Advance Directives

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Definitions

Advance directives allow for the expression of end-of-life care medical wishes in the event that patients are unable to communicate these preferences as a result of incapacity. Advance directives, a form of extended autonomy, can take on three forms: oral directives, a written instructional directive, and a durable power of attorney for health care (also referred to as a healthcare proxy in some states) (Lo, 2004). *Living wills* are specific written instructions about the kinds of health care that should be provided or forgone in particular healthcare situations. A *durable power of attorney for health care* or *healthcare proxy* is a document that appoints an agent the person trusts to make decisions in the event of the appointing person's subsequent decisional incapacity. In some states, oral advance directives do not meet the criteria of "clear and convincing evidence" needed to legally document patient treatment preferences. Advance directives are part of the ongoing advance care planning process whereby patients, family members, decision-making surrogates, and healthcare professionals collaboratively clarify patient goals, values, and preferences about future healthcare treatments.

Specific Issues Related to Palliative Care

Conversations related to advance care planning can be difficult for a myriad of complicated reasons. Medical culture has been characterized as "valu[ing] technology over discussion" (Lynn et al., 2000, p. 218), and some medical professionals may be concerned that frank and open discussion about end-of-life care issues can diminish patient and family hope (Steinhauser et al., 2001). Waiting for the clinician to take the lead, patients may be reluctant to bring up advance care planning issues themselves, although researchers indicate that most patients want to be fully informed about their condition and prognosis (Jenkins, Fallowfield, & Saul, 2001; Steinhauser et al.).

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Without timely, meaningful, and ongoing advance care planning, families relate narratives of their loved ones' dying being needlessly prolonged by undesired treatment or being hastened when treatment is withheld or withdrawn. Patients realistically fear that they will lose control of decision making as their voices can be stifled or ignored when they want aggressive therapy to be withheld or discontinued or when they demand aggressive life-sustaining therapy that a clinician judges to be medically futile. Factors contributing to physician reluctance to withhold or withdraw life-sustaining therapy include lack of familiarity with ethical and legal guidelines for withholding and withdrawing medical treatment, misunderstandings about the legal consequences of withholding or withdrawing treatment, failure to embrace preparation for a comfortable and dignified death as a legitimate aim of medicine, and a general lack of ease in initiating discussions about the plan of care as a patient's condition declines. Advances in knowledge and technology have proliferated treatment options and complicated healthcare decision making for many conditions. Patients and families need ongoing and easily understood education about treatment options so that they can make informed decisions about the direction of treatment.

In the context of modern healthcare systems, numerous obstacles to engaging in advance care planning exist, but the benefits of purposefully including these discussions over the course of treatment outweigh the costs. As part of this collaborative process, advance directive documents can be drafted and the medical team educated about the patient's end-of-life care wishes as the illness trajectory progresses, not just during the final throes of the illness. The completion of advance directives is not a one-time event. As patient preferences can and do change, particularly when a substantial change occurs in the patient's condition and/or quality of life, the documents should be revisited and revised as needed. Clinicians should educate themselves about patient and family cultural values and backgrounds as they relate to and influence end-of-life care issues and the actual completion of advance directives. For example, some cultural groups may prefer not to have direct discussions about diagnosis and prognosis, particularly if the outlook is grim (Van Winkle, 2000; Yeo & Hikoyeda, 2000).

Support for and Barriers to Advance Care Planning

A. Support for advance care planning (Emanuel, von Gunten, & Ferris, 1999): Common law, federal and state legislation, and official policies of medical organizations support advance care planning.
   1. U.S. Supreme Court, 1990 (in the case of Nancy Cruzan): The court upheld the patient's right to self-determination, establishing that the right applies even to patients who are no longer able to direct their own health care and that decisions for incompetent patients should be based on their previously stated wishes.
   2. Federal law, 1990: The Patient Self-Determination Act (PSDA) requires that patients be informed of their rights to accept or refuse medical treatment and to specify, in advance, the care they would like to receive should they become incapacitated.

3. State law: The patient's right to specify wishes in advance has been codified into statute in all 50 states, but state policies vary widely. Statutory documents recognized by law include the living will and the durable power of attorney for health care (i.e., healthcare proxy). Some states also have policy that gives family members, stated in an explicit hierarchy, the right to make decisions for a decisionally incapacitated patient in the absence of written documents.
4. Statutory documents: These documents are specifically described and defined in state statutes to help to protect clinicians who honor a patient's wishes. When such documents are used, rights, obligations, and protections are clearly defined.
5. Nonstatutory or advisory documents: These are legal and based on common law rights. They are intended to accurately reflect a patient's wishes. In some states or settings, an advisory document is enough; in others, a statutory form should be used, as well. In some states, a legal guardian may be necessary if no statutory power of attorney exists for health care.
6. Professional policy
   a) In 1997, the American Medical Association's Council on Ethical and Judicial Affairs identified advance care planning as an essential component of standard medical practice. It called for physicians to conduct advance planning discussions on a routine basis, using advisory documents as an adjunct to statutory documents, such as the living will and the durable power of attorney for health care. The American College of Physicians' (2005) *Ethics Manual* also supports advance care planning.
   b) The American Nurses Association (ANA) has a position statement on nursing and the PSDA. The ANA (1991) position is that "nurses should play a primary role in implementation of the PSDA. It is the responsibility of nurses to facilitate informed decision making for patients making choices about end-of-life care. The clinician's role in education, research, patient care, and advocacy is critical to implementation of the PSDA within all healthcare settings."

B. Explanations for the failure of many to execute advance directives
   1. Drafting an advance directive means admitting one's mortality; this is an uncomfortable subject for many in our death-denying culture.
   2. Healthcare professionals may wait for patients to initiate conversation about advance directives, and patients also may wait for healthcare professionals to do the same.
   3. Advance care planning takes time. Given clinical time constraints and the fragmented nature of the modern healthcare system, healthcare professionals may see themselves as "too busy" to have these conversations, and advance care planning does not have an *International Classification of Diseases* code.
   4. Some people may fear that the mere existence of an advance directive will prejudice healthcare professionals to withhold desired care.

Strategies to Promote Use of Advance Directives in Palliative Care

A. Familiarize yourself with state and institutional policies that address the completion and implementation of advance directives.

B. Educate the public and healthcare professionals about advance directives.

C. Incorporate advance care planning discussions into everyday patient care, including family members and decision-making surrogates whenever possible. Address not only issues related to specific medical treatments but also patient goals and values, which can inform the medical care plan. See Figure 1-1 for suggested questions to promote advance care planning discussions.

D. Make advance directives a part of the medical record, and ensure that all parties (i.e., the patient, the decision-making surrogate, family members) understand the implications for treatment and care (American Hospital Association, 1991).

E. Presume nothing about an advance directive until you have read it carefully. For patients with completed advance directives, review and discuss the contents with the patient and, if applicable, the designated surrogate and/or family members.

F. Resolve implementation problems, including
   1. Conflicts about when an advance directive becomes operative
   2. Conflicts when an attending clinician elects to ignore advance directives
   3. Conflicts when designated surrogates ignore patient preferences documented in an advance directive
   4. Conflicts about how to interpret the content of the directive.

Patient Outcomes

A. A documented record exists of the patient's preferences for end-of-life care and identification and contact information of the person the patient trusts to make his or her decisions should the patient lack decisional capacity.

B. Advance care planning discussions can promote shared decision making and a stronger sense of patient control over the dying process.

C. Clearly developed advance directives and inclusive advance care planning discussions can decrease conflict over the directions of the patient's future care.

Evaluating the Evidence

A. Conflicting evidence exists about the number of adults who have completed advance directives. Estimates range from less than 25% (Emanuel, Barry,

Figure 1-1. Suggested Questions for Advance Care Planning Discussions

Patient Understanding of Illness
- What do you understand about the current state of your illness? (Lo et al., 1999)
- What do you know about your treatment options?

Patient Preferences Regarding Information Delivery
- How much do you want to know about your illness?
- Who would you like to be present during such discussions?

Considerations in Choosing Decision-Making Surrogates
- Who would you want to make decisions for you if something happened and you were unable to make decisions about your care?
- Have you spoken with this person about being your decision maker? Have you discussed your wishes with him or her?
- Have you informed other important people in your life about your choice of decision maker?
- How well do you think this person can deal with any disagreements others may have about your wishes?
- If you anticipate any disagreements, what do you believe the best way is to address this?
- To what extent do you want your family and loved ones to have input in decisions that are made about your health care?
- How important is it that your family as a whole agrees with the decisions that are made on your behalf?

Patient Goals
- What is important for you to accomplish at this point in your life?
- As you think about the future, what is most important to you (what matters the most to you)? (Lo et al., 1999)
- What are your hopes and fears for the future?
- If you were to die sooner rather than later, what would be left undone? (Quill, 2000)
- What type of legacy do you want to leave your family and loved ones? (Lo et al., 1999)

Patient Values
- What makes life worth living? (Quill, 2000)
- What would have to happen for your life to be not worth living?
- What nourishes your spirit?
- How do you feel about quality versus quantity of life?
- What are your thoughts about pain control? Would you want your pain controlled even if it meant that you might not be as alert?

Personal Experiences With Illness, Death, and Dying
- Has anyone close to you died of an illness? What happened? What was it like for you?
- What other significant losses have you experienced?
- What would you consider a “good death”?

Spirituality and Existential Issues
- What thoughts have you had about why you got this illness at this time? (Lo et al., 1999)
- Is faith (religion, spirituality) important to you in this illness, and has it been important to you at other times in your life? (Lo et al., 1999)
- Would you like to explore religious or spiritual matters with someone? Do you have someone to talk to about these things? (Lo et al., 1999)
- Do you have any spiritual or religious beliefs that should be taken into consideration by your healthcare providers?

Note. From “Communication Issues and Advance Care Planning,” by C.D. Moore, 2005, *Seminars in Oncology Nursing, 21,* p. 18. Copyright 2005 by Elsevier. Adapted with permission.

Stoeckle, Ettelson, & Emanuel, 1991; Hanson & Rodgman, 1996; Lo, 2004) to 71% (Teno, Gruneir, Schwartz, Nanda, & Wetle, 2007).

B. Evidence from the seminal SUPPORT study (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment) indicate that advance directives have a limited role in guiding patient care (SUPPORT Principal Investigators, 1995).

C. Consistent with other more recent findings, one national study found that written advance directives were associated with "less use of life-sustaining treatment, greater use of hospice, and less likelihood of terminal hospitalization" (Teno et al., 2007, p. 192).

Resources

Advance directives and supporting information may be obtained from the following sources.

A. American Academy of Family Physicians: http://familydoctor.org

B. National Hospice and Palliative Care Organization: www.caringinfo.org

C. Aging With Dignity and Five Wishes: www.agingwithdignity.org

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Anemia

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Definition

Anemia is a decrease in the number of circulating red blood cells resulting from some underlying disorder. It may be seen as an acute or chronic condition.

Pathophysiology and Etiology

Patients with cancer or chronic illness often develop anemia. The cause is generally multifactorial and may include chemotherapy treatment, radiation therapy, nutritional deficits, blood loss, or damaged bone marrow (Dunn, Carter, & Carter, 2003; Griffin, 2001). Although no data exist to support a direct correlation between fatigue scores and hemoglobin level, the resulting overall effect of anemia can severely affect the patient's quality of life (Munch, Zhang, Willey, Palmer, & Bruera, 2005). Appropriate treatment of anemia as part of palliative care should be based on the uniqueness of each patient's situation.

Manifestations

- Fatigue
- Weakness
- Shortness of breath: pulmonary edema and congestive heart failure possible
- Malaise
- Dizziness/orthostasis
- Headache
- Cold intolerance
- Tachycardia/tachypnea
- Palpitations
- Pallor
- Depression

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• Cognitive changes
(Davis, 2004; Loney & Chernecky, 2000)

Management

The goal of treatment is to correct anemia. An increase in hemoglobin level will promote improved quality of life through enhanced physical, emotional, and cognitive function (Dunn et al., 2003). Extent of testing and treatment is based upon survival expectancy and disease status (Davis, 2004).

A. Death is not imminent.
   1. **Level I—high level of evidence**
      a) Oral iron supplements ($)—Ferrous sulfate, 325 mg po tid. Beneficial if the individual is iron deficient. Iron deficiency is typically identified through a low serum ferritin level. However, a serum ferritin level can be raised by conditions such as inflammation, malignancy, and liver disease, which may mask iron deficiency. Although readily available and inexpensive to administer, iron supplements can have a number of unpleasant side effects, such as gastrointestinal upset and constipation. Should a patient have difficulty with oral iron, administration of IV iron is an option (Davis, 2004).
      b) Blood transfusion ($$)—Administration early in care often can palliate symptoms but also may provide no benefit. Patient evaluation post-transfusion should occur to evaluate for a decrease in symptoms. In situations where bone marrow is compromised, blood transfusions serve a very temporary benefit, if any. Careful justification of transfusion should be made before initiating this treatment (Monti, Castellani, Berlusconi, & Cunietti, 1996).
      c) Erythropoietin administration ($$$)—Use of erythropoietin agents is debatable in palliative care settings. Their use may decrease cancer-related fatigue but may not benefit all individuals. Weekly injections include side effects such as fever, chills, and bone pain. The benefit generally is not seen for several weeks following initiation of treatment and requires that patients have adequate ferritin levels for it to be effective (Micromedex, 2001). Concurrent administration of iron is recommended. Hematocrit levels should be checked regularly, twice a week for two to six weeks following any dose adjustment. Dose reduction should be made if hemoglobin increase is more than 1 g/dl in a two-week period. Because of the risk of severe and life-threatening cardiovascular events, target hemoglobin level should be within a range of 10–12 g/dl (U.S. Food and Drug Administration Alert, 2006). Anemia that fails to respond to erythropoietin agents is indicative of a poor prognosis (Davis, 2004). The cost of this agent may not be covered by the patient's insurance. Anticipated benefits should be evaluated carefully prior to use in this setting. When a target

hemoglobin of ≥ 12 g/dl is maintained, clinical trials demonstrated that overall survival and/or time to tumor progression may be decreased (U.S. Food and Drug Administration Alert, 2007).

2. **Level II—moderate level of evidence**
   Folic acid ($)—Folic acid 1,000 mcg po daily. A portion of patients with anemia in the palliative care setting have folic acid deficiency (Dunn et al., 2003). The body stores of folic acid can be depleted within four to five months. Although little research supporting this intervention exists, the prevalence was identified through a prospective audit involving 105 patients, and administration of folic acid should be considered for patients with a documented deficiency (Dunn et al.).

B. Death is imminent.
   Level III—low level of evidence
   1. Attempts to treat manifestations of the anemia and not the anemia itself should be instituted.
   2. Interventions include oxygen (use a nasal cannula, as masks often make people feel as though they are suffocating), rest, warm clothing, and blankets. Avoid sudden movements.

Patient Outcomes

A. Anemia is corrected when feasible.

B. Anemia-associated symptoms are relieved.

C. Quality of life is improved.

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Anorexia, Cachexia, and Nutrition Support

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Definitions

Anorexia is a lack of appetite resulting in an involuntary decline of food intake. *Cachexia,* of which anorexia is typically a feature, encompasses the disordered metabolism characteristic of certain diseases or conditions. Common causes of cachexia include cancer, sepsis, chronic infections, HIV/AIDS, liver disease, and other conditions resulting in systemic inflammation. Cachexia and subsequent anorexia can lead to weight loss, loss of lean body mass and functional status, and decline in quality of life for patients with advanced illness. Cachexia is reported as the main cause of death in 20% of patients with advanced cancer (Del Fabbro, Dalal, & Bruera, 2006).

Pathophysiology and Etiology

Patients with advanced cancer often develop cachexia and subsequent anorexia. The cause of cachexia is not completely understood; recent data suggest that derangements in the lysosomal system, the ubiquitin-proteasome pathway, and cytosolic proteases may contribute to its development (Melstrom, Melstrom, Ding, & Adrian, 2007). Of these three mechanisms, the ubiquitin-proteasome pathway may account for the majority of skeletal muscle degradation in cancer cachexia through the action of cytokines, including tumor necrosis factor-alpha, interleukin-1 beta, interleukin-6, interferon-gamma, and proteolysis-inducing factor (Bhogal, Lorite, & Tisdale, 2006; Kuroda et al., 2007; Melstrom et al.; Skipworth, Stewart, Dejong, Preston, & Fearon, 2007). Additionally, new research points to alterations in the dystrophin glycoprotein complex as an important early event in the development of cachexia (Acharyya & Guttridge, 2007).

Regardless of the cause, it is clear that cachexia contributes to anorexia, hypermetabolism, and alterations in normal metabolic pathways. In simple starvation, the body readily adapts to calorie deficit by shifting to fatty acids as a major source of energy, thereby preserving lean body mass. In the cachectic state, the body fails to make this adaptation, which can lead to disproportionate wasting of lean body mass and loss of strength and functional status. This results in a marked decline in

quality of life for individuals with terminal illness (Fornari & McCallum, 2006; Hutton et al., 2006; MacDonald, 2007; Marin Caro, Laviano, & Pichard, 2007; Melstrom et al., 2007). An understanding of this process is important because even in patients who are overweight or obese, cachexia-related weight loss will decrease lean body mass and quality of life and should be addressed in order to provide optimal palliative care.

Manifestations

- Anorexia
- Weight loss
- Lean body mass loss
- Weakness
- Early satiety
- Malaise
- Anemia
- Dehydration
- Electrolyte imbalances
- Taste alterations
- Xerostomia
- Nausea
- Fatigue
- Lethargy
- Micronutrient deficiency
- Thyroid dysfunction

Management

A. Death is not imminent.
   1. **Level I—high level of evidence**
      a) Megestrol acetate ($$)—Megestrol acetate is a synthetic progestational agent with a long history of use for treating anorexia and weight loss associated with cancer cachexia. Several clinical trials have been conducted on the use of megestrol acetate to manage anorexia and weight loss in a variety of populations, but most predominantly in patients with cancer cachexia. Two comprehensive reviews, a Cochrane Database review, and a meta-analysis concluded that this medication is effective and beneficial for managing anorexia associated with cachexia in advanced cancer cases (Berenstein & Ortiz, 2005; Mateen & Jatoi, 2006; Melstrom et al., 2007; Pascual et al., 2004). Typical dosing for megestrol acetate is 800 mg (20 ml oral suspension) po once daily, taken in the morning (Von Roenn, 2006).
      b) Referral to a registered dietitian ($)—Referral to a registered dietitian can improve nutritional status and outcomes for patients who are treated palliatively or with curative intent. Several controlled trials demonstrated

that for better symptom management and improved outcomes in oncology populations, dietitian-delivered nutrition intervention was superior to usual nutrition care by other healthcare professionals. Individuals randomized to receive intensive nutrition intervention, dietitian-guided nutritional management, or the American Dietetic Association Medical Nutrition Therapy protocol lost significantly less weight; had significantly smaller deteriorations in global quality of life, physical functioning, and nutrition status; and were significantly more satisfied with the quality of overall cancer and nutrition care as compared to patients randomized to receive usual (non-dietitian-directed) nutrition care (Isenring, Bauer, & Capra, 2007; Isenring, Capra, & Bauer, 2004a, 2004b; Odelli et al., 2005; Ravasco, Monteiro-Grillo, Marques Vidal, & Camilo, 2005). In curative oncology care, nutrition intervention contributes to reduced postoperative infection rates, better cancer-related symptom control, decreased length of hospital stays, and improved treatment tolerance. In palliative care, nutrition intervention focuses on controlling symptoms and improving quality of life (Marin Caro, Laviano, & Pichard, 2007).

2. **Level II—moderate level of evidence**
   a) Insulin ($$)—One controlled clinical trial in a palliative care setting demonstrated that insulin therapy can significantly increase dietary intake, decrease serum free fatty acids, improve metabolic efficiency during exertion, and improve quality of life without apparent stimulation of tumor growth. Data indicate an effective dose of 0.11 +/– 0.05 units/kg/day with blood glucose monitoring as required to further guide dosing (Lundholm et al., 2007).
   b) Oxandrolone ($$)—Two small controlled trials of oxandrolone, a synthetic oral anabolic agent, demonstrated that this medication increases weight and lean body mass, as well as quality of life and performance status in patients with cancer-related weight loss (Boughton, 2003; Von Roenn, Tchekmedyian, Sheng, & Ottery, 2002). Oxandrolone is contraindicated for use in patients with breast and prostate cancer who have hypercalcemia, or in any individual with severe hepatic dysfunction or nephrosis. It should be used with caution in conjunction with warfarin and in patients with existing cardiac, renal, or hepatic disease (Von Roenn, 2006). Typical dosing for oxandrolone is 10 mg po bid.
   c) Dronabinol ($$)—Dronabinol is a synthetic version of delta-9-THC (delta-9-tetrahydrocannabinol), a naturally occurring compound found in marijuana that is responsible for its orexigenic effects. Dronabinol is administered po and is approved for chemotherapy-induced nausea and vomiting in patients with cancer who have failed to respond adequately to conventional treatments and for treating patients with AIDS-related anorexia and weight loss (Solvay Pharmaceuticals, 2007). Data demonstrate that dronabinol is well tolerated (Cannabis-In-Cachexia-Study-Group et al., 2006) and possibly effective for treating anorexia associated with cancer- and AIDS-associated cachexia (Von Roenn, 2006; Walsh,

Nelson, & Mahmoud, 2003). Dronabinol should be used with caution in combination with other sedative and psychoactive medications. Typical dosing for dronabinol is 2.5 mg po two to three times per day. Initiating dronabinol at the lowest dose range and gradually increasing dosage will help to manage medication side effects and provide the best therapeutic outcomes (Von Roenn, 2006).

d) Metoclopramide ($)—Use of metoclopramide, a prokinetic agent, may provide significant relief, lessen nausea and vomiting, lessen bloating, and improve appetite (Bruera et al., 2000; Wilson et al., 2002). One possible side effect of metoclopramide is diarrhea caused by hypermotility. A dose reduction or treatment with diphenhydramine will resolve this issue (Von Roenn, 2006). A suggested dosing schedule for metoclopramide is 10 mg four times per day (Von Roenn).

e) Corticosteroids ($)—Decreased nausea, increased sense of well-being, and increased appetite have been documented, although no persistent increase in weight has been seen (Del Fabbro et al., 2006). The beneficial effects appear to be time limited and must be balanced against long-term side effects of administration, including Cushing syndrome, proximal myopathy, immunosuppression, and exacerbation of delirium.

3. **Level III—low level of evidence**

a) Eicosapentaenoic acid (EPA), fish oil—Several phase I and phase II studies have demonstrated that EPA-enriched dietary supplements (Prosure®, Resource Support®) can ameliorate symptoms of cachexia, including weight loss and loss of lean body mass; other clinical trials have provided mixed results (Barber & Fearon, 2001; Barber, McMillan, Preston, Ross, & Fearon, 2000; Dewey, Baughan, Dean, Higgins, & Johnson, 2007; Fearon et al., 2003; Moses, Slater, Preston, Barber, & Fearon, 2004).

b) General measures (patient tips)—Treat and manage symptoms affecting nutritional intake and desire to eat, including constipation; bloating; diarrhea; feelings of fullness, early satiety, and poor appetite; altered sense of taste or smell; dry mouth or thick saliva; sore mouth or throat; nausea or vomiting; and pain.

(1) Constipation (See Constipation.)

(2) Bloating

(a) Limit beverages and foods that cause gas, such as carbonated drinks, broccoli, cabbage, cauliflower, cucumbers, peppers, beans, peas, onions, and garlic.

(b) Lessen the amount of air swallowed by encouraging the patient to limit talking while eating.

(c) Encourage the patient to avoid using straws to drink.

(d) Encourage the patient to avoid chewing gum.

(3) Diarrhea (See Diarrhea.)

(4) Feelings of fullness, early satiety, and poor appetite

(a) Offer the patient several smaller meals and snacks each day instead of three larger meals.
(b) Make eating more enjoyable by setting an attractive table, playing favorite music, or watching television.
(c) Keep snacks handy for the patient to eat immediately (hunger may only last a few minutes), such as granola bars, nuts, pudding, chips, crackers, pretzels, trail mix, canned fruit, fresh fruit, and single-serving sizes of tuna or chicken.
(d) Offer favorite foods any time of the day (e.g., if breakfast foods are appealing to the patient, offer them for dinner).
(e) Encourage the patient to eat every few hours—do not wait for the patient to express feelings of hunger.
(f) Treat food like medicine—set times to eat, such as every one to two hours, and be sure the patient has at least a couple of bites of some food at each "medication" time. Quantity and type of food are less important; frequency of eating is more important.
(g) Offer high-calorie, high-protein drinks or fortified juice-based supplements.
(h) Offer fluids between meals rather than with meals (i.e., separate liquids from solids).
(i) Provide favorite foods and encourage the patient to be in control of food choices.
(j) Make dining area as appealing and pleasant as possible by removing bed pans, medication bottles, and the like.

(5) Altered sense of taste/smell
(a) Encourage the patient to be fastidious with mouth care.
(b) Avoid food smells.
(c) Avoid meal preparation by the patient.
(d) Try foods that have minimal odors and short cooking time, such as scrambled eggs, French toast, pancakes, oatmeal, and Cream of Wheat® (Nabisco).
(e) Season foods with tart flavors, such as lemon, citrus, and vinegar (avoid if sore mouth/throat is present).
(f) Flavor foods with basil, oregano, rosemary, tarragon, mustard, ketchup, or mint.
(g) Marinate and cook meats in sweet fruit juices, dressings, or wine, such as sweet and sour pork, chicken with honey glaze, or beef with burgundy wine or Italian dressing.
(h) Instruct the patient to rinse the mouth with tea, ginger ale, salted water, or baking soda and water to clear taste buds before eating.
(i) Offer the patient lemon drops, mints, or gum (avoid if sore mouth/throat is present; avoid sugarless gum and candy if diarrhea is present).

(6) Sore mouth and throat

(a) Encourage the patient to be fastidious with mouth care.
(b) Offer the patient bland foods, such as creamed soups, cooked cereals, macaroni and cheese, yogurt, pudding, mashed potatoes, eggs, custards, casseroles, cheesecake, and milk shakes.
(c) Instruct the patient to drink through a straw to bypass mouth sores.
(d) Offer high-protein, high-calorie foods to speed healing.
(e) Blend or moisten foods with olive oil, gravy, butter, cream, or sauces.
(f) Soften foods such as bread by soaking them in milk.
(g) Try nonacidic juices such as apple juice; peach, pear, or apricot nectars; and grape juice (do not use grape juice if diarrhea is present).
(h) Avoid offering the patient tart, acidic, or salty beverages and foods, such as citrus, pickled items, and tomato-based foods.
(i) Encourage the patient to avoid alcohol, caffeine, and tobacco.
(j) Avoid mouth care products that contain alcohol or other drying, irritating ingredients; try specialty mouth care products.

(7) Nausea and vomiting (See Nausea and Vomiting.)
(8) Dry mouth or thick saliva (See Xerostomia.)
(9) Pain (See Pain.)

4. **Level IV—inconclusive level of evidence**

A number of randomized trials have been reported in the literature both supporting and refuting the use of artificial nutrition in palliative care (Hoda, Jatoi, Burnes, Loprinzi, & Kelly, 2005; Shang, Weiss, Post, & Kachler, 2006; Strasser & Bruera, 2002). As a result, the authors find the level of evidence for the use of artificial nutrition to be inconclusive at this time. Based on this, general guidelines concerning the use of various types of artificial nutrition will be presented.

a) The American Dietetic Association recommends that the following issues be considered when deciding upon initiation or continuation of artificial nutrition support (Fornari & McCallum, 2006).
(1) The patient's desire for nutrition intervention must be taken into account.
(2) The decision to forgo hydration or nutrition support should be carefully contemplated because it may be difficult to reverse outcomes of following this path, even for a short period of time.
(3) The benefits, risks, and burdens of nutrition support, including whether oral or parenteral nutrition will improve quality of life and well-being during the final stages of life, must be weighed.
(4) Whether nutrition support will provide the patient with emotional comfort, decreased anxiety, relief from anorexia and cachexia, improved self-esteem, improved relationships with family and friends, and relief from fear of abandonment must be considered.

b) Enteral nutrition support ($$$) may be an option if
   (1) It can contribute to quality or length of life in a meaningful way.
   (2) The patient wants it.
   (3) The patient has a functioning gut.
   (4) It is not contraindicated by conditions such as intractable nausea and vomiting, obstruction, or gastroparesis (may be able to bypass these with a jejunal feeding tube instead of a gastric feeding tube).

c) Indications
   (1) The patient meets < 50% of required nutrient intake orally for five to seven days or more.
   (2) Inadequate oral intake occurs for five or more days.
   (3) Protein-energy malnutrition is present.
   (4) The patient is suffering from severe dysphagia.

d) Contraindications
   (1) The patient is diagnosed with an intestinal obstruction, ileus, or hypomotility of the intestine.
   (2) The patient has severe, intractable diarrhea that is unresponsive to treatment (i.e., treatment of underlying infection, diet modification, antidiarrheals).
   (3) High-output enterocutaneous fistula is present.
   (4) The patient is diagnosed with acute pancreatitis.
   (5) The prognosis does not warrant aggressive nutrition support; this is an individual decision that must be discussed with the patient and family and treated on a case-by-case basis.

e) Starting enteral feeding
   (1) A registered dietitian should be consulted to determine nutrient needs and to select a formula (e.g., high-protein, fiber-containing, elemental) and administration method (i.e., pump, gravity feeding, bolus feeding).
   (2) Micronutrient deficiencies should be addressed ($)—If death is not imminent, use of vitamin and mineral supplements, such as an iron supplement for iron-deficiency anemia (microcytic) or vitamin B_{12} and folic acid supplements for macrocytic/megaloblastic anemia, may be beneficial. However, the benefit of such supplementation must be weighed against the potential discomfort it can cause. It may be more beneficial to discontinue vitamin and mineral supplements that contribute to gastrointestinal distress, nausea, constipation, or diarrhea if they diminish quality of life by a significant degree (Fornari & McCallum, 2006). This issue must be discussed with the patient, family, and caregivers. The costs and benefits of micronutrient supplementation should be decided on a case-by-case basis.

d) Parenteral nutrition support ($$$$)—The most important issue is to help the family and patient to understand the risks, benefits, and cost of total parenteral nutrition on a case-by-case basis. Parenteral nutri-

tion is almost never indicated in the patient who is terminally ill for the following reasons.

(1) It adds very little in terms of quality and length of life.
(2) The risks (e.g., infection, hepatic and renal complications, fluid management problems) often outweigh the benefits.
(3) Treatment is very expensive.
(4) It requires frequent blood work (no less than weekly) and intensive management.
(5) It can contribute to other problems and complications, such as ascites, edema, and hepatic and renal complications.

B. Death is imminent.

1. Decreased food and fluid intake appears to be a normal part of the "physiology" of dying.
2. In the last few weeks to days of life, a marked decline occurs in the functioning of the upper and lower gastrointestinal system, as well as a decrease in sensations of taste and smell.
3. Education of family members and caregivers at this stage is important.
4. Facilitate understanding that the physical sensations of "starving" are not present. The patient feels little discomfort strictly from decreasing nutrition status. Hunger is nonexistent, and forcing the issue of food often is counterproductive.
5. Maintenance of strength and nutrition status at this time is unrealistic. Caregivers should be encouraged to show love and support in ways that do not involve preparation or provision of food.
6. Dehydration also may be normal during the end stage of the dying process. Often, the only discomfort associated with dehydration is a dry mouth, which can be alleviated with sips of water, ice chips, or moistened swabs (Fornari & McCallum, 2006). Explaining that dehydration is a normal part of the body shutting down in the final stages of life will ease the anxiety of caregivers. (See Dehydration.)
7. Artificial hydration and nutrition support at this time can decrease quality of life simply by the nature of their invasiveness. Starting these measures when death is imminent is not advised.
8. If artificial hydration or nutrition support is already in place, decreasing the amount of the infusion to 500–600 ml/day may help to avoid discomfort from increased urinary output, gastrointestinal and pharyngeal secretions, and pulmonary edema. Discontinuing hydration altogether is an option that should be determined by the patient and family (Fornari & McCallum, 2006).
9. According to the American Medical Association's Code of Ethics, human dignity is the primary obligation if it conflicts with prolonging life. All competent patients have the right to accept or reject any or all forms of medical treatment. If an advance directive is in place, this should specify the patient's desires with regard to supportive interventions, including fluids and artificial nutrition, at the end of life (American Medical Association, 2001).

10. If the patient expresses a desire for voluntary cessation of eating and drinking, the following issues must be considered and addressed (Byock, 2000; Miller, Fins, & Snyder, 2000; Quill & Byock, 2000a, 2000b).
    a) Patient characteristics: Persistent, unrelenting, otherwise-unrelieved symptoms that are deemed unacceptable to the patient and family, including pain, seizures, weakness, and extreme fatigue
    b) Patient informed consent
        (1) Patient must be fully competent.
        (2) Patient must be fully informed of all treatment and symptom management options.
        (3) Patient must be evaluated by a mental health professional to rule out treatable depression or other mental health conditions; a second opinion is strongly recommended.
        (4) A written informed consent must be in place.
    c) Terminal prognosis: Typically days to weeks (possibly months)
    d) Palliative care: Must be available, in place, and able to adequately relieve suffering
    e) Family participation: Clinicians should encourage discussion; consensus should be reached, if possible, among the patient, immediate family members, and caregivers.
    f) Patient incompetence: Food and fluids (oral) should not be denied from incompetent patients who are willing and able to eat.
    g) Second opinions: Must be obtained by experts in underlying disease, mental health, pain management, and palliative care.
11. If all of the aforementioned issues are addressed and managed, voluntary refusal of food and fluids may be an appropriate option. Artificial nutrition and hydration are considered life-sustaining medical therapies similar to medications, surgery, dialysis, mechanical ventilation, or other medical interventions. Therefore, decisions regarding this issue should be handled using the same ethical and legal standards as other interventions. If the benefits of an intervention outweigh the costs, it is justified. If it is not beneficial or if the costs are higher than the benefits, it is not justified. Discontinuation of nutrition and hydration generally is not considered justified in the following situations (Byock, 2000; Miller et al., 2000; National Comprehensive Cancer Network Nutrition Support Panel, 2006; Quill & Byock, 2000a, 2000b).
    a) The patient will die of malnutrition before he or she would succumb to the disease process. An example includes a patient with severe dysphagia secondary to head and neck cancer, in which the primary diagnosis will not result in death before malnutrition.
    b) Untreated mental health issues are present, such as depression.
    c) The patient has a strong desire to "get affairs in order," such as writing a will or attending a specific family event.
    d) A new acute, but treatable, diagnosis arises.

Patient Outcomes

A. Malnutrition, dehydration, micronutrient deficiencies, weakness, wasting, and weight loss are corrected when possible.

B. When maintenance of nutrition and hydration status is no longer a reasonable goal, comfort needs should be met.

C. Patient maintains control over his or her intake.

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Anxiety

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Definition

Anxiety is a multifaceted, emotional response that vacillates along a continuum from a normal feeling of apprehension and fear to debilitating anxiety disorders, such as generalized anxiety disorder, panic disorder, post-traumatic stress disorder, social anxiety disorder, acute stress disorder, phobias, obsessive-compulsive disorder, or anxiety disorder caused by a medical condition (Heidrich & Esper, 2007; Kelly, McClement, & Chochinov, 2006; National Comprehensive Cancer Network [NCCN], 2007). Anxiety is the most common disorder seen in the general public as shown by the *National Comorbidity Survey* and the cause of significant social debility (Katon & Roy-Byrne, 2007). Anxiety is included in the top seven disorders in the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition), (DSM-IV) (NCCN). The four most frequent anxiety disorders seen in primary care are generalized anxiety disorder, social anxiety disorder, panic disorder, and post-traumatic stress disorder (Katon & Roy-Byrne; Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007). The most frequently identified anxiety disorder in the palliative care setting is generalized anxiety disorder, followed closely by panic disorder (Wilson et al., 2007).

Anxiety is manifested in degrees, which can be described as mild, moderate, severe, and panic (Heidrich & Esper, 2007), and may have physical, emotional, psychosocial, and spiritual roots. Mild anxiety can be a stimulus to get something accomplished, whereas severe or continual anxiety can be physically or psychologically harmful.

Pathophysiology and Etiology

The human body is programmed to respond to potentially dangerous situations through the sympathetic branch of the autonomic nervous system evoking the fight-or-flight response. When this response is prolonged or occurs too frequently,

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problems ensue. Physical problems associated with excess anxiety in the palliative population can include hypertension, palpitations, hypercoagulation, hyperglycemia, nausea, and tissue destruction (Heidrich & Esper, 2007). Anxiety can be a risk factor for the development of Parkinson disease, as well as an early symptom of the disease (Ferreri, Agbokou, & Gauthier, 2006).

Assessment of anxiety includes subjective feelings, objective findings, and review of physical functions. The palliative care patient may describe feelings of apprehension, fear, anger, uneasiness, helplessness, nervousness, vulnerability, and changes in attention span. The observer may see fidgeting, tenseness, and trembling. Other physical characteristics include increased vital signs, dilated pupils, diaphoresis, dyspnea, pallor, flushing, dry mouth, nausea, and urinary frequency (Heidrich & Esper, 2007). Low systolic blood pressure has been linked to anxiety and depression in the older population (Hildrum et al., 2007).

Many patients experience some level of anxiety during the course of their illness. Although 14%–60% of patients experience a substantial degree of anxiety or distress (Katon & Roy-Byrne, 2007; Kelly et al., 2006; Kroenke et al., 2007; NCCN, 2007; Wilson et al., 2007), less than 10% of anxiety disorders are recognized and treated (NCCN). This can be attributed in part to the stigma associated with emotional issues. NCCN prefers the term *distress* to relate to any psychosocial disorders, including anxiety, because *distress* is more socially acceptable with less negative connotations.

Depression frequently is present in patients who are also experiencing anxiety. Increased symptom burden, existential suffering, and decreased functionality lead to a decreased quality of life for patients experiencing the comorbid conditions of anxiety and depression (Badger, Segrin, Dorros, Meek, & Lopez, 2007; Heidrich & Esper, 2007; Katon & Roy-Byrne, 2007; Kelly et al., 2006; Wilson et al., 2007). The *Canadian National Palliative Care Survey* reported that 66% of patients receiving palliative care who are identified as having anxiety also met DSM-IV criteria for depression and that 45% also met the DSM-IV criteria for an additional anxiety disorder. Other significant findings of this survey were that 83% of palliative care patients with anxiety and depression reported a moderate to extreme level of global suffering. These patients reported physical symptoms, social concerns, and existential issues; were younger; were more likely to be female; had smaller social networks; and were less active in organized religion (Wilson et al.).

Manifestations

- Restlessness
- Trembling
- Uneasiness
- Sweating
- Dilated pupils
- Dry mouth
- Urinary frequency
- Increased systolic blood pressure

- Tachypnea
- Tachycardia
- Dyspnea
- Dizziness
- Breathlessness
- Flushing
- Pallor
- Chest pain
- Abdominal pain
- Nausea and vomiting

(Ferreri et al., 2006; Heidrich & Esper, 2007)

General Management Principles

A. Pharmacologic interventions

1. Pharmacologic treatment of anxiety is suggested when anxiety is severe, limits quality of life, or is accompanied by depression. Antidepressants, selective serotonin reuptake inhibitors (SSRIs), and venlafaxine have shown efficacy for concomitant treatment of depression and anxiety. Anxiety with pronounced sympathetic symptoms, such as tremors and palpitations, may be treated with propranolol prior to the anxiety-provoking stimulus (National Guidelines Clearinghouse [NGC], 2003).
2. A substantial number of patients fail to respond to first-line medication interventions, and relapse is common (Ipser et al., 2006). Sustained remissions are more likely with long-term maintenance treatment of anxiety disorders following improvement of acute symptoms. Panic disorder and social phobia medications should be continued for six months, and medications for obsessive-compulsive disorder should be continued for one year. Discontinuation of anxiolytics should be done gradually and under careful supervision (NCCN, 2007). Patients taking antidepressants must be monitored for suicidal ideations (NGC, 2003).

B. Nonpharmacologic interventions

1. Psychotherapy with or without antidepressants and anxiolytics is the recommended first-line of treatment for anxiety (Kroenke et al., 2007; NGC, 2003). If the patient is not responsive to these treatment modalities, the psychotherapy should be reevaluated, in conjunction with a review of the medication. Additional support, education, and neuroleptics also may be necessary at this point. If the patient's condition remains unchanged, further evaluation is necessary to assess for other anxiety disorders (NGC). All patients should be screened for anxiety along the continuum of care, including at the initial visit, at routine intervals, with changes in disease status, and as clinically indicated. Canada has made emotional distress its sixth vital sign to be assessed routinely, but no minimum standards exist for psychosocial care in the United States (NCCN, 2007).

2. Cognitive behavioral therapy has the strongest support of all psychotherapies for the treatment of anxiety disorders (Ayers, Sorrell, Thorp, & Wetherell, 2007; Hill & Brettle, 2005; Hunot, Churchill, Teixeira, & Silva de Lima, 2006; Katon & Roy-Byrne, 2007; Kroenke et al., 2007). Cognitive behavioral therapy is equally effective in older and younger adults without the added burden of potential polypharmacy (Hill & Brettle). Separation anxiety can be seen in adults with panic disorder, which may begin in adulthood or be carried over from childhood and may respond to cognitive behavioral therapy (Harvard Mental Health Letter, 2007).
3. Exercise is likely to be effective in the treatment of anxiety (Badger et al., 2007; Saxena, van Ommeren, Tang, & Armstrong, 2005). Any type of exercise can be helpful and would be worthwhile for patients in the palliative care setting who are physically able to participate in an exercise regimen.
4. The current mental-health care system is challenged to meet the need for care of anxiety disorders. Paraprofessionals may have a role in the treatment of anxiety disorders, especially when compared to no treatment at all (den Boer, Wiersma, Russo, & van den Bosch, 2005). Collaborative care models, based on evidence-based practice utilizing paraprofessionals and allied healthcare professionals such as nurses, have been shown to be successful in managing depression (Katon & Roy-Byrne, 2007). These same models could likely be effective in assisting with the management of anxiety disorders as well, with clinicians as the key to initial identification of anxiety issues because of their unique role in patient care (Christie & Moore, 2004; NCCN, 2007). Telephone-delivered psychosocial interventions are another promising way to meet the needs of patients with anxiety disorders (Badger et al., 2007).
5. Complementary and alternative therapies are used by as many as 91% of patients with cancer (Stephenson, Swanson, Dalton, Keefe, & Engelke, 2007; Wyatt, Sikorskii, Siddiqi, & Given, 2007; Zick et al., 2006).
   a) Complementary therapies such as meditation, relaxation, reflexology, massage therapy with or without aromatherapy, guided imagery, humor, and virtual reality may have a role in anxiety management (Arias, Steinberg, Banga, & Trestman, 2006; Christie & Moore, 2004; Fellowes, Barnes, & Wilkinson, 2004; Krisanaprakornkit, Krisanaprakornkit, Piyavhatkul, & Laopaiboon, 2005; Lane, Seskevich, & Pieper, 2007; Roffe, Schmidt, & Ernst, 2005; Schneider & Hood, 2007; Wyatt et al., 2007). Reflexology was shown to have a significant effect on anxiety and may be taught to caregivers to be used with patients (Stephenson et al., 2007).
   b) Herbal therapies are included in complementary and alternative therapies. Essiac, a combination of at least four different herbs, consumed as a tea mostly by patients with breast cancer, was not shown to positively affect anxiety (Zick et al., 2006). Valerian is another herbal therapy that may not be effective for treating anxiety (Miyasaka, Atallah, & Soares, 2006). On the other hand, passiflora, or passionflower extract (Miyasaka et al.),

and kava may have some benefit. Kava extract was the most promising herb in the treatment of anxiety (Pittler & Ernst, 2002), but its use poses a potential risk for hepatic toxicity or failure (Wasik, 2008).

Management

A. Death is not imminent.
   1. **Level I—high level of evidence**
      (Arias et al., 2006; Heidrich & Esper, 2007; Hill & Brettle, 2005; Kapczinski, Lima, Souza, Cunha, & Schmitt, 2003; NCCN, 2007; NGC, 2003; Wasik, 2008)
      a) Cognitive behavioral therapy
         (1) Improvement seen in two-thirds of patients at six months
         (2) Shown to have the most consistent evidence of support
         (3) May increase efficacy of drug treatments
         (4) Useful in treatment of adults age 50 years and older
      b) SSRIs—First-line medication
         (1) Paroxetine (Paxil®) ($$$)—10–60 mg every morning; max 60 mg/day
            (a) Most studied
            (b) Few side effects
         (2) Sertraline (Zoloft®) ($$$)—start 25 mg po daily; max 200 mg/day
         (3) Fluoxetine (Prozac®) ($$$)—20–40 mg po every morning; max 80 mg/day
         (4) Citalopram (Celexa®) ($$$)—20 mg po daily; max 60 mg/day
            (a) Monitor for suicidal ideation.
            (b) Weigh risk versus benefit.
            (c) Avoid abrupt cessation.
      c) Antidepressants preferred over benzodiazepines
         (1) Clomipramine (Anafranil®) ($$$)—150–250 mg po at bedtime
            (a) Start 25 mg, increase gradually to effective dose.
            (b) Monitor for suicidal ideation.
         (2) Imipramine (Tofranil®) ($$$)—50 mg po daily; maximum 200 mg/day, 100 mg/day in older adults
            (a) Monitor for suicidal ideation.
            (b) Avoid abrupt cessation.
            (c) Monitor drug levels.
      d) Benzodiazepines
         (1) Alprazolam (Xanax®) ($)—0.25–0.5 mg po two to three times daily; max 2 mg/day in older adults
            (a) Short half-life (< 12 hours)
            (b) Multiple drug interactions
         (2) Lorazepam (Ativan®) ($$$)—0.5 mg po every six to eight hours; max 3 mg/day in older adults

(a) Medium half-life of 10–20 hours
(b) Preferred benzodiazepine with hepatic impairment
(3) Diazepam (Valium®) ($)—2–10 mg po two to four times daily
(a) Long half-life of 20–120 hours
(b) Active metabolites
(4) Clonazepam (Klonopin®) ($$)—start 0.25–0.5 mg po two to three times daily; max 4 mg/day
(a) Half-life of 18–50 hours
(b) Rapid relief
(c) Monitor patient closely when discontinued.

e) Serotonin norepinephrine reuptake inhibitors (SNRIs)
(1) Venlafaxine (Effexor®) ($$$)—75–225 mg po daily
(a) No anticholinergic, sedative, or orthostatic hypotension effects
(b) Overdose more likely to be fatal
(2) Trazodone ($)—50–100 mg po two or three times a day
(a) Monitor for suicidal ideation.
(b) Advise males of the possibility of priapism.

f) Complementary therapies
(1) Meditation
(2) Relaxation

2. **Level II—moderate level of evidence**
(Chessick et al., 2006; Christie & Moore, 2004; Fellowes et al., 2004; NGC, 2003; Roffe et al., 2005; Saxena et al., 2005; Schneider & Hood, 2007; Stephenson et al., 2007; Wasik, 2008; Wyatt et al., 2007)

a) Benzodiazepines
b) Azapirone antidepressants
(1) Imipramine (Tofranil) ($$$)—50–300 mg po at bedtime
(a) May lower seizure threshold.
(b) Monitor for suicidal ideation.
(c) Weigh risk versus benefit.
(2) Buspirone (BuSpar®) ($)—7.5–15 mg po bid daily
(3) Benzodiazepines may be more effective and better accepted than azapirones in the treatment of anxiety; however, studies show conflicting evidence.

c) Antidepressants
(1) Nefazodone ($$$)—150–300 mg po bid; max 600 mg/day
(a) Rarely, neuroleptic malignant syndrome may be seen.
(b) Monitor for suicidal ideation.
(c) Monitor liver function for possible hepatic failure.
(2) Mirtazapine (Remeron®) ($$$)—15 mg at bedtime; max dose 45 mg
(a) Make dose changes at one- to two-week intervals.
(b) Monitor for suicidal ideation.

d) Nonbenzodiazepine antianxiety agents

(1) Hydroxyzine (Vistaril®) ($)—50 mg po daily; may increase to four times daily; maximum 400 mg/day
(2) Promethazine—25–50 mg po, pr, IM, or IV every four to six hours, as needed
(a) Monitor for respiratory depression.
(b) Avoid use with other respiratory depressant–effect drugs.

e) Beta-blockers
(1) Propranolol (Inderal®) ($$)—10–40 mg po
(a) Take 45–60 minutes prior to anxiety-provoking stimulus that produces pronounced sympathetic symptoms, such as tremors and palpitations.
(b) Avoid abrupt cessation.
(c) Taper gradually.
(2) Atenolol (Tenormin®) ($$)—start 50 mg po daily
(a) Avoid abrupt cessation.
(b) Dose may be increased after seven days.

f) Physical activity and exercise

g) Complementary therapies
(1) Reflexology (can be taught to caregivers)
(2) Humor
(3) Massage
(a) Provides short-term benefit
(b) Conflicting evidence regarding the addition of aromatherapy to massage
(4) Guided imagery
(5) Virtual reality

3. **Level III—low level of evidence**
Herbal treatment (Miyasaka et al., 2006; Pittler & Ernst, 2002; Wasik, 2008)
a) Passiflora (passionflower extract)—May be as effective as benzodiazepines
b) Kava extract—Potential for hepatic toxicity or failure

B. Death is imminent.
1. Treatment of anxiety should be continued as long as needed for the actively dying patient.
2. Comfort measures should be continued or initiated as appropriate.
3. Support should be available as needed.
4. Overstimulation should be avoided.

Patient Outcomes

A. Anxiety is at an acceptable level.

B. Patient experiences restful sleep.

C. No physical manifestations of anxiety are present.

D. Comfort is maintained.

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Ascites

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Definition

Ascites is the abnormal accumulation of fluid in the peritoneal cavity.

Pathophysiology and Etiology

The most common cause of ascites is liver disease, usually cirrhosis. Ascites associated with liver disease is caused by a combination of portal hypertension and sodium retention. Fibrosis in the liver interferes with hepatic venous outflow, leading to portal hypertension. Portal hypertension overloads lymphatic drainage and initiates activities that increase sodium retention (Lingappa, 2003; Wongcharatrawee & Garcia-Tsao, 2001). These factors also may contribute to ascites associated with congestive heart failure and nephrotic syndrome (Kichian & Bain, 2004).

About 10% of patients with ascites have a malignancy as the primary cause (Rosenberg, 2006). The mechanisms causing ascites associated with liver cancer may be the same as for liver disease (i.e., portal hypertension and sodium retention) (Kichian & Bain, 2004). Tumors that seed the peritoneum may release vascular endothelial growth factor (VEGF), which increases capillary permeability, thus allowing proteins to enter the peritoneal space. This increase in microvessel permeability is believed to be the main contributor to malignant ascites (Adam & Adam, 2004). In addition, tumors may directly obstruct lymphatic channels, causing chylous ascites (Kichian & Bain).

Manifestations

- Weight gain
- Increasing abdominal girth, often identified by a change in the way clothes fit
- Abdominal pressure, discomfort, or pain
- Anorexia, early satiety, nausea and vomiting, or indigestion
- Dyspnea and orthopnea
- Constipation
- Urinary frequency

- Edema of lower extremities and scrotum
- Skin of abdomen taut and shiny
- Shifting dullness on percussion of abdomen
- Fluid wave felt on examination of abdomen

(Heidrich, 2007; Kichian & Bains, 2004)

Management

A. Death is not imminent.

1. **Level I—high level of evidence**
   a) Sodium restriction and diuretics are first-line treatment for ascites caused by cirrhosis (Runyon, 2004). These interventions often are not effective for malignant ascites (unless portal hypertension is a contributing factor) and can deplete intravascular volume.
      (1) Restrict dietary intake of sodium to 2 g/day or less.
      (2) Initiate diuretic therapy using spironolactone ($) 100 mg po combined with furosemide 40 mg po. The dosages may be increased every three to five days, maintaining the 100 to 40 mg ratio; the maximum dose of spironolactone is 400 mg/day and of furosemide is 160 mg/day (Runyon, 2004; Sandhu & Sanyal, 2005; Zebrowski et al., 1999).
   b) Peritoneovenous shunt should be considered for patients with refractory ascites associated with cirrhosis who are not candidates for paracentesis, transplant, or transjugular intrahepatic portasystemic stent-shunt ($$$$) (Runyon, 2004). The role of these procedures in ascites related to malignancy is not clear.
   c) Patients with ascitic fluid polymorphonuclear (PMN) leukocyte counts > 250 cells/mm^3 should receive empiric antibiotic therapy (e.g., cefotaxime 2 g every eight hours) ($$) (Runyon, 2004).
2. **Level II—moderate level of evidence**
   a) Fluid restriction is not necessary unless serum sodium is < 120 to 125 mmol/L (Runyon, 2004).
   b) Paracentesis ($$$) provides symptomatic relief from a tense abdomen (Runyon, 2004).
      (1) Up to 5 liters can be safely drained from the abdomen without replacement of albumin in patients with diuretic-resistant tense abdomens (Runyon, 2004; Stephenson & Gilbert, 2002).
      (2) If > 5 liters is removed in patients with portal hypertension-related ascites, albumin replacement ($$) is recommended at a dose of 8–10 g per liter of ascites removed (Runyon, 2004; Wongcharatrawee & Garcia-Tsao, 2001). The role of albumin replacement after large-volume paracentesis for malignancy-associated ascites is not clear.
      (3) If ascites is related to portal hypertension, paracentesis should be followed by diuretic therapy.

(4) Consider placement of a tunneled drainage catheter ($$$$) to allow intermittent drainage without repeat paracentesis in malignant ascites (Iyengar & Herzog, 2002; Rosenberg, Courtney, Nemcek, & Omary, 2004).

c) Intracavitary chemotherapy ($$$–$$$$) may control ascites in patients whose tumors initially responded to systemic therapy, especially in patients with ascites related to ovarian or breast cancer (Adam & Adam, 2004).

d) Patients with ascitic fluid PMN counts < 250 cells/mm^3 and who have fever or abdominal pain or tenderness should receive empiric antibiotic therapy ($$) while awaiting results of cultures (Runyon, 2004).

3. **Level III—low level of evidence**

a) Pharmacologic interventions

(1) Analgesics ($–$$) for comfort.

(2) Octreotide (Sandostatin®) ($$$)—Subcutaneous administration of 200–400 mcg/day has been reported to be effective in some cases of intractable ascites. The true cost-benefit ratio of this intervention has not been adequately evaluated (Cairns & Malone, 1999; Mincher, Evans, Jenner, & Varney, 2005; Waller & Caroline, 2000).

(3) Anti-VEGF antibodies, anti-VEGF receptor antibodies, tumor necrosis factor, metalloproteinase inhibitors, interleukin-2, and beta-interferon are in phase I and II trials for treatment of malignant ascites (Adam & Adam, 2004; Numnum, Rocconi, Whitworth, & Barnes, 2006).

b) Nonpharmacologic interventions (Heidrich, 2007; Kichian & Bain, 2004)

(1) Elevate head of bed.

(2) Encourage small, frequent meals and increase protein.

(3) Employ measures to prevent constipation and to maintain bowel function.

(4) Encourage the patient to wear loose-fitting clothing.

(5) Elevate lower extremities when sitting.

(6) Encourage meticulous skin care.

(7) Place indwelling Foley catheter for urinary retention.

B. Death is imminent.

1. Position for comfort.
2. Discontinue any sodium or fluid restrictions.
3. Continue to remove abdominal fluid via paracentesis if this promotes comfort for the patient.

a) If a catheter has been placed for drainage of abdominal fluid, the cost and discomfort associated with the procedure is minimal and can greatly enhance comfort.

b) If needle puncture is required, the discomfort associated with the procedure must be weighed against the potential increase in comfort

following the procedure. In addition, in the event that arrangements cannot be made to perform this procedure at the patient's current location, the physical, emotional, and financial burdens of transporting the patient to a clinic or hospital must be evaluated.

Patient Outcomes

A. Relief of abdominal discomfort is provided.

B. Dyspnea and orthopnea are relieved.

C. Ascites is controlled.

D. Regular bowel movements are present.

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