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Most patients with advanced cancer (60% to 80%) require treatment for pain. Pain may also be experienced in many patients with earlier stages of cancer or who have been successfully treated but have persistent pain. Effective management for cancer-related pain is well established and guidelines exist for its treatment, which have been endorsed by the World Health Organization (WHO) and other professional societies and government agencies. Despite the availability of effective treatments, cancer pain remains undertreated.

Educational Objectives

- Describe nonpharmacologic approaches to the management of persistent cancer pain, including interventional, neurostimulatory, neuroablative, physical, and psychological.
- Describe the issues of cancer pain management at the end of life.

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This continuing medical education program is intended for primary care physicians and those physicians who care for patients experiencing pain.

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CME Needs Assessment

Pain is one of the most common reasons for patients to seek medical attention and one of the most prevalent medical complaints in the US.¹⁻³ According to the 2006 National Center for Health Statistics Report, one in 10 Americans overall and three in five of those 65 years or older said that they experienced pain that lasted a year or more.² More than one-quarter of adults said they had experienced low back pain, and 15% of adults experienced migraine or severe headache in the past three months. Between the periods 1988-94 and 1999-2002, the percentage of adults who took a narcotic drug to alleviate pain in the past month rose from 3.2 percent to 4.2 percent.

For the millions of Americans who experience persistent pain, the impact on function and quality of life can be profound.²⁻⁴ Pain is associated with high utilization of health care⁴ and the societal costs related to treatment are compounded by the loss in productivity associated with persistent pain. Lost productive time from common pain conditions among workers costs an estimated \$61.2 billion per year and most of this is related to reduced performance while at work.⁵ The total annual cost of poorly controlled persistent pain most likely exceeds \$100 billion.

Physicians and other clinicians need current, state-of-the-art education to assist them in developing the necessary skills to evaluate and manage patients with persistent pain. This CME program reviews assessment and management of persistent pain syndromes that are frequently seen in primary care.

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Introduction

Patients with cancer pain may require multimodality therapy to manage difficult pain problems, applied within the broader palliative care context of concerns affecting the patient and family. These concerns usually derive from the complex interaction between pain and suffering. With optimal administration of pharmacologic therapy, only a small minority of patients will require an invasive analgesic modality.

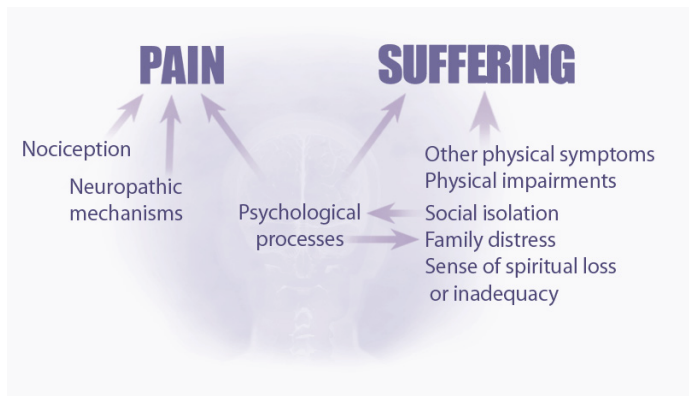


Figure: Distinctions and Interactions Between Nociception, Pain, and Suffering
Reproduced with permission from: Portenoy RK. Cancer pain: pathophysiology and syndromes. *Lancet*. 1992;339:1026-1031.

Interventional

The invasive analgesic therapies are known generically as interventional approaches.^{1,2} These include varied injection therapies, many types of neural blockade, and implant therapies.

Injection therapies

The injection therapies comprise a diverse array of approaches that differ in technical complexity and objectives. The simplest approaches—trigger point injections into tender muscles or their connections and joint injections—usually are within the purview of the primary care physician. Cancer patients commonly report musculoskeletal pains, the ability to identify and inject trigger points and joints can be a valued skill in the management of patients with cancer pain.

Other injections target specific structures, such as the spinal epidural space, the small joints that connect vertebral bodies, or scars that may entrap neuromas. In some cases, the technical skills required to inject these sites is relatively minor and the primary care physician can provide the treatment. In other cases, referral to an interventional-trained pain specialist is necessary.

Vertebroplasty and kyphoplasty are two injection therapies that are used for the treatment of pathologic vertebral fractures. Although there have been no controlled trials of either of these techniques, a large and growing clinical experience has been positive.³ In both approaches, a needle is introduced into a fractured vertebra. Cement is injected to stabilize the fracture; this is preceded by balloon expansion of the fracture in kyphoplasty. With careful patient selection, the risks of these approaches appear to be low and the clinical observations suggest prompt reduction in pain, which persists over time.

Neural blockade

Neural blockade includes many specific procedures that transiently or more permanently block somatic nerves, sympathetic nerves, or both.^{1,2,4} Somatic nerve blocks reduce afferent nociceptive input, and sympathetic nerve blocks are used to block afferent input from viscera or, occasionally, to manage neuropathic pains that are presumed to be perpetuated at least in part by sympathetic efferent function.

Temporary nerve block

Temporary nerve blocks with local anesthetic may be diagnostic, prognostic, or therapeutic. Diagnostic blocks elucidate the afferent pathways involved in the experience of pain. Prognostic blocks are implemented prior to implantation of a device or a neurolytic procedure. Though a favorable response does not predict permanent relief following implantation of a device or a neurolysis, the failure to achieve pain relief is a contraindication to a surgical implant or destructive procedure. Repeated therapeutic blocks with local anesthetic are occasionally used in cancer patients who obtain substantial and fairly prolonged relief after a temporary block. More prolonged neural blockade also can be achieved through techniques of perineural or epidural infusion. Prolonged infusion of epidural local anesthetic is the most common approach.⁵

Neural blockade with neurolytic solutions, usually alcohol, phenol, or glycerol, have been in use for many decades, and approaches have been developed to denervate virtually any area of the body.⁴ The risks associated with the injection of neurolytic substances suggest that these techniques generally should be reserved for patients with refractory pain in the setting of advanced cancer or with an appropriate risk-benefit ratio. The one commonly accepted exception is celiac plexus blockade for the management of epigastric pain due to neoplastic invasion of the celiac axis or organs innervated by splanchnic nerves. In patients with pancreatic cancer, the favorable response to neurolytic celiac plexus blockade warrants its use if routine opioid-based systemic pharmacotherapy is unable to control the pain.^{6,7}



Implant therapies

Pain specialists may be able to perform sophisticated, non-destructive therapies, which include implantation of a pump to deliver medication intraspinally or a generator to deliver an electric current adjacent to the spinal cord (spinal cord stimulation) or a specific nerve (peripheral nerve stimulation). The advent of these therapies has markedly reduced the use of neural blockade or other neurodestructive therapies.

Neuraxial infusion is usually considered when intolerable side effects attend systemic treatment with an opioid. In a controlled trial, continuous intrathecal infusion of morphine via an implanted drug delivery system yielded better pain control, less fatigue and improved survival than comprehensive medical management alone.⁸ The flexibility (and perhaps, the overall effectiveness) of this approach has increased with the use of multiple agents. Treatment may be implemented with one of several opioids (the most common being morphine and hydromorphone), a local anesthetic (such as bupivacaine), clonidine (an alpha-2 agonist approved as an epidural analgesic), ziconotide (an N-type calcium channel blocker available solely for intraspinal use and approved for the neuraxial treatment of refractory pain), baclofen (a GABA_B agonist approved for the neuraxial treatment of spasticity and sometimes used for pain), and potentially, several other drugs.⁹

Neuraxial infusion can be undertaken using any of number of specific techniques, varying from a percutaneous epidural catheter to an implanted pump delivering drug continuously into the subarachnoid space.⁵ Patients who are assessed as having a life expectancy of several months or more, and who are candidates for neuraxial infusion, often are considered candidates for an implanted pump. Patients with shorter life expectancies, including those who are largely bedbound, may still benefit from this therapy if a catheter can be placed, usually tunneled under the skin, and then either connected to a subcutaneous infusion device (which is then connected to an external pump via a needle through the skin) or brought through the skin and directly connected to an external infusion device.

Regardless of the delivery approach selected, neuraxial drug administration should begin with a trial. The trial is designed to determine whether the injection or infusion of one or more than one intraspinal drug is able to reduce pain sufficiently to warrant the burden and risks of a procedure. Pain specialists should be consulted concerning the nature and duration of the trial.

Spinal cord stimulation and other implanted neurostimulatory techniques
Patients with cancer pain refractory to conventional therapies are rarely considered for a trial of an implanted neurostimulatory approach. These include spinal cord stimulation and peripheral nerve stimulation. These techniques are performed by pain specialists in highly selected patients.^{1,2,5}

Rehabilitative approaches

The use of modalities, such as cold, heat, vibration, ultrasound and electricity, are often considered among the rehabilitative therapies that may be used for pain. Therapeutic exercise, the use of orthoses and prostheses, and occupational therapy techniques are others.

The use of modalities appears to benefit some cancer patients but there is little experience in their application to this population. Transcutaneous electrical nerve stimulation (TENS) in particular is sometimes adapted for the treatment of cancer pain, notwithstanding minimal published experience.¹⁰ A trial of TENS may be considered in patients with localized neuropathic pain that has proven difficult to manage with opioids or adjuvant analgesics.

The potential for analgesic effects from the use of orthoses or prostheses, or specific occupational or physical therapy approaches is insufficiently recognized. For example, refractory movement-induced pains, such as those related to bone metastases, may be partially relieved by bracing the painful part, and a well-fitting prosthesis may reduce stump pain. Therapeutic exercise may lessen pain associated with immobility, trigger points in muscle, and ankylosis. None of these rehabilitative techniques have been adequately studied. Nonetheless, the extensive clinical experience is favorable and a focus on function may have a positive impact on quality of life.

Surgical

Procedures designed to surgically denervate the painful area have been developed for every level of the nervous system, from peripheral nerve to cortex.¹¹ Although these techniques are now rarely performed, the most useful has been cordotomy (spinothalamic tractotomy), which is performed percutaneously in the awake patient with unilateral pain below the mid thoracic level. It has been reported to provide more than 80% of patients with initial pain relief. Efficacy gradually declines over time, and the technique was usually reserved for patients with far advanced disease, generally with unilateral nonaxial pain. Potential adverse effects include ipsilateral leg and arm paresis, ataxia, and bladder dysfunction. Postcordotomy dysesthesia, a neuropathic pain that is often refractory to treatment, can appear many months after cordotomy and is an infrequent but potentially serious complication.

Cordotomy and other denervating procedures (such as neurectomy or rhizotomy) were previously considered for pain syndromes refractory to routine drug therapies. They have been supplanted by more sophisticated techniques of pharmacotherapy and interventional approaches that are not neurodestructive, the most important of which is neuraxial infusion.



Specific surgical approaches also have been developed to address pain related to metastases. These included conventional surgical resection and stereotactic radiosurgery.^{12,13} These approaches should be considered for patients with refractory pain and those whose lesions are at high risk for fracture.

Psychological

Throughout the entire spectrum of cancer care, some patients or families who present with severe psychological distress may benefit from a multidisciplinary approach in which specific psychological interventions are emphasized within a program designed to palliate symptoms and provide family support. Occasionally, patients with pain have psychiatric disorders, indicating the need for further assessment and treatment by an appropriate specialist.¹⁴

Many specific psychoeducational, and cognitive and behavioral approaches have been applied successfully in the management of pain and related symptoms.¹⁵ Cognitive approaches include relaxation training, distraction techniques, hypnosis, and biofeedback, which may enhance a patient's sense of personal control over the pain and result in pain reduction. Although many of these techniques require experienced personnel to implement, several forms of relaxation training can be taught by the nonspecialist. More formal cognitive-behavioral therapy, which has achieved wide acceptance in the management of nonmalignant pain, is occasionally considered for patients with limited disease, whose level of functional impairment is perceived to be out of proportion to the effects of the neoplasm.

Alternative or Complementary Medicine Approaches

Therapies that are typically considered complementary or alternative have had a growing role in pain management.^{16,17} These approaches often are very attractive to patients because they endorse a holistic strategy that is perceived as providing hope and an element of self-control over the pain. Some interventions that are termed "complementary" are actually used routinely by specialists in pain medicine or palliative care. These include mind-body therapies (e.g., relaxation, meditation, and others), nutritional support, acupuncture, movement therapies such as yoga, and massage. Other interventions, such as homeopathy and naturopathy, have little or no documented clinical data on which to base therapeutic decisions.^{16,17} Healthcare professionals have the difficult task of being well-informed and expressing concerns about some of the latter therapies, while respecting patients' pursuit of complementary treatments that may be beneficial or, at the very least, cause no harm. The NIH (www.nccam.nih.gov) continues to support research in this area.

Cancer Pain and Palliative Care, and the Role of Palliative Sedation

Palliative care is an interdisciplinary therapeutic approach that focuses on the management of the physical, psychological, social, and spiritual needs of patients with serious or life-threatening diseases and their families.¹⁸ The goal is to reduce suffering and maintain an acceptable quality of life throughout the course of the illness. A focus on palliative care increases the likelihood that the values and decisions of the patient and family are respected; communication is supported; comfort needs are addressed; psychosocial and spiritual distress is managed; care is coordinated across treatment settings; practical support is available in the home; and expertise is available to manage the challenging period of active dying. "Generalist-level" palliative care should be considered part of best practice in the care of every appropriate clinical population and clinicians should be aware that palliative care also is a growing practice subspecialty for physicians, nurses, social workers, chaplains, and others. In 2006, Hospice and Palliative Medicine became a recognized subspecialty for physicians in the United States. Most palliative medicine specialists focus on end-of-life concerns, when the need for specialist-level care is likely to be greatest.

Some patients develop refractory pain or other symptoms, which cannot be addressed symptomatically despite best efforts. A specialist in palliative medicine may be a valuable consultant in this setting. Among the therapies that may be offered for refractory suffering is induced somnolence, a therapeutic intervention that might be best termed "palliative sedation." Sedation at the end-of-life may be controversial, especially if the ethical foundation is not adequately understood.¹⁹⁻²² Although it is certainly true that sedation, which is usually induced with a sedative-hypnotic drug, could potentially accelerate the dying process, the ethics of the approach are acceptable if the intention is to relieve suffering and not to kill. This is known as the "principle of double effect" and guides the administration of any intervention that carries substantial risk in the medically frail population.^{18,19} It should not be confused with euthanasia, and from an ethical perspective, it is founded on the patient's right to be free of suffering, not a patient's right to assistance in achieving death. When properly implemented, it is viewed by the American Medical Association and other professional societies as an appropriate medical treatment for defined indications.^{23,24}

Sedation should be implemented only after the medical situation has been carefully assessed, a thorough discussion with the patient and family has taken place, consent has been obtained, and the goals of care have been clearly established. Once sedation has been activated, ongoing information should be provided to family and staff, questions should be answered, and ethical and legal implications should be clarified. With prior approval by the patient or proxy, a plan for reducing sedation at times, to determine symptom burden and state of mind, may be put in place.



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