Many developments have occurred in prevention and treatment of cancer, but death from this disease is still common. Of the 58 million people who died worldwide in 2005, 7.6 million died of cancer (http://www.who.int/cancer/en/). For dying patients, it is most important to improve quality of life and relieve suffering. Palliative care is the active total care of patients whose medical condition is not responsive to curative treatment. It encompasses all therapeutic modalities designed to enhance quality of life rather than eliminating disease. Each patient’s definition of quality of life is unique, and therefore, it is important to treat each as an individual and holistically. Controlling cancer-related symptoms can ameliorate the limited remaining time patients have with family and friends. Palliative chemotherapy, rehabilitation, radiation therapy, surgery, and interventional pain management can help to achieve this objective.

In this online update of an article published in a 2005 series on pain management, a case presentation describes the typical course of a patient with cancer who receives palliative care to reduce pain.

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In the United States, society places the highest value on preserving and maximizing quality of life. When a loved one has a terminal illness diagnosed, many emotions pour out from the patient and the family. After they pass through stages of bereavement, both patient and family eventually accept the illness. They are faced with difficult decisions of holding onto hope for a cure and continuing aggressive treatment versus palliative care.

According to the World Health Organization (WHO), palliative care is defined as the active total care of patients whose disease is not responsive to curative treatment. The term palliative care is often used interchangeably with hospice care, and its goal is to ensure that the patient and family achieve the best possible quality of life.

In 1842, Mme Jeanne Garnier, who founded the Dames de Calvaire in Lyons, France, was the first to use the term hospice as referring to the care of the dying. In 1967, Dame Cicely Saunders founded St Christopher’s Hospice in London, the first research and teaching hospice that included home care, family support throughout the illness, and bereavement follow-up. This inpatient facility paved the way for the hospice movement in North America and the beginning of palliative medicine.

Worldwide, 10 million new cases of cancer are diagnosed annually. By 2020, that figure will double. For patients with cancer, up to 70% suffer from pain caused by their disease or its treatment. In those with advanced cancer, pain is described as “moderate to severe” in 40% to 50%, and as “very severe” in 25% to 30%. Studies examining pain control in cancer patients find that up to half receive appropriate analgesia and 30% receive inappropriate medications for their pain.

As we continue to develop increasingly sophisticated technology and delve further into an understanding of pain pathophysiology, a major gap remains in our ability to adequately treat pain. Palliative medicine can be defined as the study and management of disease in patients with active, progressive, far-advanced disease for whom the prognosis is limited and the focus of care is the quality of their remaining life. Interdisciplinary teamwork is vital to ensure that every patient need is fulfilled and a holistic approach to both patient and family is maintained.

Providing comfort and control of cancer-related symptoms can optimize the limited remaining time a patient has with his or her family and friends. The hope is to achieve this goal through palliative chemotherapy, radiation therapy, appropriate surgical management, interventional pain management, and rehabilitation to improve patient function and enable self-care.
Palliative Chemotherapy

Antitumor therapy is provided to control cancer-related symptoms and prolong survival, thus optimizing quality of life. Many adult cancers are responsive to chemotherapy (Figure 1), and such treatment improves numerous symptoms (Figure 2).4 Tumor response to chemotherapy has been shown to correlate with improvement of symptoms. For example, a combination treatment regimen combining irinotecan hydrochloride with cisplatin for esophageal cancer was shown to have a response rate of 57% with associated improvement in dysphagia in 35 patients.5-7 A recent study in patients with ovarian cancer showed that chemotherapy can improve overall survival and cancer-related symptoms.8

Even without evidence of tumor response to chemotherapy, patients can clinically benefit. In those with pancreatic cancer, gemcitabine hydrochloride did not prolong life; however, its use was associated with less requirement for analgesics and improvement in patient function.9

Cytotoxic drugs used in palliative chemotherapy attack cells during cell division; these agents are phase-specific and cycle-specific. Phase-specific drugs terminate cells only if given during a certain phase of the cell cycle. Prolonging treatment increases the number of cells killed because dividing cells cycle at random; it is therefore a reasonable approach.

Cycle-specific drugs target cells during any phase of division; thus, higher doses kill more cells than lower doses. Cytotoxic drugs can also be classified according to their specific cellular mode of action. Antimetabolites (5-fluorouracil, fludarabine phosphate, methotrexate, gemcitabine) interfere with the incorporation of nucleic acid bases into DNA; their activity peaks during the S phase of the cell cycle. Alkylating drugs (cyclophosphamide, ifosfamide, chlorambucil, melphalan, cisplatin, carboplatin) form linkages between the strands of DNA that prevent this biogenic substance from separating during the M phase of the cell cycle.

Antitumor antibiotics (bleomycin, doxorubicin hydrochloride, epirubicin hydrochloride) typically interfere with binding of base-pair molecules and prevent separation of DNA strands during the M phase of the cell cycle. Plant alkaloids act as either mitotic spindle inhibitors (vincristine, vinblastine, paclitaxel) or topoisomerase inhibitors (topotecan hydrochloride, irinotecan, and etoposide).10 Given the potential toxicities of chemotherapeutic agents, it is critical to educate patients about their illness and to discuss their expectations of treatment. Many drugs are available for palliation, and it is important to be aware of their potential adverse effects (Figure 3). Ideal candidates for palliative treatment are patients with excellent performance status (a measure of a patient’s functional capacity) and tumor sensitivity to chemotherapy. Use of an evaluation tool such as the Karnofsky scale enables assessment of a patient’s ability to accomplish self-care activities (Table).10 A patient with clinically significant comorbidities and poor functional status will have difficulty tolerating treatment and may become more disabled.

The most challenging issue for both patient and physician is balancing symptom relief against treatment toxicity. When adverse effects of palliative chemotherapy begin to cause a decline in performance status, physicians must reconsider treatment and patient goals. Working together as a team, the patient, family, and physician can make the best decision.

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Symptoms Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Bone pain, tumor ulceration, chest wall pain, lymphedema</td>
</tr>
<tr>
<td>Lung</td>
<td>Dyspnea, chest pain, bone pain</td>
</tr>
<tr>
<td>Prostate</td>
<td>Bone pain, lymphedema</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Pain from adenopathy; systemic symptoms, eg, fever</td>
</tr>
<tr>
<td>Head and neck</td>
<td>Pain</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>Performance status, pain</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Pain, bowel obstruction</td>
</tr>
</tbody>
</table>

Figure 1. Chemotherapy and cancer-related symptom control.

<table>
<thead>
<tr>
<th>Response</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially Curable</td>
<td>Germ cell tumor, testicular cancer, non-Hodgkin lymphoma, Hodgkin lymphoma, acute lymphoblastic leukemia</td>
</tr>
<tr>
<td>May Prolong Survival</td>
<td>Breast, non-Hodgkin lymphoma, colon, myeloma, small cell lung cancer, bladder, ovary</td>
</tr>
<tr>
<td>Little Effect on Survival, but Potential Improvement in Quality of Life</td>
<td>Non-small cell lung cancer, cervix, melanoma, esophagus, pancreas, stomach, head and neck ovary, colorectal</td>
</tr>
<tr>
<td>Resistant</td>
<td>Renal, metastatic melanoma, liver, endometrium, prostate, mesothelioma</td>
</tr>
</tbody>
</table>

Figure 2. Cancer response to chemotherapy.
Palliative Rehabilitation

Maintaining a holistic view of patients with cancer and helping them to achieve the best possible quality of life is critical. Palliative chemotherapy, radiation, surgery, and interventional pain management can alleviate cancer-related physical symptoms; however, healthcare providers must not forget the patient’s dignity, self-worth, and personal goals. After multiple hospitalizations, patients often become debilitated and deconditioned. Because they desire to remain independent in maintaining their self-care and mobility, they may become concerned about becoming a burden to their family.\textsuperscript{11-13} Patients can slide into depression as they perceive their increased reliance and dependency on others.\textsuperscript{11}

Cancer rehabilitation provides patients with a chance to achieve optimal functional capacity within the limits of the disease. By setting realistic goals, they can have a better sense of control and reduce their dependency on others. Rehabilitation teams can consist of an oncologist, physiatrist, physical therapist, occupational therapist, speech therapist, social worker, nurse, dietitian, and psychologist. Cancer rehabilitation goals are not universal but should be set according to the prognosis of each patient.

Preventive rehabilitation focuses on preserving strength, flexibility, and endurance before cancer treatment such as radiation therapy, which can lead to soft tissue and muscle contracture. Patients can mitigate such contracture if they are taught to stretch their muscles when radiation therapy begins.

Restorative rehabilitation is directed toward returning patients—specifically those with a good prognosis—to their pre-illness state. For example, a patient with breast cancer who undergoes mastectomy is expected to recover strength and full shoulder range of motion.

Supportive rehabilitation attempts to help patients adapt to permanent functional deficits caused by cancer and to maximize their autonomy. After brain tumor resection, for instance, patients may have cognitive deficits for which they can be taught to compensate with therapy.

Palliative rehabilitation concentrates on patients with advanced cancer to provide comfort and support and to maximize independence with various assistive devices. For example, providing a bedside commode with grab bars allows patients with bladder dysfunction to be independent.\textsuperscript{11}

Cancer rehabilitation can be beneficial even for those patients with advanced disease. In a case series of 115 patients with cancer who were admitted to an inpatient rehabilitation unit, there was no significant difference in functional gains achieved between patients with limited and those with advanced disease. In a case series of 115 patients with cancer who were admitted to an inpatient rehabilitation unit, there was no significant difference in functional gains achieved between patients with limited and those with advanced disease.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkylating Drugs</strong></td>
<td>Syndrome of inappropriate antidiuretic hormone secretion, bone marrow suppression, hair loss, mucositis, bladder, lung, vomiting</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Nausea, vomiting, kidney, neuropathy, ototoxicity, marrow suppression</td>
</tr>
<tr>
<td>Cisplatin/carboplatin</td>
<td>Bone marrow suppression, mucositis, diarrhea</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>Bone marrow suppression, neuropathy, mucositis</td>
</tr>
<tr>
<td><strong>Antitumor Antibiotics</strong></td>
<td>Bone marrow suppression, lung</td>
</tr>
<tr>
<td>Anthracyclines: Adriamycin, epirubicin</td>
<td>Cardiac, bone marrow suppression, hair loss, nausea, vomiting</td>
</tr>
<tr>
<td><strong>Plant Alkaloids</strong></td>
<td>Neuropathy, bone marrow suppression, hair loss, constipation</td>
</tr>
<tr>
<td>Vincristine/vinblastine</td>
<td>Bone marrow suppression, diarrhea</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Bone marrow suppression, hair loss, neuropathy, constipation</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Bone marrow suppression, lung</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Bone marrow suppression, neuropathy</td>
</tr>
</tbody>
</table>

**Figure 3.** Common toxicities of frequently used chemotherapy agents.

**Table**

Karnofsky Scale for Measuring Performance Status of Patients Treated for Cancer*  

<table>
<thead>
<tr>
<th>Physical Ability</th>
<th>Score, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complaints; no evidence of disease</td>
<td>100</td>
</tr>
<tr>
<td>Able to carry on normal activity; minor signs or symptoms of disease</td>
<td>90</td>
</tr>
<tr>
<td>Some signs or symptoms of disease; normal activity with effort</td>
<td>80</td>
</tr>
<tr>
<td>Cares for self; unable to carry on normal activity or to do active work</td>
<td>70</td>
</tr>
<tr>
<td>Requires occasional assistance but is able to care for personal needs</td>
<td>60</td>
</tr>
<tr>
<td>Requires considerable assistance and frequent medical care</td>
<td>50</td>
</tr>
<tr>
<td>Disabled; requires special care and assistance</td>
<td>40</td>
</tr>
<tr>
<td>Severely disabled; hospitalization indicated although death not imminent</td>
<td>30</td>
</tr>
<tr>
<td>Very sick; hospitalization necessary; requires active supportive treatment</td>
<td>20</td>
</tr>
<tr>
<td>Moribund; fatal processes progressing rapidly</td>
<td>10</td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
</tr>
</tbody>
</table>

*This scale (sometimes called the Karnofsky index) was devised by two American physicians (David Karnofsky and Joseph Burchenal) in the 1940s.
lytic lesions in bone yields pain relief in more than 75% of patients treated. Healing and reossification of nonfractured bone occurs in 65% to 85% of lytic bone lesions treated with radiation.

Malignancies most commonly subjected to palliative XRT are lung cancer, bone metastases, brain metastases, advanced pelvic malignancies, lymph node metastases, and spinal cord metastases. Lung cancer is the most frequent neoplastic disease in North America and is the most common cause of cancer-related mortality in both men and women. Palliative XRT is an integral part of treatment of patients with lung cancer-related lesions that are causing atelectasis, post-obstructive pneumonia, shortness of breath, large airway obstruction, and pain.

Palliative Surgery
Palliative surgery, often considered noncurative, is performed to alleviate symptoms of tumors or complications that can arise from tumors or medical or surgical treatment. The goal of palliative care, and by definition palliative surgery, is to improve quality of life for the patient. The first surgical entity to officially recognize palliative surgery was the American College of Surgeons in its Statement of Principles Guiding Care at End of Life in February 1998. This statement was one of many important events in the history of palliative care and its growing acceptance since the late 1980s. Achieving recognition of palliative surgical care has always been a topic for surgeons as well as other medical specialists.

The concept of monitoring and reducing morbidity and mortality is difficult when the goal may not be to extend life. Improvement in quality of life is more difficult to measure than a decrease in hospital days or infections. Although death within the 30-day postoperative period is universally considered a failure by surgical and medical teams, this view must be overcome when dealing with procedures of palliative intent.

Selecting patients for surgery requires a definitive understanding of disease and surgical morbidity, severity of presenting symptoms, and the likelihood that surgery will relieve them. It is also imperative to determine if the intended relief is outweighed by potential risks involved in surgery.

Approximately 250,000 gastrointestinal cancers are diagnosed in the United States each year. Of those, nearly 80% comprise gastric, pancreatic, and colorectal cancers. Although the incidence of gastric cancer is declining in the United States, it continues to be a substantial cause of overall morbidity and mortality. This disease is often diagnosed during laparotomy, and in nearly half of these cancers, the subsequent resection is considered palliative because of local or systemic spread and high mortality.

Surgical resection of gastric tumors usually offers the best form of palliative care by relieving symptoms of obstruction or bleeding. Repair of hemorrhage and perforation are fairly common operations in patients with gastric cancer. These procedures can be considered forms of palliative surgical care, though their purpose serves a more acute problem.

Pancreatic cancer is diagnosed in nearly 30,000 patients each year in the United States. Palliative surgery in such patients with terminal disease is focused on three areas: obstructive jaundice, duodenal obstruction, and general cancer pain. The most common symptom of pancreatic and cholangiocarcinoma is painless jaundice secondary to mechanical obstruction of the distal common bile duct. Various endoscopic and percutaneous stents are aimed at palliation of symptoms related to mechanical obstruction of pancreatic or biliary ducts or both.

Tumor debulking via hepatojejunostomy is also commonly done for palliation of pancreatic and biliary cancer symptoms. Pancreatoduodenectomy is a surgical option usually reserved for curative candidates. Surgical palliation of duodenal obstruction is usually accomplished via gastrojejunostomy unless life expectancy is only 3 to 6 months. Pancreatic cancer–associated pain is often the most debilitating symptom of this disease.

Surgical palliation is aimed at the specific structure or organ causing the painful symptoms. Often, pain is well controlled with opioids or a combination of opioids and interventional pain
management procedures. Neurosurgical procedures including cordotomy, dorsal rhizotomy, hypophysectomy, myelotomy, and deep brain stimulation are relatively commonly performed for their palliative intent. Other forms of cancer amenable to surgical palliation are too numerous for the scope of this article, but interest in and acceptance by surgeons and other medical practitioners in this area of care are growing rapidly.

**Interventional Palliative Procedures**

Interventional palliative procedures are a mainstay treatment modality for patients with intractable cancer pain. If medical therapy including opioids fails to achieve pain relief, more invasive methods (eg, celiac plexus blocks) are used. However, one of the most important tenets in this field is to provide maximal benefit with the least invasive treatment. Interventions such as celiac plexus blocks, splanchnic nerve blocks, sympathetic plexus blocks, and ganglion impar blocks are common palliative procedures for patients with cancer. Additionally, epidural and pudendal blocks can be considered for reduction of pain in certain circumstances (eg, pancreatic cancer, renal cancer, gastric cancer).

Temporary or permanent placement of intrathecal and epidural catheters is frequently used to deliver opioids, local anesthetics, and a limited number of other adjuvant medications to patients with cancer and other patients with diagnosed terminal diseases, as well as in select nonterminally ill patients.

**Sympathetic and Splanchnic Blocks**

Visceral cancer pain uncontrolled by opioids or other analgesics is an appropriate target for sympathetic and splanchnic blocks. Advantageously, visceral afferent fibers that transmit visceral-type pain are situated with autonomic nerve fibers, which allows for their blockade without deleterious effects on somatosensory or motor nerves.

- **Celiac Plexus Block**—Celiac plexus block is for sympathetic nerves and is intended to denervate abdominal organs from the gastroesophageal junction to the splenic flexure of the large intestine. This plexus is located at L1 posterior to the vena cava on the right side and just lateral to the aorta on the left side. It is a standard palliative procedure for intractable pain secondary to pancreatic or upper abdominal cancer in which surgery is either not an option or has failed to relieve pain. Adverse effects and complications, an important source of morbidity, include postural hypotension, diarrhea, sexual dysfunction, pneumothorax, retroperitoneal hemorrhage, kidney damage, infection, and, rarely, paraplegia.

  - Splanchnic nerve block is similar to celiac plexus block but is done at the level of T12.

- **Superior Hypogastric Plexus Block**—The superior hypogastric plexus block is indicated for patients with pelvic pain originating from cancers of the cervix, uterus, adnexa, bladder, prostate, and rectum. This bilateral plexus of nerves is located retroperitoneal at the L5-S1 region extending from the anterior aspect of L5 to the superior portion of the sacrum. The first documentation of a hypogastric block for palliative pain relief of cervical cancer was in 1990.

- **Ganglion Impar (Walther) Block**—The ganglion is a solitary retroperitoneal structure located at the level of the sacrococcygeal junction. This unpaired ganglion marks the end of the two paravertebral sympathetic chains.

Patients with sympathetically-mediated visceral pain in the perineal region associated with malignancies may be effectively treated with neurolysis of the ganglion impar. Although this block has not been evaluated in controlled trials, it tends to benefit patients with complaints of poorly localized, vague pain that is frequently accompanied by sensations of burning and urgency.

**Other Palliative Interventional Modalities**

- **Intrathecal Catheters**—Intrathecal catheters represent another modality of palliative intervention. Patients with intractable pain not adequately controlled by systemic analgesics including opioids may be candidates for spinal analgesia. Similarly, if adverse effects from systemic analgesics are unacceptable, spinal analgesia is an option, assuming that appropriate adjuvants to opioids have failed prior to considering spinal analgesia. The spinal catheter can be a simple percutaneous system with continuous or intermittent injection or a portion of a totally implantable system.

Contraindications to spinal or epidural administration are similar to those for most interventional procedures and include, but are not limited to, patient refusal, bleeding disorders, sepsis, and local infection. Relative contraindications include spinal metastasis and coexisting disease such as severe cardiovascular or pulmonary compromise.

- **Ziconotide**—Ziconotide, a synthetic peptide, produces antinociception by selectively blocking the N-type voltage-sensitive calcium channels in zone II of Rexed’s laminae of the dorsal horn. The efficacy of this peptide for patients with severe cancer pain who have failed to obtain relief from intrathecal opiate therapy was shown in a randomized double-blind study. Pain relief was moderate to complete in 53% of patients receiving ziconotide as compared with 17.5% of those receiving placebo. Overall efficacy was not reduced in the maintenance phase. Intrathecal ziconotide provided clinically and statistically significant analgesia in patients with pain from cancer or AIDS in this study (P<.001).

- **Ketamine Intravenous Infusion**—Studies have suggested that activation of N-methyl-D-aspartate (NMDA) receptors may contribute to development of chronic and intractable pain. Ketamine is a noncompetitive NMDA receptor antagonist with analgesic and dissociative anesthetic properties. Its use in both intravenous and oral forms has been investigated in the treatment of neuropathic pain associated with malignancy. Continuous intravenous infusions of ketamine were found to significantly reduce total daily doses of morphine in patients with intractable cancer pain.

- **Percutaneous Vertebral Body Augmentation**—Percutaneous vertebroplasty and kyphoplasty offer minimally invasive techniques to treat painful vertebral compression fractures due to a variety of pathologic states including metastatic neoplasms. These techniques offer an adjuvant therapy to both radiation therapy and surgery by providing stabilization and pain relief.
The following typical case presentation describes the palliative care of a terminally ill patient with cancer.

Case Presentation
Connie, a 65-year-old woman with metastatic breast carcinoma, came to the hospital with intractable spinal pain in the thoracolumbar region. She had widespread bony disease documented by positron magnetic tomography (PET) scans, bone scans and magnetic resonance imaging (MRI). The sites of metastases included the spine, hips, and femur. Connie had previously undergone radiation therapy from C6 to T1 and T8 to L2. Additionally, an intrathecal morphine pump was implanted to provide pain control. Connie continued to require oral oxycodone for breakthrough pain control. In spite of escalating doses of these intrathecal and oral analgesics, Connie continued to have excruciating pain in the thoracolumbar region. She was admitted to the hospital for pain control and required intravenous hydromorphone in addition to upward titration of her intrathecal morphine. She continued to have pain rated at a score of 10 on the 10-point Verbal Integer Scale; pain was exacerbated by movement with focal tenderness over T10. Connie did not demonstrate any motor or sensory deficits. An MRI scan showed a pathologic compression fracture of T10 without epidural involvement. She underwent percutaneous vertebroplasty without complication. Following the procedure, her pain score was reported as 1/10. She subsequently entered a brief inpatient rehabilitation stay secondary to deconditioning before she was discharged to home.

Comment
Palliative care of patients who are terminally ill with cancer has greatly improved during the past two decades. Even with the great advancements of curative cancer treatment, nearly 50% of patients with diagnosed cancer will die of their disease.19 Multiple modalities of palliative care as presented here are available, but more exist that are outside the scope of this article. The entirety of palliative modalities is a vast and important area of medical knowledge.

Relief of pain at the end of life is an issue many will encounter either personally or professionally. As physicians, we need to acknowledge and communicate to these patients that there are treatment options available that can improve their quality of life. Providing them with education about their illness and the different palliative care choices can make both patients and families feel empowered to make the best decision.

References