for adenomas of the upper GI tract,75 and routine upper-GI endoscopy is indicated. The frequency of these examinations depends on the number of adenomas found and whether dysplasia is present.

Genetic testing for the APC gene in familial polyposis and mismatch repair genes in HNPCC is available, and patients with colorectal cancer in the setting of these syndromes should undergo genetic counseling to discuss genetic testing.76 The demonstration of a mutated gene can then be used to screen the remainder of the family and identify those members who need intensive monitoring.

Diagnosing a Second Primary

Since people with one colorectal cancer are at risk for a second, they should undergo regular colonoscopy. The cumulative incidence of new cancers is about 1.5 percent at five years.77 This is higher than in the general population. Although no studies have shown improved survival because of frequent endoscopies, it would seem prudent to examine the entire colon within one to two years after surgery, and then, if that is negative, on a less frequent schedule perhaps every three to five years.

The risk of other second primary cancers in patients who have had sporadic colorectal cancer is not higher than in an age-matched population. Because the adjuvant chemotherapy used is fluorouracil based, hematologic malignancies would not be expected. Irinotecan has been proposed as a potential adjuvant drug; it has not yet been shown to cause secondary malignancies.

HNPCC is associated with other primary cancers.78 Endometrial cancer is the second most common cancer found in HNPCC carriers. Its risk has been estimated at 30 to 40 percent by age 70.79 Stomach and ovarian cancer are next in frequency, followed by several other cancers.80 Both the endometrial and ovarian cancers associated with HNPCC appear 15 to 20 years earlier than do the sporadic ones. Some authors have recommended intensive surveillance for
endometrial cancer and ovarian cancer in affected females.68

Upper GI adenocarcinomas are a major cause of death in patients with FAP who have had prophylactic colectomy.72 As stated above, periodic upper tract endoscopies are therefore indicated. In patients who have been treated with prophylactic colectomy but still have their rectum, monitoring for the development of a second cancer must be rigorous.81

Monitoring and Treating Complications of Treatment

The major long-term problems after colorectal cancer treatment stem from surgery and radiation therapy for rectal cancer. Complications arising from radiation therapy are mainly related to bowel function and occur 6 to 18 months after treatment.62 The main symptom is persistent diarrhea that is due to radiation damage to the bowel. Severe radiation proctitis may result in episodic bleeding. Another cause of diarrhea may be small bowel enteritis.83 Small bowel obstruction caused by adhesions can also occur. Sometimes the only treatment for these complications is surgical resection and re-anastomosis.

Dealing With Altered Physiologic Status

The two main problems of altered physiologic status result from damage to or removal of the rectum and the sequelae of pelvic irradiation. The care of a permanent colostomy requires special training for the patient; consultation and follow-up with an enterostomal therapist will assist the patient in adapting to his or her new condition. Maintaining hygiene, the use of appliances, skin protection, irrigation, and sexual activity are just some of the issues that need to be addressed.

Damage to the rectum in rectum-sparing surgeries can lead to anal incontinence in some patients.64 It is not clear whether radiation contributes to this problem. A study from the Mayo Clinic found an increase in rectal incontinence and diarrhea after radiation therapy for rectal carcinoma.65 But this may have been caused in part by radiation enteritis, since others have found no change in anal sphincter function after radiation therapy.66 Treatment is primarily symptomatic with antidiarrheal drugs.

Sexual and urinary function may be affected by rectal surgery. In general, urinary function can be preserved by nerve-sparing surgery. Sexual function may be lost, particularly in older men.67 Sexual function is also affected by radiation therapy. In the more carefully studied prostate cancer, sexual function is often diminished after radiation therapy (see below). Treatment with sildenafil may help some men achieve erections.68

Psychosocial Problems of Colorectal Cancer Survivors

Psychological problems are not prominent after treatment of colorectal cancer. A study from Sweden reported that the overall levels of anxiety and depression were low in cured patients.89 The one exception may be people who had treatment for rectal cancer that included radiotherapy.90 They seemed to have some decrease in functioning and independence caused mostly by their sub-optimal rectal function; sexual dysfunction may also play a role.91 The presence of a colostomy will also contribute to decreased functioning.

Routine follow-up care has little influence on quality of life. A Danish study found little psychological benefit from frequent follow-up.92 On the other hand, patients do report a strong preference to be followed closely and have few psychological qualms about surveillance.93 One issue that seems to stress patients and cause anxiety is genetic testing. Patients undergoing testing are often anxious.
before receiving their results. They also experience anxiety if they are mutation positive, but this decreases with time.94

PROSTATE CANCER

Its high incidence and low mortality make prostate cancer the second most prevalent cancer after breast cancer in the United States in 1999. The SEER review estimates that almost 1.5 million men were alive with this diagnosis; nearly 760,000 were diagnosed within the previous five years. This number exceeds the five-year prevalence for breast cancer.

Surveillance After Primary Treatment

Prostate specific antigen (PSA) testing has simplified surveillance of men after primary treatment for prostate cancer. A rising PSA level from the nadir reached after primary radiation therapy or any detectable PSA after radical prostatectomy (RP) is evidence of recurrence.95 Survival after biochemical failure (rising PSA) may be quite lengthy. A study from Cleveland of 936 men treated with radiation therapy found that the 10-year survival of those with rising PSAs was no worse than those with stable PSAs.96 Similar results were reported in a study of 1,844 men.97 Recurrences may be local or disseminated, and based on the particular scenario, further radiation, surgery, hormonal therapy, or even watchful waiting may be indicated.98

It is probably prudent to take serial PSA measurements every six months along with annual digital rectal exams as recommended by the NCCN.99 The American Urological Association recommends periodic PSA measurements without specifying their frequency.100 Other routine imaging studies, such as bone scans, are not recommended unless the PSA level rises.

Assessing Genetic Susceptibility

Prostate cancer can be inherited. It is more likely to be familial in men diagnosed under age 55; up to nine percent of all prostate cancer can be considered “hereditary.”101 Most hereditary cases appear to be transmitted as autosomal dominant genes found on chromosome 1.102 Another locus on the X chromosome has been described.103 Without genomic analysis, the best clue to hereditary prostate cancer is the family history as defined by: (1) at least three first-degree relatives have the disease; (2) two of these were under 55 at diagnosis, or men in at least three successive generations have had prostate cancer.104 Suspecting familial prostate cancer should lead to early screening of male family members, i.e., aged 40, because these men tend to present at a more advanced stage.105 Sons of men who have prostate cancer have a higher risk themselves even if there is no indication of familial prostate cancer.106

Diagnosing a Second Primary

An increased incidence of bladder cancer may be found in patients with prostate cancer; this may be falsely elevated because these patients have such intense evaluation of their pelvic organs.107 A study of Detroit-area patients found that this excess of bladder malignancies occurred in men treated with radiation therapy for their prostate cancer.108 Other cancers were not found to occur at an excessive rate. A large Swedish study109 and a large Swiss study110 both found significantly reduced incidence of other cancers in prostate cancer patients that ranged from relative risks of 0.6 to 0.8.

Monitoring and Treating Complications of Treatment

Probably no frequently used cancer therapy leads to as many complications as do surgical
and radiation treatments of prostate cancer. The major complications of surgical prostatectomy are impotence and incontinence. Rates of these sequelae vary depending on the age of the patient, the size of the cancer, the skill of the surgeon, and whether a nerve-sparing procedure was done. It must be acknowledged that since prostate cancer patients are a relatively elderly population (median age at diagnosis = 69), some of these problems may have preceded the treatment. For external radiation therapy, bowel problems are added to the major complications and urinary difficulties subtracted. Their frequency will vary depending on the dose and means of delivery.

A study from the Prostate Cancer Outcomes Study\(^\text{111}\) sheds considerable light on the dimensions of the problem. The study surveyed 1,334 patients two years after treatment. By this time, the long-term effects of radiation should have become apparent, and the short-term effects of surgery had resolved. Almost 30 percent of radical prostatectomy (RP) patients wore pads to keep dry. Close to 10 percent of all RP patients were totally or almost totally incontinent. Men who received external beam radiation therapy had a very low incidence of wearing pads (2.6%) and of major incontinence (3.5%). With respect to sexual function, almost 80 percent of the RP patients were unable to have an erection sufficient for intercourse compared with 61 percent of radiation-treated patients. Although around 10 percent of both groups had pain with their bowel movements, 37 percent of the radiation patients complained of diarrhea compared with 21 percent of RP patients.

Brachytherapy is associated with similar side effects, but the pattern of side effects more resembles those of surgery, with a high rate of urinary and sexual dysfunction but few bowel symptoms.\(^\text{112}\)

### Dealing With Altered Physiologic Status

Because all of the major side effects of prostate cancer treatment can be considered alterations in physiology, they will be discussed here. Unfortunately, many of the side effects are not treatable. Transurethral collagen injections, which have had some success in treating stress incontinence in women, have had limited success in men after RP.\(^\text{113}\) Most incontinent men are committed to wetness for life. Little treatment is available for radiation proctitis, although one group has reported success with topical sucralfate suspensions.\(^\text{114}\) The one bright spot is treatment for impotence. Treatment with sildenafil can help men who have become impotent after radiation therapy to the prostate.\(^\text{115}\) Men who have become impotent after RP may also respond to sildenafil, but also will often become potent with other treatments, such as vacuum devices, intra-corporeal injections, or both.\(^\text{116}\)

### Psychosocial Problems of Prostate Cancer Survivors

Most studies of quality of life after treatment for prostate cancer have focused on urologic symptoms but not on psychosocial ones. Yet psychosocial disturbances must occur in men who might very well be experiencing incontinence, impotence, or rectal problems. These, however, have not come to light in the numerous quality-of-life studies of post-therapy men. One major study found that 81 percent of men treated with RP and 90 percent of men treated with radiotherapy “were either delighted, satisfied, or pleased with their treatment decision.”\(^\text{117}\) But men do experience psychosocial difficulties and perceive they are not receiving adequate help.\(^\text{117}\) One source of support has been support groups.\(^\text{118}\) These may be quite helpful.\(^\text{119}\) Finally, partners of the men may also suffer psychological distress, which may be greater than that of the patients.\(^\text{120}\)

### TESTES CANCER

This is a relatively uncommon (low incidence) cancer with a low prevalence of only
126,000 in 1999;\textsuperscript{3} only 33,600 were diagnosed within five years. Since these tumors occur relatively early in life (median age at diagnosis = 34 years) and have a high cure rate, the total patient years of follow-up is large.\textsuperscript{3} An excellent review of their long-term care is available.\textsuperscript{121}

**Surveillance After Primary Treatment**

Most patients with testicular cancer are cared for by specialists during the period of early surveillance because most recurrences occur early,\textsuperscript{122} and the disease is still curable with aggressive, prompt therapy. Eventually these men will leave their specialist and receive care from a primary care physician. At this point, surveillance with serum tumor markers, human chorionic gonadotropin, and alpha-fetoprotein would be recommended on an annual basis along with chest x-ray and physical examination.\textsuperscript{123} The latter is directed to palpation for abdominal lymph node enlargement and examination of the remaining testicle. It is important to note that recurrences have been found 10 years or more after the original treatment.\textsuperscript{124}

**Assessing Genetic Susceptibility**

Testicular cancer does cluster in some families; one study suggested that it was carried as a recessive gene on the Y chromosome.\textsuperscript{125} No specific gene has been identified. The major importance of finding a familial occurrence aside from counseling male family members is that the patients have a higher risk of second testicular cancers as well as other cancers.\textsuperscript{126}

**Diagnosing a Second Primary**

Second cancers occur more commonly in testicular cancer survivors than in the normal population. The risk has been estimated as 40\textsuperscript{127} to 60\textsuperscript{128} percent higher than expected. Leukemias are increased in patients who received either radiation or chemotherapy. Solid tumors are also increased. Patients who receive radiotherapy are at particular risk of GI cancers, particularly stomach cancer. Finally, these patients have a significant risk (1% to 5%) of developing a second testicular cancer.

**Monitoring and Treating Complications of Treatment**

The major complication of testicular cancer treatment is infertility. In the past, patients undergoing retroperitoneal lymph node dissection suffered from retrograde ejaculation. Now with nerve-sparing surgery, this is uncommon.\textsuperscript{129} Chemotherapy can lead to oligospermia in some patients along with poor sperm motility.\textsuperscript{130} It is important to note that patients often have oligospermia or azoospermia before surgery.\textsuperscript{131} Patients often recover fertility.\textsuperscript{132}

**Dealing With Altered Physiologic Status**

Perhaps the only physiologic problems are related to chemotherapy, namely pulmonary damage from bleomycin and neuropathy from the cisplatin. These should mostly resolve and not interfere with normal function.

**Psychosocial Problems of Survivors**

Psychosocial problems do not occur much more often than in a normal population.\textsuperscript{133} The major problems reported are decreased sexual enjoyment and desire.

**HODGKIN DISEASE**

SEER estimates that there were 117,596 survivors of Hodgkin disease in 1999; nearly 31,000 were diagnosed within the previous five years.

**Surveillance After Primary Treatment**

The NCCN\textsuperscript{134} recommends intensive follow-up of up to five years after treatment,
preferably by an oncologist. But some form of later surveillance will still be important as late relapses as well as second primaries do occur. Most relapses in patients with Hodgkin disease will occur within the first five years, but may continue to occur up to 10 years after treatment.\textsuperscript{135} It would be reasonable to assess the primary disease sites in these individuals with imaging techniques, such as CT scans or PET scans, annually or earlier if there are signs or symptoms of recurrence.

**Assessing Genetic Susceptibility**

Hodgkin disease has not been tied to any specific genetic disorder. But it can be found clustered in families,\textsuperscript{136} and there is also a high concordance of Hodgkin disease in young adults who are identical twins.\textsuperscript{137} Some of this may relate to specific human leucocyte antigen (HLA) determinants.\textsuperscript{138}

**Diagnosing a Second Primary**

Probably no other malignancy is associated with as many second primary cancers in survivors as is Hodgkin disease. Most of these tumors are probably related to the carcinogenic effects of the radiation and chemotherapy the patients receive. Various risk ratios are cited depending on type of treatment, length of follow-up, and age at diagnosis. Patients that are younger at diagnosis have higher relative risks although absolute risks are higher in patients diagnosed as adults.\textsuperscript{139} Interestingly, the type of second primary tumor is related to the age of treatment: solid tumors such as lung, breast, and GI malignancies occur more frequently after treatment at a younger age compared with leukemia, which is more frequent in patients treated at an older age. For those who were treated when they were younger than 15, the relative risk of a second malignancy is 26 times that in a healthy individual. This drops to 1.9 for those treated when they are over 55.

The major types of malignancy seen are leukemia, non-Hodgkin lymphoma, lung cancer, breast cancer, and GI malignancies.\textsuperscript{140} Acute nonlymphocytic leukemia is a major risk in patients treated by chemotherapy, especially by those regimens containing alkylating agents.\textsuperscript{141} The rate following the use of the ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) regimen is much lower,\textsuperscript{142} and this has now become the regimen of choice in most centers. If leukemia develops, it will arise early after treatment with its peak occurrence being in the first and second decades after treatment. Non-Hodgkin lymphoma is another high-risk hematologic cancer for Hodgkin disease survivors. The majority of these lesions have diffuse, intermediate-grade histology.\textsuperscript{143} The cause of these secondary lymphomas is unknown and may occur as a result of the therapy, immunosuppression, or as a natural sequel.

Hodgkin disease survivors may also develop solid tumor second primaries. The risk of breast cancer in women treated with mantle irradiation before the age of 30 is markedly increased.\textsuperscript{144} Most of these cancers will occur at the edge of the radiation field. Increased lung cancer risk is found in patients treated with radiation and chemotherapy with alkylating agents. It increases markedly in smokers.\textsuperscript{145} Other major cancer sites that are affected are GI and female genital,\textsuperscript{146} probably in association with multimodality therapy. Many other, less common cancers, such as sarcomas and thyroid carcinomas, are also found. Surveillance should consist of annual physical examinations, including pelvic exams and screening mammography for all women treated at a young age (less than 30). Many centers recommend starting the mammography screening around eight years following treatment. Thus, many women will start their breast surveillance at a much earlier age than the general population. Although not proven as a screening technique, yearly chest x-rays would be prudent. Any smokers should be intensively urged to stop, and be given pharmacological
Monitoring and Treating Complications of Treatment

The effects of chemotherapy and radiotherapy are problematic. Both doxorubicin and radiation that involves the heart can damage heart muscle; heart failure is always a concern. Also, cardiac radiation can lead to coronary artery disease and subsequent myocardial infarction. Pericardial disease secondary to radiation is becoming less of a problem with newer techniques. Lung function can also be disturbed either as a result of treatment with bleomycin or radiation. Usually the disturbance in function is mild. Hypothyroidism is a common complication of neck radiation. Often it is subclinical and can only be discovered by tests of thyroid function. Other complications are neurotoxicities that arise from chemotherapy drugs, such as vinca alkaloids and platinum compounds. These usually take the form of slowly resolving peripheral neuropathies.

Dealing With Altered Physiologic Status

Other than what is described above, the major issue that many survivors face is fatigue. This has been described particularly for Hodgkin disease survivors. This may result, according to some, from decreased pulmonary function. Sexual dysfunction has also been reported. Unfortunately, there have been no reports of systemic evaluation and treatment of these symptoms. Problems with fertility may occur, although in one series, 35 of 43 women and 25 of 51 men were able to conceive. For patients who do conceive, the health of their offspring is not affected.

Psychosocial Problems of Survivors

Representatives of the Cancer and Acute Leukemia Group B performed a large study of Hodgkin disease and acute leukemia survivors. Both groups had vocational problems and serious marital problems. Fifty-six percent of the Hodgkin disease survivors were divorced or separated—many presumably because of their cancer. Sexual problems manifested by decreased interest, problems with erections for men, and painful intercourse for women along with poor self-image occurred in these individuals. Finally, 21 percent of Hodgkin disease survivors had high levels of psychological distress. These findings highlight the need for psychological therapy for these people.

LEUKEMIAS AND NON-HODGKIN LYMPHOMAS

SEER prevalence estimates for these cancers from 1999 are 491,000 with 220,000 having been diagnosed within five years. Many of these individuals are probably not cured because they have indolent lymphoma or chronic leukemia.

Surveillance After Primary Treatment

There are no studies that assess the value of intensive surveillance versus routine observation for any of these diseases. Many of these patients will have ongoing problems and be under the care of their oncologists or hematologists. Only some with non-Hodgkin lymphoma, and an even smaller number with cured leukemia, will no longer be under a specialist’s care.

The recurrence pattern seen after treatment of intermediate- and high-grade non-Hodgkin lymphomas resembles that of Hodgkin disease. Most recurrences are discovered within five years of treatment. It would be reasonable to assess the primary disease sites in these individuals for at least five years after treatment with imaging techniques such as CT scans or PET scans annually, or earlier if there are signs or symptoms of recurrence.
Most acute leukemia patients that relapse will do so in the first five years. For leukemia survivors, routine blood counts would be warranted at intervals of every three to six months.

Assessing Genetic Susceptibility

Although genetic abnormalities such as Down syndrome, Fanconi anemia, and others are associated with acute leukemias, these are not typically a problem in adults. Likewise non-Hodgkin lymphomas have not been tied to any specific genetic disorder although it can be found clustered in families. Although it is wise to seek a familial connection in any patient with these diseases, the great majority of patients will have no recognizable genetic susceptibility.

Diagnosing a Second Primary

Although second primaries do occur at a higher than expected frequency after treatment of non-Hodgkin lymphoma, they are not as common as they are in Hodgkin disease. Large studies from Australia, and from Sweden, Ontario, and Iowa reported a 19 to 37 percent increase, respectively, in the incidence of second cancers. Both studies found specific increases in melanomas and bladder cancer. Other cancers that were increased in one or the other study were kidney, lung, brain, lip and tongue, thyroid, and soft tissue sarcomas. Hodgkin disease and acute leukemia were also increased in incidence in the non-Australian study. The bladder and kidney cancers are thought to result from cyclophosphamide therapy. No specific recommendations can be made for surveillance other than careful evaluation of any symptoms referable to these sites.

Except for the special case of stem cell transplantation, which is discussed below, second primaries do not appear to occur at an increased frequency after treatment of acute leukemia.

Monitoring and Treating Complications of Treatment and Altered Physiologic Status

Those who have received multiple blood transfusions may develop chronic hepatitis B or C transmitted by blood products. This is becoming less prevalent as the safety of the blood supply increases. The risk of hepatitis B is one in 220,000 and that of hepatitis C, one in 1,600,000. The two most common long-term complications of therapy for non-Hodgkin lymphoma are cardiotoxicity secondary to doxorubicin therapy and hepatitis C virus infection related to transfusions. Although much has been written about the cardiac, cognitive, CNS, and other sequelae in children who are cured of their leukemia, the literature on long-term effects of therapy in adults refers mostly to stem cell therapy.

Allogeneic stem cell transplantation causes major changes in physiologic status because of graft versus host disease. Since these patients are still under the active care of their specialized oncology team, the clinician involved in routine follow-up of survivors will not be responsible for managing this complex problem. Patients who have undergone autologous stem cell transplants have problems that are similar to people who have received standard chemotherapy. They may have significant fatigue, and sleep disturbances are common.

Psychosocial Problems of Survivors

Representatives of the Cancer and Acute Leukemia Group B performed a large study of Hodgkin disease and acute leukemia survivors. Both groups had vocational problems and serious marital problems. Thirty-three percent of the leukemia survivors were divorced or separated because of their cancer. Sexual problems manifested by decreased
interest, problems with erections for men, and painful intercourse for women along with poor self-image occurred in both groups. Finally, 14 percent of leukemia survivors had high levels of psychological distress. These findings highlight the need for psychological therapy for many of the survivors.

LUNG CANCER

Although its incidence is high, the prevalence of lung cancer is relatively low because of its high lethality. The SEER estimated prevalence of this cancer was 327,000 in 1999. Slightly over 193,000 were diagnosed within five years and another 61,000 between five and ten years. This leaves approximately 71,000 patients surviving 10 years after diagnosis.

Surveillance After Primary Treatment

Most patients are not treated with curative intent. Only 40 percent of 1,398 patients with non-small cell lung cancer in a series from Walter Reed Army Medical Center underwent curative surgery, and of these, only 58 percent survived five years. For those who are treated curatively, there is no standard guideline for follow-up. A study from Brazil compared strict surveillance with frequent physical examinations, chest x-rays, and biannual CT scans with a less intensive approach that saw patients only if they had symptoms. Mortality was the same in both groups, but the authors thought some close follow-up, perhaps without CT scans, was justified because it alerted physicians to imminent health problems.

Assessing Genetic Susceptibility

Lung cancer can be inherited. Smoking is a necessary cofactor, but in families where young (under 55) individuals have developed the disease, a family trend consistent with dominant inheritance has been described. In assessing a family where first-degree relatives develop lung cancer at an early age, a physician must redouble efforts to discourage smoking.

Diagnosing a Second Primary

The most common second cancer in patients with lung cancer is another lung cancer. The risk is around one to two percent annually in patients with non-small cell lung cancer and at least double that rate in those with small cell lung cancer. Surgical resection may be warranted and can be successful if a second primary does develop. Finally, other smoking-related cancers, particularly aero-digestive cancers, can occur.

Monitoring and Treating Complications of Treatment

In non-small cell lung cancer survivors for whom surgery appears to be the major curative treatment, pulmonary insufficiency might result from the surgery, since many patients have smoking-related comorbidity. Radiation therapy may contribute to pulmonary complications, particularly by damaging remaining lung tissue. The major complications of treatment of small cell lung cancer relate to chemotherapy. Since platinum drugs are often used, neuropathies and diminished renal function can occur. In addition, cognitive functioning may decline in patients treated for small cell lung cancer. Although a decline in cognitive function might be due to prophylactic cranial irradiation, this is not certain; it can occur in patients not receiving cranial radiation.

Dealing With Altered Physiologic Status

The major physiologic problem for lung cancer survivors is reduced pulmonary function due to surgery, chronic obstructive pulmonary disease, and any radiation they may have...
received. Also, as mentioned above, some with small cell lung cancer may have reduced cognitive functioning.

**Psychosocial Problems of Survivors**

Depression is not a major problem of survivors after surgery. A study from Japan found an incidence of only around six percent. Psychological distress was frequent however and may be associated with reduced pulmonary function. It appeared that a positive relationship with their physician helped many patients.

**GYNECOLOGIC CANCERS: CERVIX, ENDOMETRIUM, AND OVARY**

Although these are different cancers, follow-up patterns are similar. Their prevalence is quite high. SEER estimates of their prevalence in 1999 are 936,000 overall and 246,000 diagnosed within five years.

**Surveillance After Primary Treatment**

There are few data supporting intensive surveillance of any of these cancers. The practice recommended by the NCCN for follow-up of women treated for ovarian cancer is frequent physical examinations—every two to four months—along with measurements of serum levels of CA-125. After two years, less intense follow-up is recommended. A recent study found pelvic MRI to be more sensitive in detecting early recurrence, but the value of this is unclear. At one time, second-look surgery was done in patients thought to be free of disease. But even when cancer was found and treated in presumably an early stage of recurrence, survival was not improved. A National Institutes of Health consensus conference recommended a follow-up schedule similar to that of NCCN, with physical examination every three to four months along with CA-125 for two years, and then less frequently.

For cervical cancer, the NCCN recommends Pap tests and pelvic examinations every three months for the first year, with decreasing frequency in subsequent years. Once again, the survival value of this is not proven. In one study, most recurrences, usually detected in the first two years after treatment, were symptomatic. Other studies have confirmed this. When the recurrence was found by active surveillance, survival was not improved.

Most literature on surveillance in gynecologic malignancies has been devoted to endometrial cancer. The NCCN recommends physical examination every three to six months and vaginal cytology every six months for two years and then less often. A more complex schedule from the MD Anderson Cancer Center also added CA-125. Although most recurrences were detected by this testing approach, it did not translate into improved survival. Most of the recurrences were found within three years after surgery. Other studies have confirmed the findings that intensive surveillance confers no survival benefit. In summary, intensive surveillance does not appear to improve survival. But that is not to say that early detection might not be valuable to a patient because it might lead to early treatment of symptoms of advanced disease. Although routine surveillance would seem to be reasonable, it need not be intensive.

**Assessing Genetic Susceptibility**

About 10 percent of ovarian cancers are familial and due to inheritance of an autosomal genetic mutation. Approximately two-thirds of these are due to BRCA mutations, and the other third due to the HNPPC mutation. In patients with a strong family history of breast, ovarian, or colorectal cancer, genetic counseling would be appropriate.

A familial pattern of endometrial cancer has
been documented, and one estimate is that about five percent of endometrial cancers are familial.\textsuperscript{191} Most of these are probably related to HNPCC,\textsuperscript{192} but other unknown mutations cannot be excluded. Cervical cancer has not been attributed to any hereditable factors.

**Diagnosing a Second Primary**

The major causes of second primaries in patients with these gynecological cancers are genetic mutations. Because endometrial cancer and ovarian cancer are associated with HNPCC, colorectal cancers as well as the other cancers described earlier in this article can occur in patients with this mutation. Women with a $\textit{BRCA}$ mutation will be at high risk for developing breast cancer.

Therapy-induced second primary tumors may also be seen. Secondary leukemia has been seen following chemotherapy for ovarian cancer.\textsuperscript{193} Secondary tumors of the rectum, vulva, and vagina have been described following radiation therapy for cervical cancer.\textsuperscript{194} In addition, cervical cancer is associated with the risk factors of HPV infection and smoking; these may lead to other cancers, such as anal\textsuperscript{195,196} vaginal, and vulvar cancers.\textsuperscript{197}

**Monitoring and Treating Complications of Treatment**

The major complications of treatment stem from the pelvic radiation used to treat endometrial and cervical cancers. The main problems patients experience are diarrhea and some lower back pain as a result of the radiation.\textsuperscript{198} Survivors may also develop urinary frequency because of radiation-induced changes in the bladder. In general, the health-related quality of life of patients with endometrial cancer treated with radiation is not significantly lower than a matched population of healthy women except in the first two years after treatment because of the symptoms described above.\textsuperscript{199}

Cervical cancer patients face an additional burden if they have been treated with radiation. The radiation causes vaginal stenosis and can lead to significant sexual dysfunction if this is not prevented at the time of radiotherapy. In addition, women may experience decreased libido and less satisfaction with sex.\textsuperscript{200}

Long-term effects of ovarian cancer treatment, other than those caused by surgery, would result from the chemotherapy. Cisplatin can cause peripheral neuropathy, hearing loss, and renal insufficiency. Neuropathy may be exacerbated by concomitant use of taxanes. Some of these sequelae may eventually resolve.

**Dealing With Altered Physiologic Status**

Lack of ovaries or uterus should not result in major functional alterations except for early menopause in young ovarian cancer patients. There is no documented reason that menopausal symptoms cannot be treated with hormone replacement therapy (HRT) except in women with a genetic susceptibility to breast cancer. But a recent review has pointed out that the safety of HRT in these cancer survivors has not been proven.\textsuperscript{201}

**Psychosocial Problems of Survivors**

Women treated with radiotherapy for carcinoma of the cervix experience mild, persistent, psychosocial problems, and their quality of life never equals that of healthy women.\textsuperscript{202} But their main problems seem to be worry about their disease and difficulty in sharing their problems with others. Other than the side effects of the treatment, they return to normal functioning. Patients with endometrial cancer react similarly.\textsuperscript{203}

Ovarian cancer survivors report their emotional well-being as good to excellent.\textsuperscript{204}
Their major problems relate to their fear of cancer recurrence. Otherwise, they cope well except for menopausal symptoms.

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**GENITOURINARY CANCERS: BLADDER AND KIDNEY**

The SEER numbers for prevalence of kidney cancer in 1999 are 188,000 overall and 77,000 diagnosed within five years. For bladder cancer, comparable figures are 450,000 and 171,000.

**Surveillance After Primary Treatment**

No specific guidelines for surveillance after treatment of renal cell cancer have been published. One recommendation that has been proposed for renal cell carcinoma is that if there is to be intensive surveillance, it should be in those patients with larger (> 5 cm) tumors or those with aneuploid tumors. A specific recommendation has been that early (T1) tumors be followed with annual chest x-rays and liver function tests. For more advanced stages, the recommendations are that these tests be done every three to six months for three years, and then annually along with abdominal and pelvic CT scans at 24 and 60 months. The reason for this active surveillance is the impression that surgical removal of isolated recurrences, particularly pulmonary, may be curative for a few patients. No randomized controlled trials have been performed to test this hypothesis.

Because patients with locally treated bladder cancer have a high risk of recurrence, they need follow-up surveillance by urologists. Frequent cystoscopy is needed. Addition of urine cytology to this follow-up regimen is useful in detecting carcinoma in situ and high-grade urothelial carcinomas. It may be more likely that nonurologists will be primarily responsible for the surveillance of patients treated with total cystectomy. In one study, 74 percent of metastases were detected in asymptomatic patients by surveillance. Most were pulmonary. The authors of the study recommend that surveillance be adjusted to the stage of the cancer, with annual chest x-rays and examinations for Stage T1 cancers, biannual exams for T2 cancers, and more frequent exams along with biannual pelvic CT scans for T3 cancers. Although there are no major studies reporting improved survival with this approach, one report did cite better palliation for pelvic recurrence because of early detection.

**Assessing Genetic Susceptibility**

Most renal and bladder cancers are sporadic. Familial occurrence of bladder cancer has been described but is uncommon. In general, first-degree relatives of patients, particularly younger ones, with bladder cancer have a 50 percent higher risk for the disease. This mostly occurs in people exposed to risk factors, such as smoking or industrial chemicals.

On the other hand, there is a distinct clinical syndrome, von Hippel-Lindau disease, which is associated with familial renal cell carcinoma. This disease, caused by a mutation on chromosome 3, is associated with multiple benign and malignant tumors, including renal cell carcinoma. These cancers generally have a good prognosis. Other tumors in this syndrome are central nervous system hemangioblastomas, pheochromocytomas, and pancreatic cysts. Another familial aggregation occurs with papillary cell carcinomas of the kidney. These also have a relatively good prognosis.

**Diagnosing a Second Primary**

Other than other tumors in the von Hippel-Lindau syndrome, second primaries are not reported to be increased in these cancers.

**Monitoring and Treating Complications of Treatment**

Quality of life is normal in patients with renal cell cancers, and there are no associated
long-term complications. Bladder cancer patients after radical cystectomy do experience long-term complications. Both men and women experience sexual dysfunction characterized by loss of interest, inability to have orgasm, and in men, impotence.

Dealing With Altered Physiologic Status

A major problem for bladder cancer patients is significant urinary leakage, particularly if they have had an ileal conduit (around 50% to 60% percent). The rate is much lower with orthotopic bladder replacements.

Psychosocial Problems of Survivors

Most renal cancer patients do not experience major problems. But patients who did not have radical nephrectomy, but rather had nephron-sparing surgery (partial nephrectomy), seem to be less anxious about their cancer and its chance of recurrence. Patients who have had cystectomy for bladder cancer also report few emotional problems. But some do have limitations in their ability to engage in social activities because of urine leakage. This is less of a problem in patients with orthotopic bladders. Dissatisfaction with sexual functioning is helped by inflatable implant prostheses.

A SPECIAL COMMENT: SECOND PRIMARY TUMORS AFTER BONE MARROW TRANSPLANT

Survivors of stem cell transplantation have a special problem with second malignancies in addition to the complications of the transplant. One prominent malignancy related to allogeneic transplantation is lymphoma, which occurs in about one percent of patients. This is usually a B-cell lymphoma that appears soon after transplantation, but may appear later. Epstein-Barr virus infection seems to be a prerequisite. A second, prominent malignancy is acute leukemia, often preceded by a myelodysplastic syndrome. This occurs much more frequently after autologous transplant. In one study, the cumulative incidence of myelodysplastic syndromes and acute myelogenous leukemia (MDS/AML) in autotransplanted Hodgkin disease patients was 13.5 percent at six years. These authors also found an increased risk of solid tumors regardless of whether the transplant was autologous or allogeneic. They estimated the risk as 5.6 percent at 13 years. Melanoma was the most common tumor. A report of 19,000 individuals who received an allogeneic transplant estimated the risk of solid (nonhematological) tumors as almost three times normal with sarcomas, melanomas, brain tumors, and liver cancers exhibiting the highest risk. Once again, there are no specific surveillance guidelines except to be sensitive to the possibilities that malignancies can arise more readily than expected in nontransplanted individuals.

CONCLUSIONS

The spectrum of medical and psychological needs of the cancer survivor is numerous, diverse, and complex. If these needs are to be fully met, the responsible physician must know the natural history of the specific tumor, the manifestations of genetic variants, the risk of second-primary tumors, the complications of therapy including alterations in normal physiologic functions, and the often subtle psychosocial sequelae. Since many of these conditions can be ameliorated, optimal management can improve both quality of life and, in some cases, survival. As the status of the cancer survivor becomes more and more recognized as a distinct clinical entity, it is hoped that targeted educational interventions and useful screening tools will be developed to enable the clinician to improve the health of this ever-increasing population.
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