Primary Care of the Patient with Cancer

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Care of patients with cancer can be enhanced by continued involvement of the primary care physician. The physician's role may include informing the patient of the diagnosis, helping with decisions about treatment, providing psychological support, treating intercurrent disease, continuing patient-appropriate preventive care, and recognizing and managing or comanaging complications of cancer and cancer therapies. Adverse effects of therapy and cancer-related symptoms include nausea, febrile neutropenia, pain, fatigue, depression, and emotional distress. 5-Hydroxytryptamine antagonists are effective in controlling acute nausea associated with chemotherapy. Febrile neutropenia requires systematic evaluation and early empiric antibiotics while awaiting culture results. Cancer-related pain, depression, and fatigue often are underdiagnosed and undertreated. Use of brief screening tools for assessing fatigue and emotional distress can improve management of these symptoms. Exercise prescription, activity management, and psychosocial interventions are useful in treating cancer-related fatigue. The physician must be alert for signs and symptoms of cancer-related emergencies like spinal cord compression, hypercalcemia, tumor lysis syndrome, pericardial tamponade, and superior vena cava syndrome. (Am Fam Physician 2007;75:1207-14. Copyright © 2007 American Academy of Family Physicians.)

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More than 1.3 million patients are diagnosed with cancer every year in the United States, and a typical family physician will have three or four patients each year who are given a new diagnosis of cancer.[1] These patients and their families face not only a life-threatening disease but a flurry of subspecialty consultations, medical tests, and treatments that may be difficult and disruptive. During the course of the patient's cancer care, the family physician can remain an important resource for the patient and family, providing an empathetic and credible source of information, support, and advice as well as medical treatment for intercurrent illness, preoperative evaluation, postoperative care, and coordination of subspecialty care *(Table 1[2])*.

Table 1. Roles and Responsibilities of the Primary Care Physician After the Diagnosis of Cancer

Be a case manager
Maintain regular contact
Be available
Have knowledge of community resources and covered services
Address ongoing health maintenance needs
Provide appropriate pain management
Assess for pathologic depression and other psychiatric pathology
Be aware of therapeutic options
Communicate with and support the patient

Information from reference 2.

Patients followed by an oncologist alone are less likely to receive preventive care, and care for noncancer chronic illness that is consistent with guidelines, than patients followed jointly by an oncologist and a primary care physician.[3] For patients with advanced disease, primary care continuity may reduce emergency department visits and make it more likely that the patient will be able to die at home.[4,5]

The responsibility to inform a patient about a cancer diagnosis may fall on the family physician. The SPIKES mnemonic, which was developed to guide this process, is provided in *Table 2*.[6] If cues indicate, touch may be beneficial in conveying concern and empathy, and the presence of significant others should be encouraged.[7] Most patients want full information about the extent of the disease, treatment options, adverse effects, symptoms, and prognosis, but want some control over the timing, mode, and extent of information they receive.[8,9] Regardless of the prognosis, some hope can and should be conveyed.

Adverse Effects of Chemotherapy and Radiation

Although chemotherapy and radiation treatments are usually directed by a subspecialist, the family physician must be aware of

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Treat chemotherapy-related nausea and vomiting with 5-hydroxytryptamine antagonists.	A	14
Manage chemotherapy-related anemia with epoetin alfa.	A	27, 28
Recommend exercise to mitigate fatigue and improve functional status in patients undergoing chemotherapy and radiation therapy.	B	38, 39
Treat cancer-related fatigue with psychosocial intervention.	B	40
Megestrol (Megace) improves weight gain and appetite in patients with cachexia caused by cancer.	A	52, 53
Massage and aromatherapy massage may enhance psychological well-being, including relief of anxiety, in patients with cancer.	B	61

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1135 or http://www.aafp.org/afpsort.xml.

potential adverse effects and, in some practice settings, may be called on to manage them.

NAUSEA AND VOMITING

Approximately 70 to 80 percent of patients treated with chemotherapy experience nausea and vomiting,[10] which may be acute (occurring within a few hours after chemotherapy), delayed (occurring 24 or more hours after chemotherapy), breakthrough or refractory (occurring despite prophylactic treatment), or anticipatory (occurring before chemotherapy treatment). The emetogenic potential of chemotherapeutic agents varies from mild to severe.[11] Drug dose, schedule and route of administration, and patient variability also are factors.

Antiemetic therapy is most effective if given before chemotherapy and maintained while the emetic potential of the agent continues. Oral formulations are as effective as parenteral or rectal routes if the patient is able to swallow and digest tablets. Lorazepam (Ativan), metoclopramide (Reglan), and prochlorperazine (Compazine) often are used for moderate- to low-emetic-risk chemotherapy and for breakthrough nausea.

The introduction of 5-hydroxytryptamine (5-HT) receptor antagonists in the early 1990s represented a significant advance in antiemetic therapy.[12] Currently, 5-HT antagonists are most widely used in practice with high- to moderate-risk chemotherapy and include ondansetron (Zofran), granisetron (Kytril), dolasetron (Anzemet), and palonosetron (Aloxi). Trials with these agents indicate that they are highly effective in controlling acute nausea and vomiting associated with chemotherapy and have minimal adverse effects.[12-14] They are equally effective for acute nausea,[15] but palonosetron, which has a much higher affinity for the 5-HT receptor and a longer half-life than the other 5-HT antagonists, is more effective than dolasetron in preventing delayed emesis.[16] The coadministration of dexamethasone improves the effectiveness of 5-HT antagonists in controlling acute emesis. However, one study found that adding a 5-HT antagonist to dexamethasone for the treatment of delayed nausea and vomiting did not result in an improved antiemetic effect over dexamethasone alone.[17] Aprepitant (Emend) augments the activity of 5-HT antagonists and dexamethasone to inhibit acute and delayed emesis induced by cisplatin (Platinol).[18,19]

Nausea and vomiting also can occur secondary to radiation treatment and are most likely in patients undergoing whole body or upper abdominal radiation. Higher total dose of radiation, larger amount of tissue radiated, and higher daily fraction of radiation are also factors in the severity of nausea and vomiting.[20]

Table 2. SPIKES Protocol for Delivering Bad News

S = Setting up the interview	Arrange for some privacy; sit down; manage time constraints and interruptions; involve significant others; make a connection with the patient
P = Perception	Before you tell, ask what patient knows
I = Invitation	Explore the patient's wishes for receiving information
K =Knowledge and information given to the patient	Warn the patient that bad news is coming
E = Addressing the patient's Emotions with Empathetic responses	Continue empathetic statements and gestures until patient is calm
S = Strategy and Summary	Discuss treatment options if patient is ready; a clear plan for the future will reduce anxiety; confirm the patient's understanding of the discussion

Information from reference 6.

FEVER AND NEUTROPENIA

Fever in a patient undergoing chemotherapy is common and worrisome. In the guidelines developed by the Infectious Diseases Society of America[21] (IDSA), fever is defined as a single oral temperature higher than 100.9°F (38.3°C) or an oral temperature of 100.4°F (38.0°C) or higher for more than one hour.

An absolute neutrophil count less than 500 per mm^3 (0.5×10^9 per L) is defined as severe neutropenia. The severity of infection is inversely related to the neutrophil count, with the greatest risk of bacteremia at absolute neutrophil levels lower than 100 per mm^3 (0.1×10^9 per L).[22] Evaluation of the patient with neutropenia includes physical examination (with attention to indwelling vascular access devices), laboratory data, radiographs, and blood and urine cultures.

After initial evaluation, patients may be risk stratified *(Table 3[21,23])* to determine if they are candidates for outpatient treatment or if hospital admission is required. In either case, empiric broad-spectrum antibiotics should be started. Delayed treatment may result in increased mortality.[21,24] No single antibiotic or antibiotic combination can be uniformly recommended for all febrile neutropenic patients. Initial therapy is selected after considering the most likely potential infecting organism, site of infection, organ function (e.g., kidney, liver), medication allergies, and recent antibiotic treatment.

Table 3. Risk Assessment in the Patient with Febrile Neutropenia

*High risk**	*Low risk†*
Inpatient status	Outpatient status
Serum creatinine greater than 2 mg per dL (180 µmol per L), LFT greater than three times the normal limit	No comorbid illness
Uncontrolled or progressive cancer	Short duration of neutropenia
Pneumonia	Creatinine less than 2 mg per dL, LFT of three times the normal limit or less
Significant comorbid illness	Good functional status, active and independent
Prolonged severe neutropenia	
ANC less than 100 per mm^3 (0.1×10^9 per L)	
ANC less than 500 per mm^3 (0.5×10^9 per L) for more than seven days	

LFT = liver function test; ANC = absolute neutrophil count.

**—Patients with any of the following should be considered high risk and treated intravenously in the hospital.*

†—Patients with most or all of the following should be considered low risk and treated daily at an outpatient clinic or at home with antibiotics.

Information from references 21 and 23.

The most widely used outpatient antibiotic choice is an oral fluoroquinolone or amoxicillin/clavulanate (Augmentin). Commonly used empiric intravenous antibiotic monotherapies include carbapenems (e.g., imipenem/cilastatin [Primaxin], meropenem [Merrem]), and extended-spectrum antipseudomonal cephalosporins (e.g., ceftazidime [Fortaz], cefepime [Maxipime]). Dual therapy agents include an aminoglycoside with antipseudomonal penicillin (with or without a beta-lactamase inhibitor) or an extended-spectrum antipseudomonal cephalosporin; and ciprofloxacin (Cipro) with antipseudomonal penicillin. Outpatients should be treated for 10 to 14 days. Inpatients should be treated three to four days pending sensitivity, then continue with oral medication as an outpatient for 10 to 14 days.[21,24]

According to IDSA and National Comprehensive Cancer Network guidelines, diagnostic reassessment should occur if fever does not improve in three to four days. Although most patients with cancer-related febrile neutropenia will recover without major complications, involvement of a subspecialist should be considered when the patient's fever does not improve after three or four days of appropriate antimicrobial treatment or when the patient has septic shock, methicillin-resistant *Staphylococcus aureus* infection, or signs and symptoms of invasive fungal infection.

Other Adverse Effects and Cancer-Related Emergencies

Other common adverse effects and their treatments are listed in *Tables 4[25-28] and 5.*[29,30] There is strong evidence that epoetin alfa (Epogen) reduces transfusion requirement and improves quality of life in cancer patients with anemia.[27,28] The maximal incremental benefit occurs between hemoglobin levels of 11 and 12 g per dL (110 to 120 g per L).[31]

The family physician must be alert to signs and symptoms indicating a cancer-related emergency *(Table 6).*[32]

Ongoing Care After Chemotherapy or Radiation

Following initial treatment, patients with persistent cancer may have multiple symptoms including pain, fatigue, weakness, anorexia, dry mouth, constipation, early satiety, dyspnea, weight loss, and insomnia; these may occur regardless of the histologic type of cancer.[33] The most significant of these are fatigue, pain, and the symptoms associated with depression. According to a National Institutes of Health consensus statement, too few cancer patients receive adequate treatment for these symptoms.[34]

Table 4. Adverse Effects of Chemotherapy

Adverse effect	*Onset*	*Evaluation*	*Treatment*
Diarrhea	Seven to 10 days after start of chemotherapy	Stool bacterial culture Stool *C. difficile* antigen Fecal occult blood testing	If *Clostridium difficile* positive, use metronidazole (Flagyl) If *C. difficile* negative, use an antimotility agent such as loperamide (Imodium) or diphenoxylate/atropine (Lomotil)
Alopecia	Seven to 10 days after start of chemotherapy	—	Shave remaining hair from head; wear wigs or scarves
Chemotherapy-induced anemia	Several weeks after start of chemotherapy	Rule out other causes of anemia (e.g., bleeding, hemolysis, nutritional deficiency)	Recombinant erythropoietin (epoetin alfa [Epogen], darbepoetin alfa [Aranesp]) if hemoglobin is less than 11 g per dL (110 g per L)

Information from references 25 through 28.

Table 5. Adverse Effects of Radiation Therapy

Site of radiation	*Adverse effect*	*Treatment*
Oral cavity	Mucositis	Saline/bicarbonate lavage; viscous lidocaine (Xylocaine), diphenhydramine elixir (Benadryl), simethicone (Mylanta), or Gelclair (oral gel that forms a protective coating that provides durable pain relief); sucralfate (Carafate) oral suspension
	Thrush	Antifungal treatments (nystatin [Mycostatin] swish and swallow, fluconazole [Diflucan] or itraconazole [Sporanox] orally)
Salivary glands	Xerostomia	Sialogogues (e.g., pilocarpine [Salagen]); intravenous amifostine (Ethyol) infusion daily before radiation therapy
Mandible	Temporomandibular joint fibrosis	Stretching exercises
	Osteoradionecrosis	Complete dental work before starting radiation therapy; hyperbaric oxygen; pentoxifylline (Trental)
Lungs	Pneumonitis	Prednisone (30 to 60 mg daily for 2 to 3 weeks) with appropriate tapering
	Fibrosis	Supportive care (e.g., oxygen, bronchodilators); pentoxifylline
Prostate	Obstructive uropathy	Alpha blockers (e.g., terazosin [Hytrin], doxazosin [Cardura], tamsulosin [Flomax]); finasteride (Propecia)
Bowel	Diarrhea	Low-residue diet; loperamide (Imodium); diphenoxylate/atropine (Lomotil); cholestyramine (Questran); octreotide (Sandostatin)
	Proctitis	Hydrocortisone cream; glucocorticoid retention enemas; mesalamine suppositories (Rowasa); sulfasalazine (Azulfidine)

Information from references 29 and 30.

FATIGUE

Fatigue is the most prevalent symptom in cancer patients, occurring in almost all patients undergoing aggressive treatments including radiation, chemotherapy, and bone marrow transplantation.[35,36] Fatigue may begin early in the course of treatment and persist for many months or years after treatment. Unlike simple tiredness or situational fatigue, it is more debilitating and severe; less likely to be relieved by simple rest; and may lead to withdrawal from meaningful and enjoyable activities. Among employed patients with cancer-related fatigue, 75 percent changed their employment status and 28 percent discontinued work entirely as a result of fatigue.[37]

Seven clinical factors have been identified as causative elements in fatigue: pain, emotional distress, sleep disturbance, anemia, nutrition, activity level, and other comorbidities.[38] These factors must be addressed in mitigating cancer-related fatigue. Patients with moderate or severe fatigue need further evaluation and intervention.[38]

It has been shown that exercise, including walking and aerobic and resistance training, have beneficial effects on some symptoms related to cancer, including fatigue, distress, anxiety, and depressive symptoms.[38] A recent systematic review indicates a trend toward improved physical functioning with exercise programs.[39] An exercise prescription should take into account the patient's

Table 6. Cancer-Related Emergencies

Condition	*Cause*	*Signs/symptoms*	*Diagnostic tests*	*Treatment*
Spinal cord compression	Spinal column metastasis, local spread intramedullary metastasis	Back pain (early); neurologic deficit of the legs (late)	Magnetic resonance imaging of the spine	Corticosteroids, radiation, surgery, treat underlying malignancy
Superior vena cava syndrome	Mediastinal tumors, venous catheters	Neck, facial, periocular swelling; dyspnea; cough; head pressure; hoarseness; nasal congestion; syncope	Computed tomography	Corticosteroids, radiation, supportive care, treat underlying malignancy
Pericardial tamponade	Lymphatic obstruction, pericardial metastasis	Dyspnea; orthopnea; chest pain; weakness	Echocardiography, pericardiocentesis	Pericardiocentesis, sclerosis, chemotherapy, pericardial window or stripping
Hypercalcemia	Bone metastasis, parathyroid hormone–related protein production, calcitriol excretion	Confusion; lethargy; sleepiness	Laboratory tests for calcium and electrolytes	Intravenous hydration, bisphosphonates
Tumor lysis syndrome	Rapid tumor cell destruction from chemotherapy, multiple electrolyte abnormalities, hyperuricemia	Nausea, weakness, myalgia, dark urine, arrhythmias	Laboratory tests for electrolytes and uric acid	Prevent by hydration, allopurinol (Zyloprim); treat electrolyte abnormalities, acidosis

Information from reference 32.

history and any physical constraints that may impact exercise safety and compliance.

There also is strong evidence that psychosocial interventions, including support groups, stress management, education, and behavioral intervention, are effective in treating fatigue in patients with cancer.[40]

PAIN

Thirty to 50 percent of patients undergoing active treatment, and about 70 to 90 percent of those with advanced solid tumors, experience chronic pain.[41] Appropriate treatment of pain can result in 90 percent of cancer patients achieving adequate relief.[41] Barriers to pain control include lack of physician knowledge of adequate treatment of pain, unrealistic concerns about narcotic addiction, patient underreporting of symptoms, and lack of emphasis on symptom control in comparison with disease management.[41] Uncontrolled severe pain is an emergency and requires aggressive treatment.

MENTAL HEALTH

Studies have shown an increased prevalence of depression in cancer patients.[42,43] The amount of other psychiatric and psychological problems in cancer patients is not different from the general population and is less than in psychiatric patients.[42]

Depression may adversely affect the course of malignant disease. Depression has been linked to a reduced chance of survival in breast cancer patients.[44,45] Older women with depression before cancer diagnosis were more likely to receive nondefinitive treatment for cancer.[45] Depression in cancer patients is underdiagnosed and undertreated for a number of reasons.[46] Physicians may accept affective symptoms as normal and may underestimate the severity of depressive symptoms.[47] Although studies have been limited, the existing data support the use of antidepressant medication to treat depression in cancer patients.[48,49]

The concept of psychosocial distress in cancer patients is useful, emphasizing the continuum of unpleasant emotional experiences ranging from normal feelings of fear, sadness, vulnerability, and spiritual crisis to more traditional clinical issues (e.g., anxiety, panic, clinical depression). This approach recognizes the considerable overlap of common "normal" distress reactions in cancer patients with pathologic reactions while encouraging intervention before symptoms rise to the level of a clinical syndrome.[50] Assessment of distress can be accomplished with an interview or a short questionnaire given periodically and at times of increased vulnerability *(Figure 1)*.[50]

NUTRITION

Maintaining adequate nutrient intake during active treatment can be challenging for cancer patients. Nausea, anorexia, and changes in taste and smell contribute to poor nutrition. Smaller, more frequent meals and nutrient-dense liquid supplements may improve nutrient intake. Supplementation with large amounts of vitamins and minerals during cancer treatment theoretically could reduce effectiveness of chemotherapy or radiation

The Family Context

Despite the obvious stress on the patient's spouse or partner, a diagnosis of cancer is not associated with a decline in the quality of the marriage relationship.[63] Although patients with cancer, in particular women with breast cancer, may fear abandonment by their spouse, most marriages remain stable.[64] A significant minority of couples coping with breast cancer report they have grown closer as a result of the diagnosis.[65]

Children of patients with cancer experience fear, mood disturbance, feelings of guilt, and distress.[66] Adolescent daughters are especially at risk of psychosomatic symptoms and mood disturbances.

As cancer progresses and the burden of care increases, the caregiver's psychological morbidity can equal or exceed that of the patient.[67] Family physicians are in an ideal position to understand the impact of a cancer diagnosis on a patient's family. They can help allay unrealistic fears, reassure the patient about ongoing care, provide realistic hope about treatment or symptom relief, assess family function and caregiver burden, allow expression of concerns by the patient and family, and express empathy. When necessary, timely and appropriate referrals for mental health and social services can be made.

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