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The 1986 NIH consensus development conference, The Integrated Approach to the Management of Pain, recommended considering pain as 3 separate constructs: acute pain associated with malignant disease, persistent pain associated with malignant disease, and persistent pain not associated with malignant disease. Most research into persistent malignant pain has been done in cancer and AIDS patient populations, but the treatment principles apply to all types of persistent pain associated with progressive, potentially life limiting disorders. Therefore, the clinical applicability of many of the treatment recommendations in this module extend well beyond patients with pain due to cancer.

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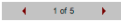
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CME Needs Assessment

The large majority of patients with advanced stage cancer (60% to 80%) will require treatment for pain. Pain may also be experienced in many patients with earlier stages of cancer and intermittently during the course of their disease. Even patients who have been successfully treated may have persistent pain due to the consequences of the original cancer or its treatment. 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. Based on the WHO guidelines for the relief of cancer pain, 70% to 90% of patients can obtain good pain relief with oral analgesics if administered as called for in the recommendations.¹

In spite of the availability of effective pain treatments, clinical studies indicate that cancer pain remains undertreated. There are a number of reasons for the undertreatment of cancer pain, including inadequate pain assessment and suboptimal use of analgesic agents such as opioids. However, the ultimate reason for the undertreatment of cancer pain is due to inadequate physician and other healthcare professional education on pain management.

Intended Audience

This continuing medical education program is intended for primary care physicians and other healthcare professionals who manage patients with cancer-related pain.

Educational Objectives

Upon completion of this activity, participants should be able to:

- Evaluate and interpret the pain complaint in the patient with cancer.
- Integrate consideration of the impact of pain on quality of life in the management of cancer-related pain.
- Describe the different cancer pain syndromes.

1. Gabriel, SE. Cancer Pain Relief: with a Guide to Opioid Availability. 2nd ed. Geneva: World Health Organization; 1996.

Introduction

Pain is very common in patients who have cancer. It is estimated that 30% to 50% of patients undergoing active antineoplastic therapy and 75% to 90% of patients with advanced disease have persistent pain severe enough to warrant opioid therapy.¹⁻³ Fortunately, effective use of opioid therapy and numerous adjunctive approaches can provide adequate control of pain and an improved quality of life for most patients. Failure to treat pain adequately continues to be a major problem, however, and this failure is rooted in clinical care deficiencies, a reluctance of patients to report unrelieved pain, and limitations in the health care system.

To address deficiencies in clinical practice, physicians must attend to pain as a significant concern and apply widely accepted management principles. These focus on pain assessment and the administration of a multimodality strategy based on optimal opioid therapy.

Assessment of Cancer Pain

The assessment of cancer pain requires an understanding of phenomenology, pathophysiology, and characteristics of typical cancer syndromes. This information is combined with a patient-specific evaluation of the malignancy and other comorbidities to clarify the nature of the pain and ensure consideration of the physical, psychological, and social concerns that could be contributing to the patient's pain (Table: Stepwise Assessment of the Patient with Cancer Pain). The goals of pain treatment in patients with cancer are to enhance comfort and improve quality of life.

Definition of Pain

According to the International Association for the Study of Pain, pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".⁴ In patients with cancer, structural disease or neuropathic processes can usually be identified as etiologic, but this does not obviate the need for a careful assessment of other factors, such as psychological disturbances, that could be influencing the intensity of the pain or contributing to pain-related distress.

The definition of pain may be clarified by distinguishing nociception, pain, and suffering (Figure: Distinctions and interactions between nociception, pain, and suffering). Nociception is the activity produced in the nervous system by noxious (potentially tissue-damaging) stimuli. Clinically, nociception is inferred whenever tissue damage is identified.

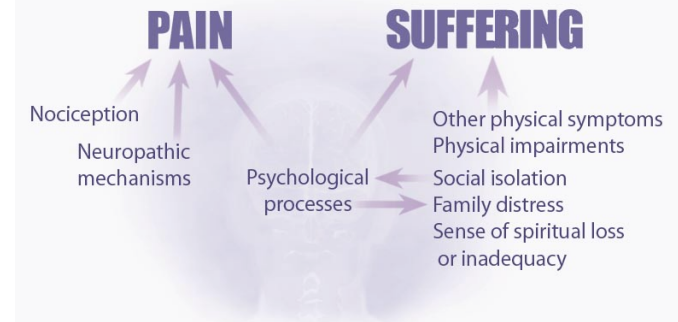


Figure: Distinctions and Interactions Between Nociception, Pain, and Suffering
Reproduced with permission from: Portenoy RK. Cancer pain: pathophysiology and syndromes. *Lancet*. 1992;339:1026-1031.

Pain is a perception. Like other perceptions, it is influenced by factors beyond the activity in the afferent nervous system alone. A pain assessment may or may not suggest that the pain is consistent with the degree of tissue injury (also called "nociceptive" pain) revealed in the physical examination or imaging studies. In all cases, factors other than tissue injury, including neuropathic processes and psychological disturbances, must be evaluated as other potential determinants of the pain. Failure to address these other factors while targeting therapy at sources of nociception can lead to a poor outcome, in which the focus of tissue damage is ameliorated but the pain continues.

Evaluation of the Pain Complaint

A comprehensive pain assessment should include information about:

- temporal characteristics (onset, duration and daily fluctuation);
- course (stable, improving, worsening, or widely fluctuating);
- severity (both average and worst);
- location;
- quality; and
- provocative and palliative factors.

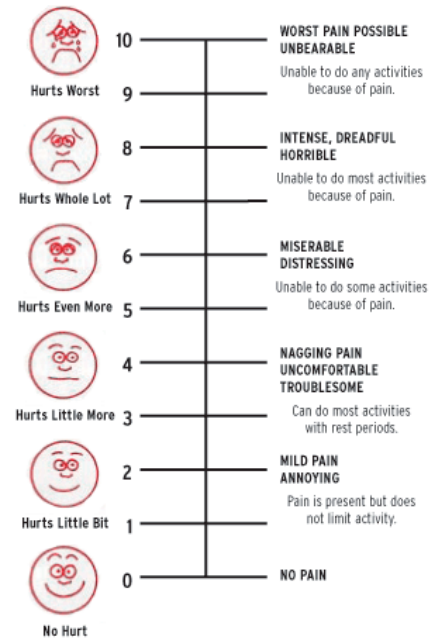
The evaluation is complemented by information about the patient's cancer and its therapy, related medical and psychosocial condition, and other issues. Pain may be acute or persistent. Acute pain usually has a well-defined onset and a readily identifiable cause; it is short-lived or anticipated to be so. It may be associated with anxiety, overt pain behaviors (moaning or grimacing), and signs of sympathetic hyperactivity (including tachycardia, hypertension, and diaphoresis). In contrast, persistent pain typically is characterized by an ill-defined onset and association with persistent focus of pathology. The course of the pain may be linked to the disease

and may change with the response to primary antineoplastic therapies. With persistent pain, overt pain behaviors and sympathetic hyperactivity are typically absent, and vegetative signs, including lassitude, sleep disturbance, and anorexia, may be present. A clinical depression evolves in some patients.

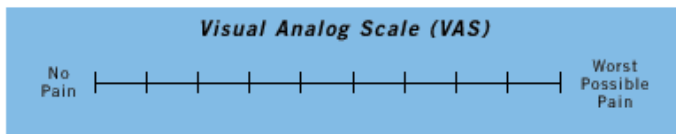
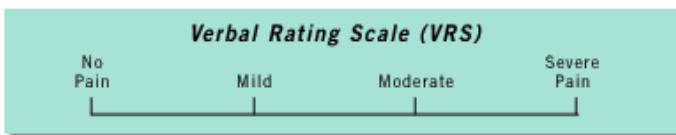
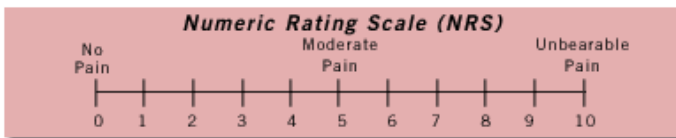
Most patients with persistent cancer pain also experience periodic flares of pain, or “breakthrough pain.”⁵ An important subtype of breakthrough pain is “incident” pain, which is precipitated by voluntary activity. Identification of breakthrough pain may suggest specific interventions, such as the use of so-called “rescue” doses, or specific treatment targeting the cause of the breakthrough pain. Pre-emptive treatment with short-acting analgesics are useful when administered in advance of known causes of incident pain (e.g., rehabilitation therapy).

Pain may be focal, multifocal, or generalized. Initiation of some therapies, such as nerve blocks, depend on the specific location and extent of the pain. In this context, “focal” means that the pain is experienced at one site. A distinction also may be drawn between focal and referred pain. From this perspective, focal pains are defined as those experienced superficial to the underlying nociceptive lesion, whereas referred pains are experienced at a site distant from the etiologic lesion. Pain may be referred from a lesion involving any of a large group of structures, including nerve, bone, muscle or other soft tissue, and viscera.⁶ Various subtypes of referred pain can be distinguished. Pain may be referred anywhere along the course of an injured peripheral nerve (such as pain in the thigh or knee from a lumbar plexus lesion) or nerve root (radicular pain). Pain also may be referred to a site remote from a nociceptive lesion and outside the dermatome affected by the lesion (e.g., shoulder pain from diaphragmatic irritation).

Pain Faces



Oucher Scale





Knowledge of pain referral patterns is needed to target assessment procedures. For example, a patient with recurrent cervical cancer may report progressive pain in the inguinal region. This would require evaluation of numerous structures to identify the underlying nociceptive lesion, including the subjacent pelvic bones and hip joint, pelvic sidewall, paraspinal gutter at an upper lumbar spinal level, and intraspinal region at the upper lumbar level. Often, missed referral sites are scars, unstable ligaments or tendons, all rich with sensory nerve fibers that when dysfunctional can refer pain in very unusual patterns.

Measurement of pain intensity is an essential element in the pain assessment. Intensity may be monitored using a Numeric Rating Scale (0-10), Verbal Rating Scale (none, mild, moderate, severe), or a Visual Analog Scale. Pictorial scales (Faces Scale, Oucher Scale) are particularly useful for the very young and patients with mild to moderate cognitive impairment. The particular scale used is less important than its consistent use to monitor and document the status of the pain over time.

Interpreting the Assessment

The pain history, combined with the information gleaned from a physical examination and appropriate imaging and laboratory studies, usually provides sufficient data to generate meaningful conclusions concerning the etiology of the pain, its pathophysiology, and its defining syndrome. The latter constructs are very useful in clarifying the need for additional evaluation, prognosticating outcomes, and developing an efficient therapeutic strategy.

Etiology

The etiology of acute pain is often obvious, and further evaluation to determine the underlying lesion is not indicated unless the course varies from the expected. In contrast, the etiology of persistent cancer-related pain may be more difficult to characterize. In most cases, pain is due to direct invasion of pain-sensitive structures by the neoplasm. The structures most often involved are bone and neural tissue, but pain also can occur when there is an obstruction of a hollow viscus, distention of organ capsules, distortion or occlusion of blood vessels, and infiltration of soft tissues. In about one-quarter of patients, the etiology relates to an antineoplastic treatment, and fewer than 10% have pain unrelated to the neoplasm or its treatment.⁸ Many patients, particularly those with advanced illness, have multiple etiologies and several sources of pain.

Given the association between pain and the underlying neoplasm, clarification of the specific relationship between the pain and the disease is an essential element of the assessment. A survey of patients referred to a pain service in a major cancer hospital noted that previously unsuspected lesions were identified in 63% of patients.⁹ This outcome altered the known extent of disease in virtually all patients, changed the prognosis for some, and provided an opportunity for a primary antineoplastic therapy in approximately 15%.

Pathophysiology

While the mechanisms underlying pain are complex and dynamic processes that may never be fully elucidated in the clinical setting, a pathophysiologic classification of pain can have utility in treatment planning. Pain syndromes may be labeled nociceptive, neuropathic, psychogenic and/or mixed. When the cause of the pain is not apparent most pain experts refer to this as an idiopathic syndrome.

Visceral pain associated with obstruction of a hollow viscus-gnawing or crampy

Visceral pain associated with injury of other visceral structures-aching or stabbing

Somatic pain-aching, stabbing, throbbing, or pressure-like

Pain is labeled nociceptive if it is inferred that the sustaining mechanisms involve ongoing tissue injury. This injury can involve either somatic or visceral structures. The quality of somatic nociceptive pain is typically described as aching, stabbing, throbbing, or pressure-like. The quality of visceral nociceptive pain is usually gnawing or crampy when arising from obstruction of a hollow viscus and aching or stabbing when associated with injury to other visceral structures, and is often referred to other sites or may be poorly localized.

Pain is labeled neuropathic if the evaluation suggests that it is sustained by abnormal somatosensory processing in the peripheral (PNS) or the central nervous system (CNS). Neuropathic mechanisms are involved in approximately 40% of cancer pain syndromes and can be disease-related (e.g., tumor invasion of nerve plexus) or treatment-related (e.g., postmastectomy syndrome or chemotherapy-induced painful polyneuropathy).¹¹ Among those with metastatic disease, neuropathic pain usually results from neoplastic injury to peripheral nerves (peripheral neuropathic pain). Other, less common, subtypes include: (1) those sustained by CNS processes (sometimes generically termed deafferentation pain); and (2) those in which the pain is believed to be maintained by efferent activity in the sympathetic nervous system (so-called sympathetically maintained pain).¹²



Pain may be labeled psychogenic if there is positive evidence from the assessment that psychological factors predominate in sustaining the symptom without evidence of any pathological etiology. Psychogenic pains may be more formally characterized according to the widely accepted taxonomy of the American Psychiatric Association (one of the Somatoform Disorders described in the Diagnostic and Statistical Manual).¹² Although psychological factors commonly influence the expression and severity of pain in the cancer population, it is not particularly helpful to identify the causation of pain as primarily psychogenic. If a credible pathophysiologic diagnosis is not apparent, and there is no strong evidence of a predominating psychological cause, it is best to label the pain idiopathic.

Assessment of Related Constructs

Persistent cancer-related pain is best addressed with consideration of a set of broader constructs, including suffering, quality of life, and the goals of care. Consideration of these associated factors enhances informed decision-making about interventions to manage pain.

Pain and Suffering

Suffering, a global construct intricately related to the experience of pain (Figure: Distinctions and Interactions between Nociception, Pain, and Suffering), has been described as a perceived threat to the integrity of the person, as a type of “total pain,”¹³ or as overall impairment in quality of life. Suffering may be primarily related to symptoms such as pain or physical losses; to psychiatric disorders such as depression or psychological processes such as disturbed body image; to social issues such as loss of role functioning, familial disruption, or tension in the relationship with a significant other; or to spiritual concerns such as loss of faith. Other factors, such as financial concerns, may be prominent. Psychosocial and spiritual strengths and weaknesses that long predated the cancer may be important factors influencing the patient’s degree of suffering.

Comprehensive pain assessment must address issues related to patient “suffering.” An understanding of the physical, psychological, social and spiritual issues important to the patient is fundamental to this process. A therapeutic approach focused only on pain may not meaningfully benefit a patient whose suffering is related to other factors.

Pain and Quality of Life

Quality of life is related to the construct of suffering but has been more formally characterized for a research context. Numerous instruments have been created to measure quality of life, and these have been developed from the perspective of two major characteristics: subjectivity and multidimensionality. The inherent subjectivity of quality of life has implications for assessment. Although clinicians commonly make inferences about patients’ well-being, or rely on proxy evaluation by family or others, the likelihood of inaccuracy in such appraisals must be appreciated. For the evaluation of quality of life and each of its contributing concerns, including pain, the “gold standard” of assessment is the self-report.¹⁴

Like pain itself, quality of life is multidimensional. Although a single question can screen for overall well-being, a fuller understanding of the factors that must be addressed to improve quality of life requires probing of issues related to physical, psychological, social, and spiritual functioning.

Pain and Symptom Distress

Most patients with persistent cancer pain experience multiple additional symptoms. Studies have demonstrated that pain, fatigue, and psychological distress are most prevalent in patients with advanced cancer. Global symptom distress is a useful construct that characterizes overall symptom burden.¹⁵

Goals of Care

A therapeutic approach to address pain requires a patient-oriented approach and the clarification of treatment goals. At any point in time, pain treatment may be guided by one or more overriding goals: (1) to cure or prolong life; (2) to maintain function; and (3) to provide comfort. These goals must be individualized and are influenced by many factors, including the status of the disease, the availability and burdens of therapy, psychosocial comorbidity, and the degree of spiritual or existential distress. Goals are very dynamic, and often evolve over time with the vagaries of the disease and the availability of treatment and optimal palliative care. Current goals continually influence therapeutic decision-making.



Cancer Pain Syndromes

As described previously, the information obtained from the pain assessment usually permits categorization of the pain according to etiology, pathophysiology and syndrome. During the past few decades, numerous syndromes have been described, each of which is defined by a cluster of symptoms and signs (Tables: Acute Pain Syndromes in Patients with Cancer and Persistent Pain Syndromes in Patients with Cancer).^{9,11} Syndrome identification can help direct the diagnostic evaluation, clarify the prognosis, and target therapeutic interventions.

Pain syndromes may be acute or persistent. Acute pain syndromes are commonly caused by diagnostic or therapeutic interventions, including surgery, or may be a form of breakthrough pain associated with a persistent pain syndrome. Persistent pain syndromes have a more complex taxonomy, related to the associated etiologies and pathophysiologies.

Tumor-Related Nociceptive Pain Syndromes

Neoplastic invasion of bone, joint, muscle or connective tissue can cause persistent somatic pain. Bone pain syndromes are the most prevalent. Only a small proportion of bone metastases become painful, and the factors that convert a painless lesion into a painful one are unknown.

The spine is the most common site of bone metastases, and back pain is an extremely common problem in patients with cancer. Extension of a neoplasm from the vertebra has the potential to damage the spinal cord or nerve roots, and back pain is a marker of potential epidural spinal cord or cauda equina compression. Specific patterns of pain suggest epidural extension and should be followed by specific imaging of the epidural space (e.g., MRI). These symptoms include rapidly progressive pain, pain flare with recumbency, and pain in a radicular pattern. Similarly, the signs of neurological impairment may portend epidural spread and should lead to referral. With early diagnosis and treatment of the tumor, the devastating consequences of spinal cord or cauda equina compression usually can be prevented. This is a compelling example of the need for syndrome recognition in cancer pain assessment.

Obstruction, infiltration or compression of visceral structures, including hollow viscus and supporting connective tissues, produce an extremely diverse group of visceral nociceptive pain syndromes (Table: Persistent Pain Syndromes in Patients with Cancer). Some of these syndromes are easily diagnosed. A few can pose diagnostic challenges, particularly when the pain syndrome precedes the diagnosis of the neoplasm.

Tumor-Related Neuropathic Pain Syndromes

Neuropathic pain syndromes may be caused by tumor infiltration or compression of nerve, plexus, or roots, or by the remote effects of malignancy on peripheral nerves (Table: Persistent Pain Syndromes in Patients with Cancer). These syndromes are highly variable. Patients may experience aching pains or dysesthesias anywhere in the dermatomal region innervated by the damaged neural structure. There may or may not be motor, sensory or autonomic dysfunction in the distribution of the involved nerve.

Treatment-Related Pain Syndromes

Nociceptive and neuropathic pain syndromes may evolve as a consequence of chemotherapy, radiation therapy or surgery (Table: Persistent Pain Syndromes in Patients with Cancer). For example, somatic pain related to osteonecrosis can be caused by radiation or corticosteroid-based chemotherapy regimens, and persistent visceral pain can follow intraperitoneal chemotherapy or abdominal radiation therapy. These syndromes can mimic tumor-related pain.

Chemotherapy-induced painful peripheral neuropathy is common and may be a consequence of treatment with a number of agents, including vincristine, cisplatin, and paclitaxel. Although most patients improve once chemotherapy is stopped, some develop persistent pain. Although rare, surgical incisions can precipitate a neuropathic pain syndrome in some patients. Limb amputation may cause a painful neuroma, causalgia, or phantom limb syndrome. Radiation-induced fibrosis can injure a peripheral nerve or nerves and cause chronic neuropathic pain that may begin months to years following treatment; however, this pain is generally less prominent than nerve injury related to neoplasm, and slowly progressive weakness, sensory disturbances, radiation changes of the skin, and lymphedema are often associated.

Table: Stepwise Assessment of the Patient with Cancer Pain

Step 1: Data collection	Step 2: Interpret the findings	Step 3: Formulating a Treatment Strategy
Pain-related history <ul style="list-style-type: none"> • Other relevant history • Disease related • Other symptoms • Psychiatric history • Social resources 	Pain-related constructs <ul style="list-style-type: none"> • Etiology • Inferred pathophysiology • Syndrome identification 	Further evaluation, if needed
Concurrent quality of life concerns <ul style="list-style-type: none"> • Other symptoms • Concerns in physical, psychological, social, and spiritual domains • Other concerns (e.g., financial) • Assessment of the family 	Extent of disease Goals of care <ul style="list-style-type: none"> • Prolonging survival • Optimizing function • Optimizing comfort 	Multimodality approach to the pain Treatments for concurrent concerns Patient/family education
Available laboratory and imaging data <ul style="list-style-type: none"> • Radiographs and scans • Tumor markers • Hematologic parameters • Biochemical parameters 		

Table: Guidelines for Opioid Therapy for Persistent Cancer Pain

Comprehensive Assessment <ul style="list-style-type: none"> • Define pain etiology, pathophysiology, and syndrome • Clarify status of disease • Determine impact of the pain and comorbid physical and psychosocial disturbances 	Dosing <ul style="list-style-type: none"> • Consider previous dosing requirements and relative analgesic potencies when initiating therapy • Start with low dose and increase until adequate analgesia occurs or dose-limiting side effects are encountered • Consider dosing schedule (e.g., around-the-clock or as needed) depending on the anticipated time course of pain • Consider rescue medication for breakthrough pain. • Recognize that tolerance is rarely the driving force for dose escalation; consider disease progression when increasing dose requirements occur.
Drug Selection <ul style="list-style-type: none"> • Consider age and whether major organ failure is present, especially renal, hepatic or respiratory • Consider drug-selective differences in side effect or toxicity profile • Consider the effects of concurrent drugs with possible pharmacokinetic and pharmacodynamic interactions • Consider individual differences (note prior treatment outcomes) and patient preference • Be aware of available preparations for route (e.g., oral, IV, subcutaneous injection, topical) and formulation (e.g., immediate or controlled-release) • Be aware of cost differences 	Treat Side Effects <ul style="list-style-type: none"> • Give laxatives prophylactically for those patients predisposed to constipation • Be prepared to treat nausea, itch, and somnolence • Trial of alternative opioids
Route Selection <ul style="list-style-type: none"> • Use least invasive route possible • Consider patient convenience and compliance 	Monitoring Monitor treatment efficacy and pain status over time and consider modification if necessary.

Adapted from Ingham J, Portenoy RK. Drug therapy for pain: NSAIDs and opioids. *Curr Opin Anaesthesiol.* 1993;6:838-44.

Table: Acute Pain Syndromes in Patients with Cancer

<p>Acute pain associated with diagnostic procedures</p> <ul style="list-style-type: none"> • Lumbar puncture headache • Bone-marrow biopsy • Lumbar puncture • Venipuncture • Paracentesis • Thoracentesis 	<p>Acute pain associated with hormonal therapy</p> <ul style="list-style-type: none"> • Painful gynecomastia • Luteinizing hormone releasing factor tumor flare in prostate cancer • Hormone-induced acute pain flare in breast cancer
<p>Acute pain associated with analgesic techniques</p> <ul style="list-style-type: none"> • Spinal opioid hyperalgesia syndrome • Acute pain following Sr-89 therapy of metastatic bone pain 	<p>Acute pain associated with immunotherapy</p> <ul style="list-style-type: none"> • Arthralgia and myalgia from interferon and interleukin
<p>Acute postoperative pain</p> <p>Acute pain associated with other therapeutic procedures</p> <ul style="list-style-type: none"> • Pleurodesis • Tumor embolization • Nephrostomy insertion • Pains associated with bone marrow transplantation 	<p>Acute pain associated with radiation therapy</p> <ul style="list-style-type: none"> • Painful oropharyngeal mucositis • Acute radiation enteritis and proctocolitis • Early-onset brachial plexopathy following radiation for breast cancer
<p>Acute pain associated with chemotherapy</p> <ul style="list-style-type: none"> • Pain from intravenous or intra-arterial infusion • Intraperitoneal chemotherapy • Headache due to intrathecal chemotherapy • Painful oropharyngeal mucositis • Painful peripheral neuropathy • Bone or muscle pain from colony stimulating factors or chemotherapies • 5-fluorouracil-induced angina 	<p>Acute tumor-related pain</p> <ul style="list-style-type: none"> • Vertebral collapse and other pathological fractures • Acute obstruction of hollow viscus (e.g., bowel, ureter, bladder outlet) • Headache from intracranial hypertension • Hemorrhage into tumor
	<p>Acute pain associated with infection</p> <ul style="list-style-type: none"> • Myalgia and arthralgia associated with sepsis • Pain associated with superficial wounds or abscesses

Source: Portenoy RK. Pain syndromes in patients with cancer and HIV/AIDS. In: Portenoy RK, ed. *Contemporary diagnosis and management of pain in oncologic and AIDS patients*. Newton, PA: Handbooks on Healthcare, 1998:44-70.

References

1. Gabriel, SE. *Cancer Pain Relief: with a Guide to Opioid Availability*. 2nd ed. Geneva: World Health Organization; 1996.
2. Kanner, RM. The scope of the problem. In: Portenoy RK and Kanner RM, eds. *Pain Management, Theory and Practice*. Philadelphia: FA Davis; 1996:40.
3. Vainio, A and Auvinen, A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. Symptom Prevalence Group. *J Pain Symptom Manage*. 1996;12:3-10.
4. Merskey, H and Bugduk, N. Classification of Chronic Pain. *Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. Seattle: IASP Press; 1994.
5. Fine, PG. Breakthrough pain. In: Bruera E and Portenoy R, eds. *Cancer Pain*. New York: Cambridge University Press; 2003
6. Torebjork, HE, Ochoa, JL and Schady, W. Referred pain from intraneural stimulation of muscle fascicles in the median nerve. *Pain*. 1984;18:145-156.
7. Cherny, NI, Coyle, N and Foley, KM. Suffering in the advanced cancer patient: a definition and taxonomy. *J Palliat Care*. 1994;10:57-70.
8. Chang VT, Janjan N, Jain S, Chau C. Update in cancer pain syndromes. *J Palliat Med*. 2006;9:1414-34.
9. Gonzales, GR, Elliott, KJ, Portenoy, RK and Foley, KM. The impact of a comprehensive evaluation in the management of cancer pain. *Pain*. 1991;47:141-144.
10. Caraceni, A and Portenoy, RK. An international survey of cancer pain characteristics and syndromes. IASP Task Force on Cancer Pain. International Association for the Study of Pain. *Pain*. 1999;82:263-274.
11. Grond, S, Radbruch, L, Meuser, T, Sabatowski, R, Loick, G and Lehmann, KA. Assessment and treatment of neuropathic cancer pain following WHO guidelines. *Pain*. 1999;79:15-20.
12. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington: American Psychiatric Association; 1994.
13. Saunders, C. A personal therapeutic journey. *BMJ*. 1996;313:1599-1601.
14. Grossman, SA, Sheidler, VR, Swedeen, K, Mucenski, J and Piantadosi, S. Correlation of patient and caregiver ratings of cancer pain. *J Pain Symptom Manage*. 1991;6:53-57.
15. Portenoy, R, Thaler, HT, Kornblith, AB, et al. Patients with cancer: the Memorial Symptom Assessment Scale. An instrument for the evaluation of symptom prevalence, characteristics, and distress. *Eur J Cancer*. 1994;1994:1326-1336.