Care CEU's

Continuing Education for Nursing Home Administrators

Last Days of LIfe

Overview

Despite advances in the treatment of cancer, many people will die from their disease. This summary is intended to address care during the last days to last hours of life, including common symptoms, ethical dilemmas that may arise, and the role of the cancer care professional in caring for patients and their families during this time.

In this summary, unless otherwise stated, evidence and practice issues as they relate to adults are discussed. The evidence and application to practice related to children may differ significantly from information related to adults. When specific information about the care of children is available, it is summarized under its own heading.

End-of-life Discussions

Although greatly feared by our death-denying society, the end of life can be a time of great personal growth for patients and their families.[1] This growth depends on thoughtful discussions and careful decision making about advance care planning, optimally beginning soon after diagnosis and continuing throughout the course of the disease. Planning includes establishing the goals of care, clarifying acceptable treatment options (including discussions regarding palliative care and hospice), and determining where a patient wishes to spend the final days of life. When these discussions do not take place and plans are not made, the final hours may be filled with suffering and distress.

In a large study of people with advanced cancer, patients who reported having end-of-life discussions with their physicians (n = 188) had significantly lower health care costs than did patients who did not have these discussions (n = 415). This was demonstrated by a reduction in resuscitation, ventilator use, and intensive care stay. There was no difference either in survival time or in the likelihood of receiving chemotherapy for patients who discussed end-of-life preferences with physicians (n = 75) and those who did not (n = 70). Higher costs were associated with worse quality of life at death, as rated by the patient's caregiver (hospice nurse or family member).[2]

In a U.S.-based multisite, prospective, longitudinal study, advanced cancer patients and their caregivers were followed to assess the association between end-of-life discussions and medical care, patient mental health, and caregiver adjustment. The cohort consisted of 332 patients who died a median of 4 months after enrollment, with 123 (37%) reporting end-of-life discussions with physicians at baseline. Results demonstrated an association between discussions and less aggressive medical care near death and earlier referrals to hospice. Aggressive care was associated with worse patient quality of life and caregiver adjustment.[3] (Refer to the PDQ summary on Transitional Care Planning for more information on home care needs.)

In a cross-sectional study of parents who lost a child to cancer, clear discussions between the primary oncologist and the parents were more likely to be associated with planning for the location of death, fewer hospital admissions, and parents feeling more prepared for the child's end of life.[4]

Palliative Care

Palliative care is an approach that can improve the quality of life for patients and their families facing life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other physical, psychosocial, and spiritual problems.[5] A randomized controlled study of early integrated palliative care with standard oncologic care versus standard oncologic care alone in patients newly diagnosed with metastatic non-small cell lung cancer revealed improved quality of life, fewer depressive symptoms, and longer median survival despite less aggressive end-of-life care in the group receiving palliative care.[6]

Inpatient palliative care services are increasingly available in hospitals with more than 50 beds; between 2000 and 2011, the prevalence increased from 24% to 67%.[7] There is also experience with outpatient palliative care clinics and home services. Regardless of the availability of palliative care services, all oncologists and other professionals caring for people with cancer must be proficient in aggressive symptom management and discussions of advance care planning. These activities are optimally conducted with the palliative care team so that both patient and family hear a consistent message and do not feel abandoned by the physician, with whom they have developed a strong bond.

Hospice

Hospice is a specialized form of interdisciplinary palliative care that alleviates physical, emotional, social, and spiritual discomfort during the last phase of life. Hospice is a program of care provided by an interdisciplinary team designed to keep a patient at home with family and friends. Pain management and symptom management are paramount, along with bereavement and volunteer components. Hospice provides palliative care, with which it is frequently confused; however, the focus of hospice is on patients with life-limiting, progressive disease (usually with a prognosis of no more than 6 months if the disease were to take its natural course).

Utilization of hospice care has increased in the United States, with more than 1.6 million individuals seeking such care. People who had cancer made up approximately 38% of these admissions in 2011.[8] However, a disturbing trend is reflected in the very short median length of stay in hospice of just 19.1 days. This trend suggests that advance care planning is not taking place early in the course of the disease, that the ability of health care providers to prognosticate is poor, and that referrals are made too late; it may also reflect denial on the part of professionals, patients, or their families regarding disease progression. (Refer to the End-of-Life Decisions section of the PDQ summary on Transitional Care Planning for more information.)

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Symptom Management

Symptoms commonly experienced at the end of life include pain, delirium, dyspnea, and rattle. In a study of 200 patients with cancer, noisy breathing or rattle, pain, and urinary dysfunction were the symptoms experienced most frequently during the last 48 hours of life.[1] In a large study of cancer patients evaluated with the Edmonton Symptom Assessment System, average scores for pain, nausea, anxiety, and depression remained relatively stable over the 6 months before death. However, shortness of breath, drowsiness, well-being, lack of appetite, and tiredness increased in severity over time, particularly in the month before death.[2] Other studies confirm that pain, fatigue, cough, delirium, dyspnea, and other symptoms are common in the final days.[3-5];[6][Level of evidence: III];[7,8][Level of evidence: II] Less common but equally troubling symptoms that may occur in the final hours include fever and hemorrhage.

Pain During the Final Hours of Life

Many patients fear uncontrolled pain during the final hours of life, while others (including family members and some health care professionals) express concern that opioid use may hasten death. Experience suggests that most patients can obtain pain relief during the final hours of life and that very high doses of opioids are rarely indicated.[9] Several studies refute the fear of hastened death associated with opioid use. In several surveys of high-dose opioid use in hospice and palliative care settings, no relationship between opioid dose and survival was found.[9-12]

Because consciousness may diminish during this time and swallowing becomes difficult, practitioners should anticipate alternatives to the oral route. In a study of cancer patients at 4 weeks, 1 week, and 24 hours before death, the oral route of opioid administration was continued in 62%, 43%, and 20% of patients, respectively. As patients approached death, the use of intermittent subcutaneous injections and intravenous or subcutaneous infusions increased.[13] Both intravenous and subcutaneous routes are effective in delivering opioids and other agents in the inpatient or home setting. For patients who do not have a pre-existing access port or catheter, intermittent or continuous subcutaneous administration provides a painless and effective route of delivery.[14] (Refer to the PDQ summary on Pain for a more complete review of parenteral administration of opioids and opioid rotation.)

Myoclonic jerking can occur at any time during opioid therapy but is seen more frequently at the end of life. The prevalence of opioid-induced myoclonus ranges greatly, from 2.7% to 87%.[15] Nocturnal myoclonus is common and often precedes opioid-induced myoclonus.[16] The precise cause of opioid-induced myoclonus is unknown; however, several mechanisms have been proposed.[17] High doses of opioids may result in the accumulation of neuroexcitatory metabolites, the best characterized of which are morphine-3-glucuronide and hydromorphone-3-glucouronide.[18];[19][Level of evidence: II] Serum and cerebrospinal fluid levels as well as the ratios of these metabolites are elevated in patients who are receiving morphine for cancer and nonmalignant pain and who have myoclonus.[20][Level of evidence: II] This may be particularly true for patients with renal dysfunction, a common phenomenon in the final hours of life.[20,21] However, clinical evidence of myoclonus does not consistently correlate with serum levels of morphine-3-glucuronide.[22][Level of evidence: II] In rodents, hydromorphone-3-glucuronide was more potent in its neuroexcitatory effects, including myoclonus, when compared with morphine-3-glucuronide.[19] Furthermore, other opioids with no known metabolites also have been shown to produce myoclonus.[23] Other opioids, including methadone,[24] meperidine,[25] and transdermal fentanyl,[26][Level of evidence: II] have been implicated in the development of myoclonus.[24]

Very high doses of an opioid may produce myoclonus. One group of investigators reported the development of acute confusion, restlessness, myoclonus, hallucinations, and hyperalgesia due to an inadvertent administration of high-dose intravenous fentanyl.[27] These symptoms were successfully treated with several doses of 0.1 mg to 0.2 mg of intravenous naloxone followed by a continuous infusion of intravenous naloxone (0.2 mg per hour).

Evaluation of the patient with myoclonus includes ruling out other known causes such as surgery to the brain,[28] placement of an intrathecal catheter,[29] AIDS dementia,[30] hypoxia,[31] chlorambucil,[32] metoclopramide,[33] and a rare paraneoplastic syndrome called opsoclonus-myoclonus.[34] The etiology of the paraneoplastic syndrome can also be viral; symptoms include myoclonus, opsoclonus, ataxia, and encephalopathic features.[35] The extent of the work-up to determine the cause of myoclonus varies with the goals of care.

When opioids are implicated in the development of myoclonus, hydration and rotation to other opioids are the primary treatments. There is great variability in individual response to opioids; thus, different agents may be more likely to produce myoclonus or other adverse effects. Because cross-tolerance between opioids is not complete, empirical evidence suggests that after an equianalgesic dose is calculated, that dose should be reduced by approximately 25%, then titrated upward to meet the patient's analgesic needs.

In patients with rapidly impending death, the health care provider may choose to treat the myoclonus rather than make changes in opioids during the final hours. Little research is available regarding the most effective agents for reducing myoclonic jerking. Benzodiazepines, including clonazepam, diazepam, and midazolam, have been recommended.[15,36,37] The mechanism of action of benzodiazepines is through binding to gamma-aminobutyric acid type A receptors within the central nervous system (CNS), leading to CNS depression. At higher doses, benzodiazepines may also limit repetitive neuronal firing, similar to several anticonvulsant compounds such as carbamazepine.

The anticonvulsant gabapentin has been reported to be effective in relieving opioid-induced myoclonus,[38] although other reports implicate gabapentin as a cause of myoclonus.[39,40][Level of evidence: III] The antispasmodic baclofen has been used to treat myoclonus due to intraspinal opioid administration.[41] Dantrolene has been used, but it produces significant muscle weakness and hepatotoxicity.[15] In one small randomized study, hydration was found to reduce myoclonus.[42][Level of evidence: I] In cases of severe myoclonus, palliative sedation may be warranted.

Dyspnea

Dyspnea, described as shortness of breath or air hunger, is a common symptom in people with cancer during the final days or weeks of life. The prevalence of dyspnea in adults diagnosed with cancer varies from 21% to 90%, correlated with lung cancer and advanced disease.[43][Level of evidence: II] Dyspnea may predict shortened survival. Patients with cancer presenting to an emergency center for treatment of dyspnea had a median overall survival of 12 weeks.[44] Patients with lung cancer had a significantly shorter survival (4 weeks) than did patients with breast cancer (22 weeks). In another study, patients presenting to an emergency department with cancer-related dyspnea who were at greatest risk of imminent death were those with an elevated pulse (100 or more beats per minute) and increased respiratory rate (more than 28 breaths per minute), with a predicted mean survival of less than 2 weeks.[45]

The etiology of dyspnea is usually advanced malignant disease, although other risk factors include ascites, chronic obstructive pulmonary disease, deconditioning, and pneumonia. Dyspnea occurs when more respiratory effort is necessary to overcome obstruction or restrictive disease (e.g., tumor or pleural effusions), when more respiratory muscles are required to maintain adequate breathing (e.g., neuromuscular weakness or cachexia), or when there is an increase in ventilatory need (e.g., hypercapnia or metabolic acidosis).[46]

Opioids decrease the perception of air hunger, regardless of the underlying pathophysiology and without causing respiratory depression.[47] This relief is dose related and, experimentally, is reversible by naloxone, an opioid antagonist. Very low doses of opioid, such as morphine 2.5 mg orally, may provide relief in opioid-naïve patients. Higher doses may be indicated in patients who have more intense dyspnea or in patients who are using opioids for pain. As with pain control, gradual upward titration may be needed to provide relief, particularly as symptoms progress.

The use of nebulized opioids for control of dyspnea remains controversial. Nebulized morphine has been administered in the belief that this route would deliver the opioid directly to opioid receptors isolated within the lung.[48] Initial uncontrolled clinical trials and case reports described efficacy using this technique.[49] However, controlled trials have not confirmed these positive results, and as a result, nebulized morphine is generally not indicated.[50] Initial trials of nebulized fentanyl, a lipophilic opioid, suggest efficacy.[26][Level of evidence: II]

A randomized controlled trial of oxygen delivered versus room air, both delivered by nasal cannula and worn at least 15 hours per day over a 7-day period, demonstrated no differences in breathlessness, with no difference in side effects between the two groups. In light of the lack of benefit of oxygen therapy, the investigators recommended that less burdensome therapies be selected.[51] Supplemental oxygen appears to be useful only when hypoxemia is the underlying cause of dyspnea and is not effective in relieving symptoms of dyspnea in people who do not have hypoxemia.[52,53] Alternate strategies include positioning a cool fan toward the patient’s face and repositioning the patient into an upright posture. Cognitive behavioral therapies such as relaxation, breathing control exercises, and psychosocial support may be effective in relieving dyspnea, although patients in the final hours of life may have limited capacity to participate in these techniques.[54][Level of evidence: I]

Complementary therapies such as acupuncture and acupressure have been demonstrated to be beneficial for relieving dyspnea, although controlled trials are lacking.[55] Antibiotics may provide relief from infectious sources of dyspnea; however, the use of these agents should be consistent with the patient’s goals of care. If the patient experiences bronchospasm in conjunction with dyspnea, glucocorticoids or bronchodilators can provide relief. Bronchodilators should be used with caution because they can increase anxiety, leading to a worsened sense of dyspnea. In rare situations, dyspnea may be refractory to all of the treatments described above. In such cases, palliative sedation may be indicated, using benzodiazepines, barbiturates, or neuroleptics.

Fatigue

Fatigue at the end of life is multidimensional, and its underlying pathophysiology is poorly understood.[56] Factors that may contribute to fatigue include physical changes, psychological dynamics, and adverse effects associated with the treatment of the disease or associated symptoms. Stimulant medications, along with energy conservation, may be warranted. (Refer to the PDQ summary on Fatigue for more information.)

Cough

In some patients, chronic coughing at the end of life may contribute to suffering.[57] Chronic cough can cause pain, interfere with sleep, aggravate dyspnea, and worsen fatigue. At the end of life, aggressive therapies are not warranted and are more likely to cause increased burden or even harm. Symptom control rather than treatment of the underlying source of the cough is warranted at this time of life. Opioids are strong antitussive agents and are frequently used to suppress cough in this setting. Corticosteroids may shrink swelling associated with lymphangitis. Antibiotics may be used to treat infection and reduce secretions leading to cough. Patients with cancer may have comorbid nonmalignant conditions that can lead to cough. For example, bronchodilators are useful in the management of wheezing and cough associated with chronic obstructive pulmonary disease, and diuretics may be effective in relieving cough due to cardiac failure. Additionally, a review of medications is warranted because some drugs (e.g., ACE inhibitors) can cause cough.

Anecdotal evidence suggests a role for inhaled local anesthetics, which should be utilized judiciously and sparingly; they taste unpleasant and suppress the gag reflex, and anaphylactic reactions to preservatives in these solutions have been documented. In cases of increased sputum production, expectorants and mucolytics have been employed, but the effects have not been well evaluated. Inhaled sodium cromoglycate has shown promise as a safe method of controlling chronic coughing related to lung cancer.[58]

Refer to the PDQ summary on Cardiopulmonary Syndromes for more information.

Death Rattle

Rattle, also referred to as death rattle, occurs when saliva and other fluids accumulate in the oropharynx and upper airways in a patient who is too weak to clear the throat. Rattle does not appear to be painful for the patient, but the association of this symptom with impending death often creates fear and anxiety for those at the bedside. Rattle is an indicator of impending death, with an incidence of approximately 50% in people who are actively dying. There is some evidence that the incidence of rattle can be greatly reduced by avoiding the tendency to overhydrate patients at the end of life.[59,60]

In one prospective study of 100 terminally ill cancer patients, rattle began at an average of 57 hours before death.[61][Level of evidence: II] Other studies suggest the median time from onset of rattle to death is much shorter at 16 hours.[62] Two types of rattle have been identified: real death rattle, or type 1, which is probably caused by salivary secretions; and pseudo death rattle, or type 2, which is probably caused by deeper bronchial secretions due to infection, tumor, fluid retention, or aspiration.[60,63] In one retrospective chart review, rattle was relieved in more than 90% of the patients with salivary secretions, while patients with secretions of pulmonary origin were much less likely to respond to treatment.[60]

The pharmacologic treatment of rattle includes antimuscarinic agents, which antagonize acetylcholine (and are thus termed anticholinergic) to reduce secretions.[64] The most commonly used agents include scopolamine, glycopyrrolate, atropine, and hyoscyamine.[59,64] Few data exist to support the use of one agent or route over another. Because most patients are unable to swallow at this time, transdermal or parenteral routes are employed most frequently. Scopolamine, also called l-hyoscine or hyoscine, is available in oral, parenteral, transdermal, and ophthalmic formulations. Some clinicians begin treatment by applying one or two scopolamine transdermal patches behind the ear. Noticeable reduction in secretions usually occurs within 1 or 2 hours after application. If the patch is ineffective, a scopolamine infusion is initiated, with a starting dose of 50 µg per hour intravenously or subcutaneously and titrated upward to 200 µg or more per hour. Adverse effects include CNS depression, although paradoxical excitation has been reported.

Glycopyrrolate (Robinul) is commercially available parenterally and in oral tablet form. Doses typically range from 1 mg to 2 mg orally or 0.1 mg to 0.2 mg intravenously or subcutaneously every 4 hours, or by continuous intravenous infusion at a rate of 0.4 mg to 1.2 mg per day. Glycopyrrolate is less likely to penetrate the CNS, and fewer adverse effects are reported than with other antimuscarinic agents, though this is probably of little consequence in the use of glycopyrrolate to relieve rattle at the end of life.

Other drugs that can assist with reducing secretions are atropine and hyoscyamine.[59,64] Doses for these agents are included in the table on Common Symptoms at End of Life and Their Treatment. In addition to these agents, diuretics such as furosemide can sometimes eliminate excess fluids that build up in the upper airways. Reducing parenteral fluids can help reduce excess secretions. None of these measures appear to be effective when the underlying cause of rattle is deep fluid accumulation, such as occurs with pneumonia.[65][Level of evidence: II]

Common Symptoms at End of Life and Their Treatment

Enlarge

Symptom	Management
Myoclonus	Consider etiology (usually high-dose opioids administered over a prolonged period).
	Hydrate.
	Rotate to alternate opioid.
	Use benzodiazepines; if patient cannot swallow, use midazolam or lorazepam.
Dyspnea	Use opioids (small, frequent doses as needed for opioid-naïve patients [e.g., 2.5 mg morphine PO every hour prn]; opioid-tolerant patients will require dose adjustment and upward titration).
	Use benzodiazepines only if anxiety is present.
	Use glucocorticoids or bronchodilators for bronchospasm.
	Use antibiotics if cause is infectious and this is consistent with goals of care.
	Use oxygen only when hypoxia is present.
	Direct a cool fan toward the face.
	Reposition (elevate head of bed; if patient has nonfunctioning lung, position on side with that lung down).
	Use cognitive-behavioral therapies such as guided imagery.
	Use integrative therapy such as acupuncture.
Fatigue	Use methylphenidate (Ritalin) 2.5 mg twice daily (in a.m. and at noon) to start; increase up to 30 mg/day; anxiety and restlessness may occur.
	Use d-amphetamine (Dexedrine) 2.5 mg/day to start; increase up to 30 mg/day; anxiety and restlessness may occur.
	Use modafinil (Provigil) 50–100 mg/day to start; increase to 100–200 mg/day.
	Suggest energy conservation methods.
	Employ sleep hygiene measures.
	(Refer to the PDQ summary on Fatigue for more information.)

Cough	Consider etiology (infection, bronchospasm, effusions, lymphangitis, cardiac failure) and treat accordingly.
	Use opioids (small, frequent doses to start for opioid-naïve patients; opioid-tolerant patients will require dose adjustment and upward titration).
	Use other antitussives such as guaifenesin or dextromethorphan.
	Use glucocorticoids such as dexamethasone to manage cough due to bronchitis, asthma, radiation pneumonitis, and lymphangitis.
	Use bronchodilators such as albuterol 2–3 inhalations every 4–5 hours for bronchospasm leading to cough.
	Use nonsedating antihistamines with or without decongestants for sinus disease. (Suggest nonsedating agents if fatigue or sedation is a problem.)
	Use diuretics to relieve cough due to cardiac failure.
	(Refer to the PDQ summary on Cardiopulmonary Syndromes for more information.)
Rattle	Use scopolamine transdermal patch, 1.5 mg (start with one or two patches; if ineffective, switch to 50 µg/hour continuous IV or SQ infusion and double the dose every hour, up to 200 µg/hour).
	Use glycopyrrolate, 1–2 mg PO; or 0.1–0.2 mg IV or SQ every 4 hours; or 0.4–1.2 mg/day continuous infusion.
	Use atropine, 0.4 mg SQ every 15 minutes prn.
	Use hyoscyamine, 0.125–0.25 mg PO or SL every 4 hours.
	Change position or elevate head of bed.
	Reduce or discontinue enteral or parenteral fluids.
	Avoid suctioning.
Delirium	Stop unnecessary medications.
	Hydrate.
	Use haloperidol, 1–4 mg PO, IV, or SQ every 1–6 hours prn.
	Use olanzapine, 2.5–20 mg PO at bedtime.
	(Refer to the PDQ summary on Delirium for more information.)
Fever	Use antimicrobials if consistent with goals of care.
	Use antipyretics such as acetaminophen.
	Apply cool cotton cloths.
	Give tepid sponge baths.
Hemorrhage	Use vitamin K or blood products for chronic bleeding if consistent with goals of care.
	Use aminocaproic acid (PO or IV).
	Induce rapid sedation with IV midazolam when catastrophic hemorrhage occurs.

	Use blue or green towels to minimize distress.

PO = by mouth; prn = as needed; IV = intravenous; SQ = subcutaneous; SL = sublingual.

Nonpharmacologic interventions include repositioning the patient by elevating the head of the bed or turning the patient to either side. Reducing or eliminating additional fluids and feedings alleviates additional fluid accumulation in the body. Family members may request suctioning, but this can be traumatic and cause bleeding or stimulate the gag reflex. If truly indicated, suctioning should not be done beyond the oral cavity.

Delirium

Delirium is common during the final days of life.[5,66] There are two general presentations of delirium: hyperactive and hypoactive. (Refer to the PDQ summary on Delirium for a complete review.) The hyperactive form of delirium includes agitation, hallucinations, and restlessness.[67] In hypoactive delirium, the patient is withdrawn and quiet; as a result, this form of delirium may be underdiagnosed.[68][Level of evidence: II][66] Although the etiology of either form of delirium is poorly understood, metabolic changes (e.g., hypercalcemia, hypoglycemia, opioid metabolites), dehydration, and drug interactions are implicated.[68-70][Level of evidence: II] Other potential causes of delirium include cancer within the CNS, a full bladder, fecal impaction, dyspnea, or withdrawal from alcohol or benzodiazepines.

Care of the patient with delirium can include stopping unnecessary medications, reversing metabolic abnormalities (if consistent with the goals of care), treating the symptoms of delirium, providing parenteral hydration,[71] and providing a safe environment. Agents known to cause delirium include corticosteroids, chemotherapeutic agents, biological response modifiers, opioids, antidepressants, benzodiazepines, and anticholinergic agents. In a small, open-label, prospective trial of 20 cancer patients who developed delirium while being treated with morphine, rotation to fentanyl reduced delirium and improved pain control in 18 patients.[70][Level of evidence: II] To limit the potential for drug interactions, medications that are no longer useful or that are inconsistent with the goals of care should be stopped. For example, cholesterol-lowering agents are rarely beneficial at this time of life, but many patients admitted to hospice remain on these medications.

Onset of effect and nonoral modes of delivery should be considered when an agent is being selected to treat delirium at the end of life. Agents that can relieve delirium relatively quickly include haloperidol, 1 mg to 4 mg orally, intravenously, or subcutaneously.[72] The dose is usually repeated every 6 hours but in severe cases can be administered every hour. Other agents that may be effective include olanzapine, 2.5 mg to 20 mg orally at night (available in an orally disintegrating tablet for patients who cannot swallow).[73][Level of evidence: II] Although benzodiazepines (such as lorazepam) or atypical antipsychotics typically exacerbate delirium, they may be useful in delirium related to alcohol withdrawal and for hyperactive delirium that is not controlled by antipsychotics and other supportive measures. Chlorpromazine can be used, but intravenous administration can lead to severe hypotension; therefore, it should be used cautiously.[74] In intractable cases of delirium, palliative sedation may be warranted. Safety measures include protecting patients from accidents or self-injury while they are restless or agitated. The use of restraints is controversial; other strategies include having family members or sitters at the bedside to prevent harm. Reorientation strategies are of little use during the final hours of life. Education and support for families witnessing a loved one's delirium are warranted; one survey of family members found high levels of distress caused by observing delirium.[75][Level of evidence: II]

In dying patients, a poorly understood phenomenon that appears to be distinct from delirium is the experience of auditory and/or visual hallucinations that include loved ones who have already died. Although patients may sometimes find these hallucinations comforting, fear of being labeled confused may prevent patients from sharing their experiences with health care professionals.[76] Family members at the bedside may find these hallucinations disconcerting and will require support and reassurance. Consultation with the patient's or family's minister, rabbi, priest, or imam; the hospital chaplain; or other spiritual advisor is often beneficial.

Fever

Terminally ill patients experience a high incidence of fever and infections.[77,78] A number of retrospective studies have shown that a large number of patients who are receiving hospice or palliative care are treated with antibiotics for suspected or documented infections.[79-81];[82][Level of evidence: II]

The benefits and burdens of the use of antimicrobials in this patient population are topics of much discussion.[79,80,82,83] Three prospective studies have suggested that symptom control may be the main objective in the decision to use antimicrobials to treat clinically suspected or documented infections in patients who are receiving palliative or hospice care.[84-86][Level of evidence: II]

Difficulties in treating symptoms include predicting which patients will obtain symptom relief and which patients will experience only the additional burdens of treatment. Determining the cause of fever (e.g., infection, tumor, or another cause) and deciding which symptoms from suspected infections might respond to various antimicrobial interventions can be difficult clinical judgments, particularly in patients who have multiple active medical problems and for whom the goal of treatment is symptom control.

Hemorrhage

Hemorrhage is an uncommon (6%–10%) yet extremely disturbing symptom that can arise from cancer or its treatment.[33,87,88] Patients at particular risk include those with head and neck cancers with tumor infiltration into the carotid artery.[88] Radiation therapy to this region can result in thinning of the walls of the vessels, increasing the risk of bleeding. Slow leakage of blood from eroded areas can signal risk of hemorrhage; however, early signs are frequently not apparent, and bleeding can occur without warning. Other cancers that can lead to sudden hemorrhage include gastric or esophageal cancers that perforate, leading to a rapidly fatal upper gastrointestinal bleed.[33,87] Leukemias and other hematologic disorders place patients at risk for hemorrhage. Disseminated intravascular coagulopathy, idiopathic thrombocytopenia, or other platelet abnormalities can lead to sudden hemorrhage.

When chronic bleeding occurs, management may include hemostatic dressings or agents, radiation therapy, endoscopy, arterial embolization, or surgery may be warranted. Systemic interventions include the use of vitamin K or blood products. However, the goals of care are comfort oriented when catastrophic hemorrhage occurs at the end of life. Optimally, code status has already been discussed; resuscitation is rarely effective. Supportive care is critical, for both the patient and family members at the bedside. Although survival after hemorrhage is very limited (usually a few minutes), patients may be initially aware of events around them. Fast-acting agents such as midazolam may sedate the patient during this distressing event.[89]

The following steps should be taken when bleeding occurs:

- Cover the area with dark-colored (e.g., blue or green) towels to limit visual exposure to the blood.
- Speak calmly and reassure the patient that he or she is not alone (and, if loved ones are in attendance, let the patient know they are there).
- Clean the area rapidly because blood can produce a foul odor that may be distressing to loved ones.
- Provide support to family members.

Oncology, palliative care, and other units that care for patients at risk for hemorrhage should have supplies (towels, sedatives) and standing orders in place for rapid employment. Support is essential for all members of the health care team, including novice clinicians or nonclinical staff who might be in attendance, such as chaplains or social workers. Team members should be encouraged to verbalize their emotions regarding the experience, and their questions should be answered.

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Ethical Issues

Nutritional Supplementation

Providing nutrition to patients at the end of life is a very complex and individualized decision. Ideally, the options for nutrition support for end-of-life care should be discussed in advance, and information on all nutritional choices and their consequences should be provided to the patient and family. Patients are best able to make decisions if they are well informed about the possible risks and benefits of artificial nutrition. Considerations of financial cost, burden to patient and family of additional hospitalizations and medical procedures, and all potential complications must be weighed against any potential benefit derived from artificial nutrition support. Supplemental nutrition may be beneficial in the treatment of advanced cancer, where quality of life would otherwise suffer and death would be caused by malnutrition rather than the underlying disease, such as in mechanical obstruction or malabsorption resulting in intolerance of oral intake.[1]

The rationale for providing artificial nutrition at the very end of life is less clear. One study has concluded that artificial nutrition—specifically, parenteral nutrition—neither influenced the outcome nor improved the quality of life in terminally ill patients.[2]

The controversial nature of providing artificial nutrition at the end of life has prompted the American Academy of Hospice and Palliative Medicine (AAHPM) to recommend that individual clinical situations be assessed using clinical judgment and skill to determine when artificial nutrition is appropriate. Recognizing that the primary intention of nutrition is to benefit the patient, AAHPM concludes that withholding artificial nutrition near the end of life may be appropriate medical care if the risks outweigh the possible benefit to the patient.[3]

The goal of end-of-life care is to relieve suffering and alleviate distressing symptoms. The patient's needs and desires must be the focus, with their best interests being the guide for decision making, influenced by religious, ethical, and compassionate issues.[4-6]

Resuscitation

Broadly defined, resuscitation includes all interventions that provide cardiovascular, respiratory, and metabolic support necessary to maintain and sustain the life of a dying patient. It is important for patients, families, and proxies to understand that choices may be made specifying what supportive measures, if any, should be given preceding death and at the time of death. People often believe that there is plenty of time to discuss resuscitation and the surrounding issues. However, many dying patients do not make choices in advance or have not communicated their decisions to their families, proxies, and the health care team. If these issues are unresolved at the time of end-of-life events, undesired support and resuscitation may result. Studies suggest that this aggressive care is associated with worse patient quality of life and worse adjustment to bereavement for loved ones.[7,8]

Narrowly defined, a Do Not Resuscitate (DNR) order instructs health care providers that, in the event of cardiopulmonary arrest, cardiopulmonary resuscitation (CPR, including chest compressions and/or ventilations) should not be performed and that natural death be allowed to proceed. DNR orders must be made before cardiac arrest and may be recommended by physicians when CPR is considered medically futile or would be ineffective in returning a patient to life. A DNR order may also be made at the instruction of the patient (or family or proxy) when CPR is not consistent with the goals of care. It is advisable for a patient who has clear thoughts about these issues to initiate conversations with the health care team (or appointed health care agents in the outpatient setting) and to have forms completed as early as possible (i.e., before hospital admission), before the capacity to make such decisions is lost. Although patients with end-stage disease and their families are often uncomfortable bringing up the issues surrounding DNR orders, physicians and nurses can tactfully and respectfully address these issues appropriately and in a timely fashion. Lack of standardization in many institutions may contribute to ineffective and unclear discussions around DNR orders.[9] (Refer to the PDQ summary on Transitional Care Planning for more information.)

Ventilator Withdrawal

Fewer patients with advanced cancer will undergo resuscitation and ventilatory support when discussions regarding goals of care and advance directives begin early in the course of the disease. However, when advance directives are not available or when the directives are not adequately communicated, intubation may occur despite low likelihood of survival.

When ventilatory support appears to be medically futile or is no longer consistent with the patient's (or family's or proxy's) goals of care, ventilator withdrawal to allow death may take place. Extensive discussions must first take place with patients (if they are able) and family members to help them understand the rationale for and process of withdrawal. When no advance directive is available and a patient can no longer communicate, it is helpful to reinterpret in a more realistic light, or reframe for family members, that they are not making a decision to "pull the plug" for their loved one. Rather, they are helping the health care team interpret their loved one's wishes or discontinuing a treatment that is no longer considered effective. Such reframing is essential to help family members and significant others understand that the underlying disease process, and not ventilator withdrawal, is the cause of the patient's death.[10]

Two methods of withdrawal have been described: immediate extubation and terminal weaning.[11] Immediate extubation includes providing parenteral opioids for analgesia and sedating agents such as midazolam, suctioning to remove excess secretions, setting the ventilator to "no assist" and turning off all alarms, and deflating the cuff and removing the endotracheal tube. Gentle suctioning of the oral cavity may be necessary, but aggressive and deep suctioning should be avoided. In some cases, patients may appear to be in significant distress. Analgesics and sedatives should be provided even if the patient is comatose. Family members and others who are present should be warned that some movements may occur after extubation, even in patients who are brain dead. Such movements are probably caused by hypoxia and may include gasping, moving extremities, or sitting up in bed.[12] Immediate extubation is generally chosen when a patient is brain dead, when a patient is comatose and unlikely to experience any suffering, or when a patient prefers a more rapid procedure.

Terminal withdrawal entails a more gradual process. Ventilator rate, oxygen levels, and positive end-expiratory pressure are decreased gradually over a period of 30 minutes to a few hours. A patient who survives may be placed on a T-piece; this may be left in place, or extubation may proceed. There is some evidence that the gradual process in a patient who may experience distress allows clinicians to assess pain and dyspnea and to modify the sedative and analgesic regimen accordingly.[13] In a study of 31 patients undergoing terminal weaning, most patients remained comfortable, as assessed by a variety of physiologic measures, when low doses of opioids and benzodiazepines were administered. The average time to death in this study was 24 hours, although two patients survived to be discharged to hospice.[14]

Paralytic agents have no analgesic or sedative effects, and they can mask patient discomfort. These neuromuscular blockers should be discontinued before extubation. Guidelines suggest that these agents should never be introduced when the ventilator is being withdrawn; in general, when patients have been receiving paralytic agents, these agents should be withdrawn before extubation. The advantage of withdrawal of the neuromuscular blocker is the resultant ability of the health care provider to better assess the patient's comfort level and to allow possible interaction between the patient and loved ones. One notable exception to withdrawal of the paralytic agent is when death is expected to be rapid after the removal of the ventilator and when waiting for the drug to reverse might place an unreasonable burden on the patient and family.[15]

Regardless of the technique employed, the patient and setting must be prepared. Monitors and alarms should be turned off, and life-prolonging interventions such as antibiotics and transfusions should be discontinued. Family members should be given sufficient time to make preparations, including making arrangements for the presence of all loved ones who wish to be in attendance. They should be given information on what to expect during the process; some may elect to remain out of the room during extubation. Chaplains or social workers may be called to provide support to the family.

Palliative Sedation

Some families may need continuous information and professional guidance when palliative sedation is used, and this need increases with the duration of the sedation. Individuals or groups outside the family and health care team may have strong opinions about palliative sedation and may offer unsolicited guidance that conflicts with what the patient desires. Concerns identified in a study conducted in The Netherlands relate to the following:[16]

- Aim of continuous sedation.
- Patient well-being.
- Family well-being.

The use of palliative sedation for psychosocial and existential symptoms can be particularly controversial. The clinician may face many ethical and clinical questions—questions that are more easily resolved in the case of palliative sedation for pain and physical symptoms. Useful resources include the framework for the use of sedation in palliative care recommended by the European Association for Palliative Care [17] and the position statement developed by the American Academy of Hospice and

Palliative Medicine.[18]

For example, the ethical basis for the use of terminal sedation (double effect) is less clearly applicable in the case of psychiatric symptoms. Under the principle of double effect, the intended effect (relieving psychological suffering) would be considered allowable as long as any risks or negative effects (i.e., shortened survival) are unintended by the health care professional. The difficulty arises because the principle only discusses the professional's intention, when it is the patient's intention that can be unclear and potentially problematic. Is the depressed patient who no longer wants to suffer depressive symptoms asking only for that relief, or does the patient also intend to ask the professional to shorten his or her life? A clinician who feels uncomfortable in such situations may wish to seek guidance from his or her ethics committee.

Other difficult questions can arise from the potentially negative value that is culturally assigned to detaching oneself, or "zoning out," as a lower form of coping. Should the anxious patient who no longer wants to face the anxiety associated with the end of life and who wants to be sedated be encouraged to work through such issues? Or is it allowable for these patients to have sedation for dealing with their anxiety? How many alternatives should be tried before anxiety is considered unacceptable? When dealing with such requests, professionals should consider their own cultural and religious biases and the cultural and/or religious backgrounds of patients and their families.

Few studies detail the use of terminal sedation for psychosocial symptoms. Four palliative care programs in Israel, South Africa, and Spain participated in one survey.[19] One unique study has described the Japanese experience around the issues of palliative sedation therapy.[20,21] A retrospective study at the MD Anderson Cancer Center in Houston included 1,207 patients admitted to the palliative care unit. Palliative sedation was used in 15% of admissions. The most common indications were delirium (82%) and dyspnea (6%). Sedation in these circumstances is often on a temporary basis and was reversible in 23% of this group of patients.[22]

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Care During the Final Hours

Although the signs of approaching death may appear obvious to health care professionals, many family members have never observed the death of a loved one as death has become more institutionalized. As a result, most people are not familiar with the signs of impending death. Educating family members about these signs is critical.

In the final days to hours of life, patients often experience a decreased desire to eat or drink, as evidenced by clenched teeth or turning from offered food and fluids. This behavior may be difficult for family members to accept because of the meaning of food in our society and the inference that the patient is “starving.” Family members should be advised that forcing food or fluids can lead to aspiration. Reframing will include teaching the family to provide ice chips or a moistened oral applicator to keep a patient’s mouth and lips moist. Massage is another strategy through which family members can provide care and demonstrate love.

Patients may withdraw and spend more time sleeping. When patients respond slowly to questions, are somewhat confused, and have a decreased interest in their environment, family should be encouraged to touch and speak to them. Professionals can model these behaviors. A patient's extremities may become mottled, cold, or cyanotic. The heart rate may increase or decrease and may become irregular; blood pressure usually drops as death approaches. Urine output may decrease dramatically or cease. Respiration often takes on an abnormal pattern called Cheyne-Stokes respiration, which ranges from very shallow breaths to alternating periods of apnea and deep, rapid breathing. These changes should be explained to family members at the bedside or when they are preparing to care for a loved one at home

It is important for health care professionals to explore with families any fears associated with the time of death and any cultural or religious rituals that may be important to them. Such rituals might include placement of the body (e.g., the head of the bed facing Mecca for an Islamic patient) or having only same-sex caregivers or family members wash the body (as practiced in many orthodox religions). When death occurs, expressions of grief by those at the bedside vary greatly, dictated in part by culture and in part by their preparation for the death. Chaplains should be consulted as early as possible if the family accepts this assistance. Health care providers can offer to assist families in contacting loved ones and making other arrangements, including contacting a funeral home. (Refer to the PDQ summary on Spirituality in Cancer Care for more information.)

Grief and Bereavement

Family members are likely to experience loss at the death of their loved one. If left unattended, loss, grief, and bereavement can become complicated, leading to prolonged and significant distress for either family members or clinicians. Furthermore, clinicians are at risk for significant grief from the cumulative effects of many losses through the deaths of their patients. Burnout has also been associated with unresolved grief in health care professionals. (Refer to the PDQ summary on Grief, Bereavement, and Coping With Loss for more information.)

Changes to This Summary (12/10/2013)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Editorial changes were made to this summary.

This summary is written and maintained by the PDQ Supportive and Palliative Care Editorial Board, which is editorially independent of NCI. The summary reflects an independent review of the literature and does not represent a policy statement of NCI or NIH. More information about summary policies and the role of the PDQ Editorial Boards in maintaining the PDQ summaries can be found on the About This PDQ Summary and PDQ NCI's Comprehensive Cancer Database pages.

Purpose of This Summary

This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about patient care during the last days to last hours of life. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

Reviewers and Updates

This summary is reviewed regularly and updated as necessary by the PDQ Supportive and Palliative Care Editorial Board, which is editorially independent of the National Cancer Institute (NCI). The summary reflects an independent review of the literature and does not represent a policy statement of NCI or the National Institutes of Health (NIH).

Board members review recently published articles each month to determine whether an article should:

- be discussed at a meeting,
- be cited with text, or
- replace or update an existing article that is already cited.

Changes to the summaries are made through a consensus process in which Board members evaluate the strength of the evidence in the published articles and determine how the article should be included in the summary.

The lead reviewers for Last Days of Life are:

- Larry D. Cripe, MD (Indiana University School of Medicine)
- Myra Glajchen, D.S.W. (Beth Israel Medical Center)
- David Hui, MD, MSC (M.D. Anderson Cancer Center)

Any comments or questions about the summary content should be submitted to Cancer.gov through the Web site's Contact Form. Do not contact the individual Board Members with questions or comments about the summaries. Board members will not respond to individual inquiries.

Levels of Evidence

Some of the reference citations in this summary are accompanied by a level-of-evidence designation. These designations are intended to help readers assess the strength of the evidence supporting the use of specific interventions or approaches. The PDQ Supportive and Palliative Care Editorial Board uses a formal evidence ranking system in developing its level-of-evidence designations.

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“This course was developed from the public domain document: PDQ® Last Days of Life. Bethesda, MD: National Cancer Institute. Date last modified 12/10/2013.”