Numerous, well-defined symptoms are associated with end of life when death is caused by a chronic or debilitating illness (or both) such as cancer, HIV/AIDS, Alzheimer’s dementia, and congestive heart failure. These symptoms, if unrelieved, are distressing to both the patients and their families and preclude any possibility of relieving psychological, social, and spiritual suffering, improving quality of life, or completing life closure. Therefore, the objective of this article is to identify some common symptoms at end of life and various management strategies for each.

(K key words: anorexia, asthenia, breathlessness, cachexia, constipation, delirium, dyspnea, fatigue, loss of appetite, nausea, vomiting, weight loss)

Palliative care is defined as “the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best possible quality of life for patients and their families.”

Although palliative care is not new, its re-emergence to its current position of prominence in the practice of medicine is a wake-up call for physicians to understand and embrace its precepts through their various practices of medical care. “Palliative care is both an art and a science,” said Joan Harrold, MD, in a symposium on end of life at the 1999 American Geriatrics Society annual meeting. She went on to say:

We are often faced with the dilemma that we know how to provide end-of-life care but may not know when the patient stops ‘living with’ a disease and starts ‘dying of’ it. A patient may be sick enough to die on a number of occasions, and we have difficulty seeing such patients as ‘dying’ when they do not actually die. It is important to provide good palliative care to patients before we are sure they are dying, or we will miss the chance.

Figure 1 outlines basic principles of palliative care.

Although palliative care has emerged as a recognized subspecialty, primary care physicians and their patients are eager to maintain strong relationships at end of life which emphasize more than just the patient’s disease. Therefore, it is imperative for physicians to equip themselves with the necessary information and training in order to ensure their patients, to the best of their ability, a “good” death. This article seeks to equip the physician, in part, to manage some common non-pain symptoms associated with end of life.

Management of Nonpain Symptoms
The Oxford Textbook of Palliative Medicine lists more than 55 symptoms that may cause significant problems at the end of life. The importance of many of these symptoms in end-of-life care is underappreciated. A recent study looking at symptom burden at the end of life in patients cared for by hospices found a “significant perceived symptom burden among these patients.” This finding raises the concern that it is “possible that terminally ill patients who are not receiving hospice care manifest an even higher symptom burden.” Obviously, the management and control of symptoms present a challenging
Anorexia and Cachexia

Anorexia (loss of appetite) with cachexia (weight loss) is usually multifactorial in the terminally ill patient. Pain, medications, depression, nausea, dysphagia, odynophagia, or advancing disease all contribute to loss of appetite. The social and physiologic implications of eating and feeding are significant. Food is identified as nurturing, and the belief held by many patients and families is that if only the patient would eat more, he or she would regain his or her former health and vigor. Decreased food intake is associated with starvation and ill health.

The perception of loss of appetite is usually minimal to the patient. To the family, the perception of anorexia with its associated weight loss is usually more acute and distressing. In the assessment of the anorectic patient, the first step is to determine qualifiers, that is, who is bothered more by the problem, the patient or the family? Next, an intake and diet history should be obtained by having the patient or family (or both) keep a log to determine the actual severity of the problem. It is helpful to determine what foods the patient likes and dislikes. Then, review all prescription and nonprescription medications the patient is taking.

The physical examination should include vital signs (temperature, pulse, and respiration) and attention to the cardiovascular, pulmonary, gastrointestinal, and musculoskeletal systems. The patient should be assessed for depression, anxiety, and fear.

The cause of the patient’s anorexia may be reversible, such as pain, depression, medication side-effect, nausea, constipation, infections, dysphagia, or odynophagia. Irreversible causes are related to the terminal disease process. Figure 2 provides a guide to interventions.

**Asthenia, Fatigue, and Weakness**

In multiple series, fatigue is the most frequent distressing symptom associated with advanced illness and end-of-life care. Patients and families will focus on the symptom rather than its underlying cause. Often this complaint is viewed as the patient has “given up” or is “not fighting.” The symptom of fatigue encompasses a spectrum of issues and is multidimensional. Little is known about fatigue in terms of pathophysiology or effective therapy. The physician can play an instrumental role in educating the patient and family about the complex nature of the symptom and give the patient “permission” to rest.
Assessment includes determining to what extent does fatigue interfere with the patient accomplishing his or her activities of daily living, reviewing all prescription and nonprescription medication, assessing hydration and the patient’s overall oral intake, and assess for sleep disturbance and insomnia related to uncontrolled pain or other uncomfortable symptoms. Appropriate physical examination and diagnostic studies should be done.

Finally, it should be determined whether the cause is reversible or irreversible. Reversible causes include medications (antihypertensives, cardiac medications, diuretics, etc), dehydration, anemia, electrolyte imbalance, and disturbed nocturnal sleep. Irreversible causes are related to terminal disease process.

**Figure 3** provides a guide to appropriate interventions for fatigue.

**Constipation**

Constipation is discomfort associated with reduced frequency of bowel movements. It is associated with an increase in stool consistency that leads to difficulty defecating. The cause of constipation at end of life is usually multifactorial, including medications, decreased mobility, ileus, mechanical obstruction, dehydration, and metabolic abnormalities.

The cause in a given patient is often not carefully assessed, and if left unmanaged, can lead to considerable patient distress. The consequences of unmanaged constipation include abdominal pain, bloating, nausea and vomiting, overflow incontinence, tenesmus, fecal impaction, and bowel obstruction.

As for the previous symptoms, assessment should include determination of the patient’s usual bowel pattern, (frequency, use of laxatives, date of last bowel movement, etc) and a review of all prescription and nonprescription medications. Physical examination should include the cardiovascular, pulmonary, and gastrointestinal systems, with a rectal examination to assess for fecal impaction. It is important to rule out bowel obstruction, hypercalcemia, and hypokalemia and to determine the patient’s food and fluid intake (amount and type).

**Figure 4** provides a guide to management of constipation.

**Delirium**

Delirium occurs in 28% to 83% of patients near the end of life. It frightens patients and families and may cause as much distress as do pain and other physical symptoms. Families may regret the premature separation from a patient who can no longer communicate. Delirium may also be a predictor of approaching death for some patients. Delirium robs patients of valuable time and curtails opportunities to make final choices and plans. For all these reasons, delirium can be a daunting obstacle to good end-of-life care if not addressed properly.

Delirium exists if two or more of the following are present:

- reduced level of consciousness;
- perceptual disturbances, such as illusions, hallucination, or paranoia;
- memory loss;
- disorientation to time, place, or person;
- disturbance of the sleep-wake cycle;
- increased or decreased psychomotor activity;
- development of symptoms over a short period and a tendency for symptoms to wax and wane throughout the day.

If uncorrected, symptoms become worse.

Assessment for delirium begins with a determination of time of onset, circumstances surrounding onset, and level of disability caused; a review of all prescription and nonpre-
INTERVENTIONS FOR CONSTIPATION

Nonpharmacologic
- Increase mobility, if possible.
- Increase oral intake, if possible.
- Increase fiber in diet with increased fluids (bran, vegetables, fruit, fruit juices).
- Encourage patient to keep a bowel log.
- Instruct patient to avoid straining.
- Teach maneuvers to encourage defecation
- Massage of only transverse and descending colon.
- Rotation of upper body while sated on toilet.
- Easily accessible bedside commode with adequate privacy.
- Taking advantage of the gastrocolic reflex that occurs after eating and having the patient sit upright on the edge of the bed or on a commode.

Pharmacologic
- Stimulant laxatives
  - Prune juice, 120 mL to 240 mL once or twice daily
  - Senna (Senokot), 2 tablets every night at bedtime; titrate up to effect (up to 9 or more daily).
- Bisacodyl (Dulcolax), 5 mg orally as needed at bedtime; titrate to effect.
- Osmotic laxatives
  - Lactulose (Chronulac), 30 mL orally every 4 to 6 hours; titrate to effect.
  - Milk of Magnesia (or other magnesium salts), 1 to 2 tablespoons one to three times a day
  - Magnesium citrate, 1 to 2 bottles as needed
  - Detergent laxatives (stool softeners)
  - Sodium ducosate (Colace), 1 to 2 tablets orally once or twice daily; titrate to effect.
- Prokinetic agents
  - Metoclopramide hydrochloride (Reglan), 10 mg to 20 mg orally every 6 hours.

Figure 4. A guide to management of constipation. ▲

INTERVENTIONS FOR DELIRIUM

Nonpharmacologic
- Orientation protocol
- Orientation board with names of care team members and the day’s schedule
- Reorienting communication.
- Therapeutic activities protocol
- Cognitively stimulating activities three times a day.
- Nonpharmacologic sleep protocol
- Warm drink of milk or herbal tea at bedtime
- Relaxation tapes or music
- Back massage
- Sleep-enhancement protocol
- Noise-reduction strategies
- Adjustment of schedules to allow sleep (rescheduling of medication)
- Early mobilization protocol
- Ambulation or active range-of-motion exercises three times a day
- Minimal use of immobilizing equipment (catheters, restraints).
- Vision protocol
- Portable amplifying devices
- Earwax disimpaction
- Volume-repletion measures (encourage intake of oral fluids).

Pharmacologic
- Adjust pharmacy regimen if drug toxicity is suggested.
- Predominantly neuroleptic effects
  - haloperidol (Haldol) tablets/liquid, 0.5 mg to 1.0 mg orally every 30 minutes (titrate to effect; not to exceed 3 mg in 24 hours)
  - olanzapine (Zyprexa), 2.5 mg to 5 mg orally every day
  - risperidone (Risperdal), 0.5 mg orally twice a day
- Predominantly sedative effects
  - lorazepam (Ativan), 0.5 mg to 1.0 mg orally, subcutaneously, intravenously, or sublingually every 4 hours (recommended for anxiety or agitation not associated with hallucinations or psychosis)

Figure 5. A guide to management of delirium. ▲

escription medications, with consideration given to drug toxicity, polypharmacy, and possible drug interactions; and determination of the presence and level of pain.

Appropriate physical examination includes measurement of vital signs; examination of head, eyes, ears, nose, and throat; and examination of the cardiovascular, pulmonary, urinary, gastrointestinal, and neurologic systems. The patient should
undergo a mini-mental status and mood assessment. The capillary blood sugar level should be measured, and laboratory studies should be done to rule out metabolic disturbances (e.g., hypercalcemia, hypokalemia).

In the elderly, risk factors—constipation; infection; change in environment, room, caretaker, routine; or sleep disturbances—should be considered.

**INTERVENTIONS FOR DYSPNEA**

**Nonpharmacologic**
- Breathing exercises (diaphragmatic/purse-lipped)
- Elevation of head of bed
- Percussion, vibration, coughing; postural drainage not indicated
- Avoidance of gas-forming foods that may cause abdominal distention
- Teaching good posture and effective use of accessory muscles
- Encouraging adequate rest periods between activities
- Positioning of an electric fan for increased airflow on the patient (can alter the feeling of breathlessness)
- Administration of oxygen, 2 L/min to 4 L/min via nasal cannula as needed
- Thoracentesis or paracentesis if indicated

**Pharmacologic**
- Prednisone, 10 mg to 20 mg orally three times a day or dexamethasone, 8 mg orally every day for tumor infiltration, bronchospasm
- Lorazepam (Ativan), 0.5 mg to 2.0 mg every 6 hours for chronic obstructive pulmonary disease or breathlessness related to anxiety
- Diuretics for congestive heart failure
- Inhalers for bronchospasm
- Adrenergics
- Anticholinergics
- Steroids
- Opioids
- Morphine, 2.5 mg to 5.0 mg (range, 2.5 mg to 20.0 mg) orally every 4 hours as needed
- Noisy breathing
- Scopolamine patch (Transderm Scop) may be useful in drying copious secretions
- Glycopyrrolate (Rubinul), 1 mg to 2 mg orally two to three times a day (maximum 8 mg/d)

**THE 11 “Ms” OF EMESIS**
- Metastasis (brain, liver)
- Meningeal irritation
- Movement (vestibular stimulation)
- Mentation (anxiety)
- Medications (numerous)
- Mechanical obstruction
- Motility
- Metabolic
- Microbes
- Myocardia (ischemia, congestive heart failure)
- Mucosal irritation

**Figure 6. A guide to appropriate management of dyspnea.**

**Figure 7.**

*Figure 5 offers a guide to interventions in management of delirium. The goal of pharmacologic treatment of delirium should be to bring patients closer to their baseline mental state, not to sedate them or suppress agitation.*

**Dyspnea**

Dyspnea (breathlessness) is one of the most frequent symptoms noted in patients at end-of-life. Like pain, dyspnea is a subjective sensation and is difficult to define. It can be caused by multiple factors, including anemia, pleural effusions, progressive tumor growth, congestive heart failure, pneumonia, pneumothorax, laryngeal obstruction, ascites, and anxiety. Treatment is directed at symptomatic control of the underlying factors or relief of the unpleasant sensation.

As with the other nonpain symptoms, assessment begins with a determination of the qualifiers based on the patient’s subjective reporting: how debilitating/disruptive is the dyspnea? A review of all prescription and nonprescription medications and appropriate physical examination (vital signs, cardiovascular, pulmonary, and gastrointestinal systems) are essential. The patient’s physical and emotional status should be evaluated.

*Figure 6 provides a guide to appropriate management of dyspnea. Although administration of oxygen may not be physiologically helpful, it may afford physiologic. Pharmacologic approaches depend on the cause of the dyspnea. Opioids provide safe, effective relief of dyspnea at end of life. They ameliorate respiratory distress by altering the perception of breathlessness, lessen the ventilatory response to hypoxia and hypercapnea, and reduce oxygen consumption. Nebulized morphine can be given to patients who cannot take the oral form.*
Noisy breathing, or death rattle, which may be misinterpreted as dyspnea, is caused by the movement of retained secretions in the hypopharynx, trachea, or main bronchus during inspiration and expiration.9

Nausea and Vomiting

Nausea and vomiting are commonly associated with many advanced diseases and also may be the result of therapeutic interventions. Nausea is expressed as an unpleasant subjective sensation as a result from stimulation of the gastrointestinal lining, the chemoreceptor trigger zone in the base of the fourth ventricle, the vestibular apparatus, or the cerebral cortex. Vomiting is an observable neuromuscular reflex that constitutes a final common pathway after stimulation of one or more of these regions. Both these symptoms, together or alone, can be very disruptive and distressing for patients and families.

A thorough assessment of nausea and vomiting is crucial to understanding which of the multiple potential causes is operant, what the likely pathophysiology is, and what would be most appropriate to prescribe.

Different causes will require different interventions if the symptoms are to be controlled effectively. The “Eleven ‘Ms’ of Emesis” (Figure 7) lists the major causes of nausea and vomiting.3

Nonpharmacologic interventions may be helpful and include the following:
- instituting measures in persons at risk for aspiration;
- providing oral care after each episode;
- applying cool, damp cloth to forehead, neck, and wrists;
- reduction or elimination of noxious stimuli:
  - pain,
  - fatigue,
  - odors,
  - food,
  - anxiety;

**PHARMACOLOGIC INTERVENTIONS FOR NAUSEA AND VOMITING**

- If stimulated by emotions, sights, or smell
  - Lorazepam (Ativan), 0.5 mg to 2.0 mg orally or sublingually every 4 to 6 hours
  - Diphenhydramine hydrochloride (Benadryl), 20 mg to 50 mg every 4 to 6 hours
  - Hydroxyzine hydrochloride (Vistaril, Atarax), 25 mg to 100 mg three to four times a day
  - Promethazine hydrochloride (Phenergan), 25 mg to 50 mg every 4 to 6 hours

- If resulting from motion sickness or vestibular stimulation
  - Metoclopramide
  - Scopolamine (Transderm Scop) behind ear every 3 days.
  - Meclizine hydrochloride (Bronine), 25-mg chewable tablets orally two to three times a day

- If resulting from toxins or drugs
  - Evaluation of drug levels
  - Haloperidol (Haldol), 0.5 mg to 2.0 mg orally, intravenously, or subcutaneously every 6 hours, then titrate (less sedating)
  - Prochlorperazine (Compazine)
    - 10 mg to 20 mg orally every 6 hours OR
    - 25 mg as needed every 12 hours OR
    - 5 mg to 10 mg intravenously every 6 hours
  - Thiethylperazine (Torecan)
    - 10 mg to 20 mg orally every 6 hours OR
    - 10 mg as needed every 6 to 8 hours
  - Metoclopramide hydrochloride (Reglan), 10 mg to 20 mg orally every 6 hours

- If resulting from visceral or gastrointestinal stimulation
  - Scopolamine OR
  - Meclizine OR
  - Diphenhydramine OR
  - Hydroxyzine

- If resulting from increased cranial pressure
  - Dexamethasone, 16 mg once daily
  - Neuroleptics (prochlorperazine, thiethylperazine, or haloperidol) may assist in controlling symptoms

Figure 8. A guide to appropriate pharmacologic management of nausea and vomiting.
Collaboration
Palliative care, though rewarding, is challenging and multifaceted. Do not hesitate to expand your ability to provide good care by using hospice providers and palliative care specialists. With the patient’s permission, you might also want to have clergy, social workers, or community volunteers singly or in combination to assist in the care and meeting the needs of the patient and the patient’s family.

Caring
Showing that you understand the distress and loss that is part of the dying process, listening to fears and anxieties, and responding with patience and gentleness can relieve many of the “psychological symptoms” associated with this process. This experience can be enriching and gratifying as we allow ourselves to be of service to people at the most difficult moments of their lives.

References

Comments—The Four Cs
The Four Cs for successful participation in patients’ end-of-life care are common sense, communication, collaboration and care.11

Common Sense
In the last weeks and months of a patient’s life, treatment options should be approached differently than with the non-terminally ill patient. All modes of therapy and interventions must be assessed in terms of providing palliation and comfort without undue burden or discomfort to the patient and family. This is a time when “less might be better.”

Communication
Being available to take calls and to answer questions from the patient and family provides a comfort and a confidence all its own. Be open. Be honest. Be available. Have a well thought-out, agreed-on, and documented plan of care so that the patient, family, other healthcare providers, and covering physicians know what to expect and how to manage any changes in the patient’s symptoms or status.

Pharmacologic treatment will vary depending on the underlying pathophysiology (Figure 8). The brain and the gut, as previously noted, are the two organ systems that are responsible for the pathophysiology of nausea and vomiting and where therapeutic treatment is targeted. When nausea and vomiting is stimulated by toxins or drugs, it may be appropriate to evaluate and monitor drug levels such as digoxin and theophylline. An attempt should be made to change or reduce the number of drugs being used that cause nausea or to change the route of administration. Antiemetic therapy should begin with a single medication, the dose of which should be optimized before adding a second drug with a different mechanism of action. It may be necessary to combine antiemetics that work at different sites.5,6,10

Teaching the patient deep breathing and voluntary swallowing techniques to suppress vomiting reflex; restriction of liquids with meals; offering cold foods that have less odor; having patient dress in loose, unrestricted clothing; encouraging the patient to sit in fresh air or in front of a fan; having the patient avoid lying flat for 2 hours after eating; encouraging frequent, small feedings; having the patient take the highest protein/caloric nutrients at a time when he or she is least nauseated; and preventing dehydration by offering fluids in small amounts (1 tablespoon per hour.)

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