Chapter 12: Palliative and End-of-Life Care

Ezekiel J. Emanuel

EPIDEMIOLOGY

CAUSES OF DEATH

In 2019, 2,854,838 individuals died in the United States **(Table 12-1)**. Approximately 74% of these deaths occurred in those aged ≥65 years. The epidemiology of death has changed significantly since 1900 and even since 1980. In 1900, heart disease caused ~8% of all deaths, and cancer accounted for <4% of all deaths. In 1980, heart disease accounted for 38.2% of all deaths, cancer 20.9%, and cerebrovascular disease 8.6% of all deaths. By 2019, there had been a dramatic drop in deaths from cardiovascular and cerebrovascular diseases. In 2019, 23.1% of all deaths were from cardiovascular disease and just 5.3% from cerebrovascular disease. Deaths attributable to cancer, however, had increased slightly to 21.0%. The proportions of deaths due to chronic lower respiratory disease, diabetes, Alzheimer's, and suicide have increased. Interestingly, in 2019, HIV/AIDS accounted for <0.18% of all U.S. deaths. While unlikely to continue being a leading cause of death in the future, COVID-19 was also the cause for >600,000 deaths in 2020–2021, and the official figure is almost certainly an undercount of the actual death toll.

TABLE 12-1

Ten Leading Causes of Death in the United States and Britain

CAUSE OF DEATH	UNITED STATES (2019)		ENGLAND AND WALES (2019)	
	NUMBER OF DEATHS, ALL AGES (%)	NUMBER OF DEATHS, PEOPLE ≥65 YEARS OF AGE	NUMBER OF DEATHS, ALL AGES (%)	NUMBER OF DEATHS, PEOPLE ≥65 YEARS OF AGE
All deaths	2,854,838	2,117,332	530,841	449,047
Heart disease[a]	659,041 (23.1)	531,583 (25.1)	87,095 (16.4)	74,967 (16.7)
Malignant neoplasms	599,601 (21.0)	435,462 (20.6)	147,419 (27.8)	118,982 (26.5)
Chronic lower respiratory diseases	156,979 (5.5)	133,246 (6.3)	31,221 (5.9)	28,235 (6.3)
Accidents	173,040 (6.1)	60,527 (2.9)	15,141 (2.9)	8999 (2.0)
Cerebrovascular diseases	150,005 (5.3)	129,193 (6.1)	29,816 (5.6)	27,210 (6.0)
Alzheimer's disease	121,499 (4.3)	120,090 (5.7)	20,400 (3.8)	20,279 (4.5)
Diabetes mellitus	87,647 (3.1)	62,397 (2.9)	6528 (1.2)	5552 (1.2)
Influenza and pneumonia	49,783 (1.7)	40,399 (1.9)	26,398 (5.0)	24,269 (5.4)
Nephritis, nephritic syndrome, nephrosis	51,565 (1.8)	42,230 (2.0)	3575 (0.7)	3323 (0.7)
Intentional self-harm	47,511 (1.7)	—	4832 (0.9)	751 (0.2)

[a]Calculated using International Classification of Diseases codes I00–I09, I11, I13, I20–I51.

Source: National Center for Health Statistics (United States, 2019), *http://www.cdc.gov.kaplanmc.idm.oclc.org/nchs;* National Statistics (Great Britain, 2019), *http://www.statistics.gov.uk*.

This change in the epidemiology of death is also reflected in the costs of illness. In the United States, ~84% of all health care spending goes to patients with chronic illnesses, and 12% of total personal health care spending—slightly less than $400 billion in 2015—goes to the 0.83% of the population in the last year of their lives.

In upper-middle- and upper-income countries, an estimated 70% of all deaths are preceded by a disease or condition, making it reasonable to plan for dying in the foreseeable future. Cancer has served as the paradigm for terminal care, but it is not the only type of illness with a recognizable and predictable terminal phase. Since heart failure, chronic obstructive pulmonary disease (COPD), chronic liver failure, dementia, and many other conditions have recognizable terminal phases, a systematic approach to end-of-life care should be part of all medical specialties. Many patients with chronic illness–related symptoms and suffering also can benefit from palliative care regardless of prognosis. Ideally, palliative care should be considered part of comprehensive care for all chronically ill patients. Strong evidence demonstrates that palliative care can be improved by coordination between caregivers, doctors, and patients for advance care planning, as well as dedicated teams of physicians, nurses, and other

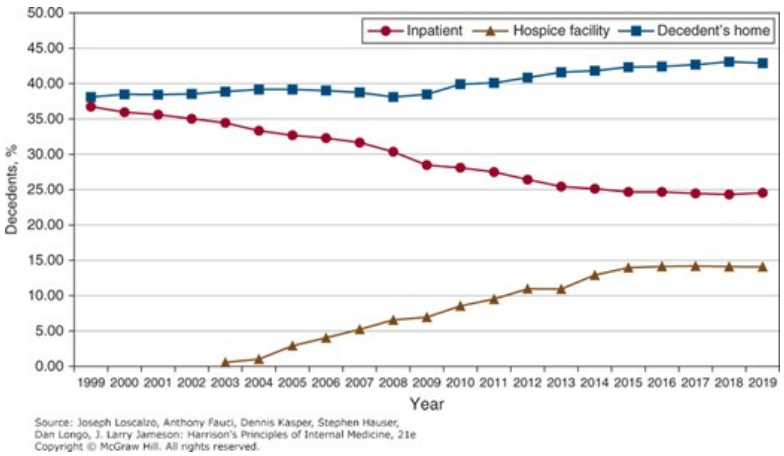
providers.

SITE OF DEATH

Where patients die varies by country. In Belgium and Canada, for instance, over half of all cancer patients still die in the hospital. The past few decades have seen a steady shift, both in the United States and other countries like the Netherlands, out of the hospital, as patients and their families list their own homes as the preferred site of death. In the early 1980s, ~70% of American cancer patients died in the hospital. Today, that percentage is ~25% (Fig. 12-1). A recent report shows that since 2000, there has been a shift in the United States from inpatient to home deaths, especially for patients with cancer, COPD, and dementia. For instance, among Medicare beneficiaries, 30.1% of deaths due to cancer in 2000 occurred in acute care hospitals; by 2009, this figure had dropped to 22.1%; by 2015, it was 19.8%.

FIGURE 12-1

Graph showing trends in cancer decedents' site of death 1999–2019. (*Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2019 on CDC WONDER Online Database. http://wonder.cdc.gov.kaplanmc.idm.oclc.org.*)



Paradoxically, while deaths in acute care hospitals have declined in the United States since 2000, both hospitalizations in the last 90 days of life and—even more troublingly—admission to the intensive care unit (ICU) in the last 30 days have actually increased. Over 40% of cancer patients in the United States are admitted to the ICU in their last 6 months of life, and >25% of cancer patients are admitted to the hospital in the last 30 days.

The shift in deaths out of the hospital has been accompanied by an increase in the use of hospice in the United States. In 2000, 21.6% of Medicare decedents used hospice at the time of death; by 2009, 42.2% were using hospice; and by 2018, 50.7% of Medicare decedents were enrolled in hospice at the time of death. Among cancer patients, ~60% were using hospice at the time of death. Hospice is also increasingly being used by noncancer patients. Today, cancer patients constitute ~20% of hospice users. But since 2014, the proportion of patients with other diagnoses using hospice has grown substantially, including those with circulatory/heart disease (17.4% in 2018 vs 13.8% in 2014), stroke (9.5% vs 6.2%), and respiratory disease (11.0% vs 9.4%). Of 2018 Medicare hospice decedents, 51.5% died at home, 17.4% in a nursing facility, 12.8% in a hospice inpatient facility, and 12.3% in assisted living.

Unfortunately, significant racial disparities exist in end-of-life care and the use of hospice, especially for noncancer deaths. Racial and ethnic minorities are less likely to receive hospice services than white decedents and are more likely to receive invasive or aggressive care in end-of-life treatment. Of people who died of head and neck cancers between 1999 and 2017, African Americans and Asians/Pacific Islanders were less likely to die at home or in hospice. Among Medicare beneficiaries who had a pancreatectomy for pancreatic cancer and lived at least 30 days, racial and ethnic minority patients remained 22% less likely than white patients to initiate hospice before death.

In 2008, for the first time, the American Board of Medical Specialties (ABMS) offered certification in hospice and palliative medicine. With the shortening of hospital stays, many serious conditions are now being treated at home or on an outpatient basis. Consequently, providing optimal palliative and end-of-life care requires ensuring that appropriate services are available in a variety of settings, including noninstitutional settings.

HOSPICE AND THE PALLIATIVE CARE FRAMEWORK

Central to this type of care is an interdisciplinary team approach that typically encompasses pain and symptom management, spiritual and psychological care for the patient, and support for family caregivers during the patient's illness and the bereavement period.

One of the more important changes in this field is beginning palliative care many months before death in order to focus on symptom relief and then switching to hospice in the patient's last few months. This approach avoids leaving hospice until the very end by introducing palliative care earlier, thereby allowing patients and families time to accommodate and transition. Phasing palliative care into end-of-life care means that patients will often receive palliative interventions long before they are formally diagnosed as terminally ill, or likely to die within 6 months.

Fundamental to ensuring quality palliative and end-of-life care is a focus on four broad domains: (1) physical symptoms; (2) psychological symptoms; (3) social needs that include interpersonal relationships, caregiving, and economic concerns; and (4) existential or spiritual needs.

ASSESSMENT AND CARE PLANNING

Comprehensive Assessment

Standardized methods for conducting a comprehensive assessment focus on evaluating the patient's condition in all four domains affected by the illness: physical, psychological, social, and spiritual.

A comprehensive assessment should follow a modified version of the traditional medical history and physical examination and should emphasize both physical and mental symptoms. Questions should aim to elucidate symptoms, discern sources of suffering, and gauge how much those symptoms interfere with the patient's quality of life. Standardized and repeated assessments to evaluate the effectiveness of interventions are critical. Thus, clinicians should use shorter, validated instruments, such as (1) the revised Edmonton Symptom Assessment Scale; (2) Condensed Memorial Symptom Assessment Scale (MSAS); (3) MD Anderson Brief Symptom Inventory; (4) Rotterdam Symptom Checklist; (5) Symptom Distress Scale; (6) Patient-Reported Outcomes Measurement Information System; and (7) Interactive Symptom Assessment and Collection (ISAAC) tool.

MENTAL HEALTH

With respect to mental health, many practices use the Patient Health Questionnaire-9 (PHQ-9) to screen for depression and the Generalized Anxiety Disorder-7 (GAD-7) to screen for anxiety. Using such tools ensures that the assessment is comprehensive and does not focus excessively on only pain.

INVASIVE TESTS

Invasive tests are best avoided in end-of-life care, and even minimally invasive tests should be evaluated carefully for their benefit-to-burden ratio for the patient. Aspects of the physical examination that are uncomfortable and unlikely to yield useful information that change patient management should be omitted.

SOCIAL NEEDS

Health care providers should also assess the status of important relationships, financial burdens, caregiving needs, and access to medical care. Relevant questions include the following: *How often is there someone to feel close to? How has this illness been for your family? How has it affected your relationships? How much help do you need with things like getting meals and getting around? How much trouble do you have getting the medical care you need?*

EXISTENTIAL NEEDS

To determine a patient's existential needs, providers should assess distress, the patient's sense of emotional and existential well-being, and whether the patient believes he or she has found purpose or meaning. Helpful assessment questions can include the following: *How much are you able to find meaning since your illness began? What things are most important to you at this stage?*

PERCEPTION OF CARE

In addition, it can be helpful to ask how the patient perceives his or her care: *How much do you feel your doctors and nurses respect you? How clear is the information from us about what to expect regarding your illness? How much do you feel that the medical care you are getting fits with your goals?* If

concern is detected in any of these areas, deeper evaluative questions are warranted.

Communication

Particularly when an illness is life-threatening, there exists the potential for many emotionally charged and potentially conflict-creating moments—collectively called "bad news" situations—in which empathic and effective communication skills are essential. Those moments include the sharing of a terminal diagnosis with the patient and/or family, the discussion of the patient's prognosis and any treatment failures, the consideration of deemphasizing efforts to cure and prolong life while focusing more on symptom management and palliation, advance care planning, and the patient's actual death. Although these conversations can be difficult, research indicates that end-of-life discussions can lead to earlier hospice referrals, rather than overly aggressive treatment, ultimately benefiting quality of life for patients and improving the bereavement process for families.

Just as surgeons prepare for major operations and investigators rehearse a presentation of research results, physicians and health care providers caring for patients with significant or advanced illnesses should develop a standardized approach for sharing important information and planning interventions. In addition, physicians must be aware that families often care not only about how prepared the physician was to deliver bad news, but also the setting in which it was delivered. For instance, one study found that 27% of families making critical decisions for patients in an ICU desired better and more private physical space to communicate with physicians.

One structured seven-step procedure for communicating bad news goes by the acronym P-SPIKES: (1) ***p***repare for the discussion, (2) ***s***et up a suitable environment, (3) begin the discussion by finding out what the ***p***atient and/or family understand, (4) determine how they will comprehend new ***i***nformation best and how much they want to know, (5) provide needed new ***k***nowledge accordingly, (6) allow for ***e***motional responses, and (7) ***s***hare plans for the next steps in care **(Table 12-2)**.

TABLE 12-2

Elements of Communicating Bad News—The P-SPIKES Approach

ACRONYM	STEPS	AIM OF THE INTERACTION	PREPARATIONS, QUESTIONS, OR PHRASES
P	Preparation	Mentally prepare for the interaction with the patient and/or family.	Review what information needs to be communicated. Plan how you will provide emotional support. Rehearse key steps and phrases in the interaction.
S	Setting of the interaction	Ensure the appropriate setting for a serious and potentially emotionally charged discussion.	Ensure that patient, family, and appropriate social supports are present. Devote sufficient time. Ensure privacy and prevent interruptions by people or beeper. Bring a box of tissues.
P	Patient's perception and preparation	Begin the discussion by establishing the baseline and whether the patient and family can grasp the information. Ease tension by having the patient and family contribute.	Start with open-ended questions to encourage participation. Possible questions to use: *What do you understand about your illness?* *When you first had symptom X, what did you think it might be?* *What did Dr. X tell you when he or she sent you here?* *What do you think is going to happen?*
I	Invitation and information needs	Discover what information needs the patient and/or family have and what limits they want regarding the bad information.	Possible questions to use: *If this condition turns out to be something serious, do you want to know?* *Would you like me to tell you all the details of your condition? If not, who would you like me to talk to?*
K	Knowledge of the condition	Provide the bad news or other information to the patient and/or family sensitively.	Do not just dump the information on the patient and family. Check for patient and family understanding. Possible phrases to use: *I feel badly to have to tell you this, but…* *Unfortunately, the tests showed…* *I'm afraid the news is not good…*
E	Empathy and exploration	Identify the cause of the emotions—e.g., poor prognosis. Empathize with the patient's and/or family's feelings. Explore by asking open-ended questions.	Strong feelings in reaction to bad news are normal. Acknowledge what the patient and family are feeling. Remind them such feelings are normal, even if frightening. Give them time to respond. Remind the patient and family you won't abandon them. Possible phrases to use: *I imagine this is very hard for you to hear.* *You look very upset. Tell me how you are feeling.* *I wish the news were different.* *We'll do whatever we can to help you.*
S	Summary and planning	Delineate for the patient and the family the next steps, including additional tests or interventions.	It is the unknown and uncertain that can increase anxiety. Recommend a schedule with goals and landmarks. Provide your rationale for the patient and/or family to accept (or reject). If the patient and/or family are not ready to discuss the next steps, schedule a follow-up visit.

Source: Adapted from R Buckman: *How to Break Bad News: A Guide for Health Care Professionals.* Baltimore, Johns Hopkins University Press, 1992.

Continuous Goal Assessment

Major barriers to providing high-quality palliative and end-of-life care include the difficulty in determining an accurate prognosis and the emotional resistance of patients and their families to accepting the implications of a poor prognosis. A practical solution to these barriers is to integrate palliative care interventions or home visits from a palliative care visiting nurse months before the estimated final 6 months of life. Under this approach, palliative care no longer conveys the message of failure, having no more treatments, or "giving up hope." The transition from palliative to end-of-life care or hospice also feels less hasty and unexpected to the family. Fundamental to integrating palliative care with curative therapy is the inclusion of a continuous goal assessment as part of the routine patient reassessments that occur at most patient-physician encounters.

Goals for care are numerous, ranging from curing a specific disease, to prolonging life, to relieving a particular symptom, to adapting to a progressive disability without disrupting the family, to finding peace of mind or personal meaning, to dying in a manner that leaves loved ones with positive memories. Discerning a patient's goals for care can be approached through a seven-step protocol: (1) ensure that medical and other information is as complete as reasonably possible and is understood by all relevant parties (see above); (2) explore what the patient and/or family is hoping for, while also identifying relevant and realistic goals; (3) share all the options with the patient and family; (4) respond with empathy as they adjust to changing expectations; (5) make a plan that emphasizes what can be done to achieve the realistic goals; (6) follow through with the plan; and (7) periodically review the plan and consider at every encounter whether the goals of care should be revised with the patient and/or family. Each of these steps need not be followed in rote order, but together they provide a helpful framework for interactions with patients and their families regarding their goals for care. Such interactions can be especially challenging if a patient or family member has difficulty letting go of an unrealistic goal. In such cases, the provider should help them refocus on more realistic goals and should also suggest that while it is fine to hope for the best, it is still prudent to plan for other outcomes as well.

Advance Care Planning

PRACTICES

Advance care planning is the process of planning for future medical care in case the patient becomes incapable of making medical decisions. A 2010 study of adults aged ≥60 who died between 2000 and 2006 found that while 42% of adults were required to make treatment decisions in their final days of life, 70% lacked decision-making capacity. Among those lacking decision-making capacity, approximately one-third did not have advance planning directives. Ideally, such planning would occur before a health care crisis or the terminal phase of an illness. Unfortunately, diverse barriers prevent this. Approximately 80% of Americans endorse advance care planning and living wills. However, according to a 2013 Pew survey, only 35% of adults have written down their end-of-life wishes. Other studies report that even fewer Americans—with some estimates as low as 26% of adults—have filled out advance care directives. A review of studies suggests that the percentage of Americans who had written advance directives did not change between 2011 and 2016 and remains slightly over one-third of Americans. Larger numbers of adults, between 50 and 70%, claim to have talked with someone about their treatment wishes. Americans aged 65 and older are more likely to complete an advance directive compared to younger adults (46% vs 32%).

Effective advance care planning should follow six key steps: (1) introducing the topic, (2) structuring a discussion, (3) reviewing plans that have been discussed by the patient and family, (4) documenting the plans, (5) updating them periodically, and (6) implementing the advance care directives **(Table 12-3)**. Two of the main barriers to advance care planning are problems in raising the topic and difficulty in structuring a succinct discussion. Raising the topic can be done efficiently as a routine matter, noting that it is recommended for all patients, analogous to purchasing insurance or estate planning. Many of the most difficult cases have involved unexpected, acute episodes of brain damage in young individuals.

TABLE 12-3

Steps in Advance Care Planning

STEP	GOALS TO BE ACHIEVED AND MEASURES TO COVER	USEFUL PHRASES OR POINTS TO MAKE
Introduce	Ask the patient what he or she	*I'd like to talk with you about something I try to discuss with all my patients. It's called advance*

advance care planning	knows about advance care planning and if he or she has already completed an advance care directive.	*care planning. In fact, I feel that this is such an important topic that I have done this myself. Are you familiar with advance care planning or living wills?*
	Indicate that you as a physician have completed advance care planning.	*Have you thought about the type of care you would want if you ever became too sick to speak for yourself? That is the purpose of advance care planning.*
	Indicate that you try to perform advance care planning with all patients regardless of prognosis.	*There is no change in health that we have not discussed. I am bringing this up now because it is sensible for everyone, no matter how well or ill, old or young.*
	Explain the goals of the process as empowering the patient and ensuring that you and the proxy understand the patient's preferences.	*Have many copies of advance care directives available, including in the waiting room, for patients and families.*
	Provide the patient relevant literature, including the advance care directive that you prefer to use.	*Know resources for state-specific forms (available at www.nhpco.org).*
	Recommend the patient identify a proxy decision-maker who should attend the next meeting.	
Have a structured discussion of scenarios with the patient	Affirm that the goal of the process is to follow the patient's wishes if the patient loses decision-making capacity.	*Use a structured worksheet with typical scenarios.*
	Elicit the patient's overall goals related to health care. Elicit the patient's preferences for specific interventions in a few salient and common scenarios. Help the patient define the threshold for withdrawing and withholding interventions. Define the patient's preference for the role of the proxy.	*Begin the discussion with persistent vegetative state and consider other scenarios, such as recovery from an acute event with serious disability; then ask the patient about his or her preferences regarding specific interventions, such as ventilators, artificial nutrition, and CPR; finally, proceeding to less invasive interventions, such as blood transfusions and antibiotics.*
Review the patient's preferences	After the patient has made choices of interventions, review them to ensure they are consistent and the proxy is aware of them.	
Document	Formally complete the advance	

the patient's preferences	care directive and have a witness sign it.	
	Provide a copy for the patient and the proxy.	
	Insert a copy into the patient's medical record and summarize it in a progress note.	
Update the directive	Periodically, and with major changes in health status, review the directive with the patient and make any modifications.	
Apply the directive	The directive goes into effect only when the patient becomes unable to make medical decisions for himself or herself.	
	Reread the directive to be sure about its content.	
	Discuss your proposed actions based on the directive with the proxy.	

Abbreviation: CPR, cardiopulmonary resuscitation.

Structuring a focused discussion is an important communication skill. To do so, a provider must first identify the health care proxy and recommend his or her involvement in the advance care planning process. Next, a worksheet must be selected that has been demonstrated to produce reliable and valid expressions of patient preferences, and the patient and proxy must be oriented to it. Such worksheets exist for both general and disease-specific situations. The provider should then discuss with the patient and proxy one example scenario to demonstrate how to think about the issues. It is often helpful to begin with a scenario in which the patient is likely to have settled preferences for care, such as being in a persistent vegetative state. Once the patient's preferences for interventions in this scenario are determined, the provider should suggest that the patient and proxy discuss and complete the worksheet for each other. If appropriate, the patient and proxy should consider involving other family members in the discussion. During a subsequent return visit, the provider should go over the patient's preferences, checking and resolving any inconsistencies. After having the patient and proxy sign the document, the provider should place the document in the patient's medical chart and make sure that copies are provided to relevant family members and care sites. Since patients' preferences can change, these documents must be reviewed periodically.

TYPES OF DOCUMENTS

Advance care planning documents are of two broad types. The first includes living wills, also known as instructional directives; these are advisory documents that describe the types of decisions that should direct a patient's care. Some are more specific, delineating different scenarios and interventions for the patient to choose from. Among these, some are for general use and others are designed for use by patients with a specific type of disease, such as cancer, renal failure, or HIV. Less specific directives can be general statements, such as not wanting life-sustaining interventions, or forms that describe the values that should guide specific discussions about terminal care. The second type of advance directive allows the designation of a health care proxy (sometimes also referred to as a durable attorney for health care), an individual selected by the patient to make decisions. The choice is not either/or; a combined directive that includes a living will and designates a proxy is often used, and the directive should indicate clearly whether the specified patient preferences or the proxy's choice takes precedence if they conflict. Some states have begun to put into practice a

"Physician Orders for Life-Sustaining Treatment (POLST)" directive, which builds on communication between providers and patients by including guidance for end-of-life care in a color-coordinated form that follows the patient across treatment settings. The procedures for completing advance care planning documents vary according to state law.

A potentially misleading distinction relates to statutory, as opposed to advisory, documents. Statutory documents are drafted to fulfill relevant state laws. Advisory documents are drafted to reflect the patient's wishes. Both are legal, the former under state law and the latter under common or constitutional law.

LEGAL ASPECTS

As of 2021, 48 states and the District of Columbia had enacted living will legislation. Massachusetts and Michigan are the two states without living will legislation. Indiana has a life-prolonging procedures declaration. States differ in the requirements for advanced directives, including whether they need to be witnessed and, if so, by how many witnesses and whether they need to be notarized. Importantly, in 25 states, the laws state that the living will is not valid if a woman is pregnant. All states except Alaska have enacted durable power of attorney for health care laws that permit patients to designate a proxy decision-maker with authority to terminate life-sustaining treatments. Only in Alaska does the law prohibit proxies from terminating life-sustaining treatments for pregnant women.

The U.S. Supreme Court has ruled that patients have a constitutional right to decide any issues related to refusing or terminating medical interventions, including life-sustaining interventions, and that mentally incompetent patients can exercise this right by providing "clear and convincing evidence" of their preferences. Since advance care directives permit patients to provide such evidence, commentators agree that they are constitutionally protected. Most commentators believe that a state is required to honor any clear advance care directive, regardless of whether it is written on an "official" form. Many states have enacted laws for the explicit purpose of honoring out-of-state directives. If a patient is not using a statutory form, it may be advisable to attach a statutory form to the advance care directive being used. State-specific forms are readily available free of charge for health care providers, patients, and families through the website of the National Hospice and Palliative Care Organization (*http://www.nhpco.org*).

REIMBURSEMENT

As of January 1, 2016, the Centers for Medicare and Medicaid Services amended the physician fee schedule to reimburse discussions of advance care planning under Current Procedural Terminology codes 99497 and 99498. The session must be voluntary and include an explanation of advance care planning but need not include a completed advance care document. There can be multiple bills for the discussion if it extends over several encounters. A study found that patients who engaged in a billed advance care planning encounter were more likely to be enrolled in hospice and less likely to receive intensive therapies, despite being more likely to be hospitalized in the ICU. However, a billing incentive in and of itself may not increase advance care planning discussions by clinicians. In 2016, just 1.6% of Medicare Advantage patients had a discussion of advance care planning that was billed. Factors beyond reimbursement, such as clinicians' lack of comfort and skill in carrying out advance care planning discussions and lack of time, appear to impede discussions of advance care planning.

INTERVENTIONS

PHYSICAL SYMPTOMS AND THEIR MANAGEMENT

Great emphasis has been placed on addressing dying patients' pain. In order to emphasize its importance, pain assessment has frequently been included as the fifth vital sign. Heightened consideration of pain has been advocated by large health care systems such as the Veterans' Administration and accrediting bodies such as The Joint Commission. Although this embrace of pain has been symbolically important, available data suggest that making pain the fifth vital sign does not lead to improved pain management practices. In light of the opioid crisis in the United States, the emphasis on pain management has begun to be reexamined. For instance, in 2017 draft standards, The Joint Commission recommends nonpharmacologic pain treatment as well as identification of psychosocial risk factors for addiction. Importantly, good palliative care requires much more than good pain management. The frequency of symptoms varies by disease and other factors. The most common physical and psychological symptoms among all terminally ill patients include pain, fatigue, insomnia, anorexia, dyspnea, depression, anxiety, nausea, and vomiting. In the last days of life, terminal delirium is also common. Assessments of patients with advanced cancer have shown that patients experienced an average of 11.5 different physical and psychological symptoms **(Table 12-4)**.

TABLE 12-4

Common Physical and Psychological Symptoms of Terminally Ill Patients

PHYSICAL SYMPTOMS	PSYCHOLOGICAL SYMPTOMS
Pain	Anxiety
Fatigue and weakness	Depression
Dyspnea	Hopelessness
Insomnia	Meaninglessness
Dry mouth	Irritability
Anorexia	Impaired concentration
Nausea and vomiting	Confusion
Constipation	Delirium
Cough	Loss of libido
Swelling of arms or legs	
Itching	
Diarrhea	
Dysphagia	
Dizziness	
Fecal and urinary incontinence	
Numbness/tingling in hands/feet	

In the vast majority of cases, evaluations to determine the etiology of these symptoms should be limited to the history and physical examination. In some cases, radiologic or other diagnostic examinations will provide sufficient benefit in directing optimal palliative care to warrant the risks, potential discomfort, and inconvenience, especially to a seriously ill patient. Only a few of the common symptoms that present difficult management issues will be addressed in this chapter. **Additional information on the management of other symptoms, such as nausea and vomiting, insomnia, and diarrhea, can be found in Chaps. 45, 31, and 46, respectively. Information on the management of patients with cancer is provided in Chap. 69.**

Pain

FREQUENCY

The frequency of pain among terminally ill patients varies significantly. Cancer (~85%), congestive heart failure (CHF; ~75%), and AIDS have been associated with a higher prevalence of pain compared to other advanced illnesses, such as COPD (~45%), chronic kidney disease (~40%), and dementia

(~40%). One meta-analysis of adults with advanced or terminal illness found pain prevalence of 30–94% in patients with cancer, compared to 21–77% for COPD, 14–78% for CHF, 11–83% for end-stage renal disease, 14–63% for dementia, and 30–98% for AIDS.

ETIOLOGY

There are two types of pain: nociceptive and neuropathic. Nociceptive pain is further divided into somatic or visceral pain. *Somatic pain* is the result of direct mechanical or chemical stimulation of nociceptors and normal neural signaling to the brain. It tends to be localized, aching, throbbing, and cramping. The classic example is bone metastases. *Visceral pain* is caused by nociceptors in gastrointestinal (GI), respiratory, and other organ systems. It is a deep or colicky type of pain classically associated with pancreatitis, myocardial infarction, or tumor invasion of viscera. *Neuropathic pain* arises from disordered nerve signals. It is described by patients as burning, electrical, or shock-like pain. Classic examples are post-stroke pain, tumor invasion of the brachial plexus, and herpetic neuralgia.

ASSESSMENT

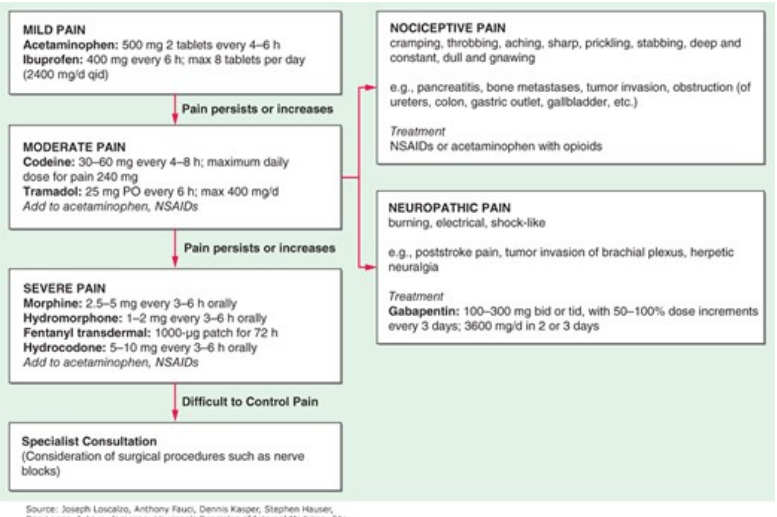
Pain is a subjective experience. Depending on the patient's circumstances, perspective, and physiologic condition, the same physical lesion or disease state can produce different levels of reported pain and need for pain relief. Systematic assessment includes eliciting the following: (1) type: throbbing, cramping, burning, etc.; (2) periodicity: continuous, with or without exacerbations, or incident; (3) location; (4) intensity; (5) modifying factors; (6) effects of treatments; (7) functional impact; and (8) impact on patient. Several validated pain assessment measures may be used, including the Visual Analogue Scale (VAS), the Brief Pain Inventory (BPI), or the Numerical Pain Rating Scale (NRS-11). Other scales have been developed for neuropathic pain, such as the Neuropathic Pain Scale and the DN4 Questionnaire. Frequent reassessments on a consistent scale are essential to assess the impact of and need to readjust interventions.

INTERVENTIONS

Interventions for pain must be tailored to each individual, with the goal of preempting chronic pain and relieving breakthrough pain. At the end of life, there is rarely reason to doubt a patient's report of pain. With the opioid crisis in the United States, there is more emphasis on making opioids one component of multimodal analgesia. Nevertheless, at the end of life, pain medications, especially opioids, remain the cornerstone of management (Fig. 12-2). If they are failing and nonpharmacologic interventions—including radiotherapy and anesthetic or neurosurgical procedures such as peripheral nerve blocks or epidural medications—are required, a pain consultation is appropriate.

FIGURE 12-2

Terminal pain management flow chart. NSAIDs, nonsteroidal anti-inflammatory drugs.



Source: Joseph Loscalzo, Anthony Fauci, Dennis Kasper, Stephen Hauser, Dan Longo, J. Larry Jameson: Harrison's Principles of Internal Medicine, 21e

Pharmacologic interventions still largely follow the World Health Organization three-step, "analgesic ladder" approach, which involves nonopioid analgesics, "mild" opioids, and "strong" opioids, with or without adjuvants (Chap. 13). Nonopioid analgesics, especially nonsteroidal anti-inflammatory drugs (NSAIDs), are the initial treatments for mild pain. They work primarily by inhibiting peripheral prostaglandins and reducing

inflammation but may also have central nervous system (CNS) effects. Additionally, NSAIDs have a ceiling effect. Ibuprofen, up to 2400 mg/d qid, has a minimal risk of causing bleeding and renal impairment and is a good initial choice. In patients with a history of severe GI or other bleeding, however, ibuprofen should be avoided. In patients with a history of mild gastritis or gastroesophageal reflux disease (GERD), acid-lowering therapy, such as a proton pump inhibitor, should be used. Acetaminophen is an alternative in patients with a history of GI bleeding and can be used safely at up to 4 g/d qid. In patients with liver dysfunction due to metastases or other causes and in patients with heavy alcohol use, doses should be reduced.

If nonopioid analgesics are insufficient, opioids should be introduced. Opioids primarily work by interacting with μ opioid receptors to activate pain-inhibitory neurons in the CNS, although they also interact variably with δ and κ receptors. Receptor agonists, such as morphine, codeine, and fentanyl, produce analgesia by activating pain-inhibitory neurons in the CNS. Partial agonists, such as buprenorphine, have a ceiling effect for analgesia and a lower potential for abuse. They are useful for postacute pain but should not be used for chronic pain in end-of-life care. Pure antagonists, such as naloxone and methylnaltrexone, are used for reversal of opioid effects.

Traditionally, "weak" opioids such as codeine were used first. If they failed to relieve pain after dose escalation, "strong" opioids like morphine were used in doses of 5–10 mg every 4 h. However, this breakdown between "weak" and "strong" opioids is no longer commonly accepted, with smaller doses of "stronger" opioids frequently being preferred over similar or larger doses of "weaker" opioids, and different pain syndromes having different preferred therapies. Regardless, nonopioid analgesics should be combined with opioids, as they potentiate the effect of opioids.

Importantly, the goal is to prevent patients from experiencing pain. Consequently, for continuous pain, opioids should be administered on a regular, around-the-clock basis consistent with their duration of analgesia, and the next dose should occur before the effect of the previous dose wears off. They should not be provided only when the patient experiences pain. Patients should also be provided rescue medication, such as liquid morphine, for breakthrough pain, generally at 20% of the baseline dose. Patients should be informed that using the rescue medication does not obviate the need to take the next standard dose of pain medication. If the patient's pain remains uncontrolled after 24 h and recurs before the next dose, requiring the patient to utilize the rescue medication, the daily opioid dose can be increased by the total dose of rescue medications used by the patient, or by 50% of the standing opioid daily dose for moderate pain and 100% for severe pain.

It is inappropriate to start with extended-release preparations. Instead, an initial focus on using short-acting preparations to determine how much is required in the first 24–48 h will allow clinicians to determine opioid needs. Once pain relief is obtained using short-acting preparations, the switch should be made to extended-release preparations. Even with a stable extended-release preparation regimen, the patient may experience incident pain, such as during movement or dressing changes. Short-acting preparations should be taken before such predictable episodes. Although less common, patients may have "end-of-dose failure" with long-acting opioids, meaning that they develop pain after 8 h in the case of an every-12-h medication. In these cases, a trial of giving an every-12-h medication every 8 h is appropriate.

Due to differences in opioid receptors, cross-tolerance among opioids is incomplete, and patients may experience different side effects with different opioids. Therefore, if a patient is not experiencing pain relief or is experiencing too many side effects, a change to another opioid preparation is appropriate. When switching, one should begin with 50–75% of the published equianalgesic dose of the new opioid.

Unlike NSAIDs, opioids have no ceiling effect; therefore, there is no maximum dose, no matter how many milligrams the patient is receiving. The appropriate dose is the dose needed to achieve pain relief. This is an important point for clinicians to explain to patients and families. Addiction or excessive respiratory depression is extremely unlikely in the terminally ill; fear of these side effects should neither prevent escalating opioid medications when the patient is experiencing insufficient pain relief nor justify using opioid antagonists.

Opioid side effects should be anticipated and treated preemptively. Nearly all patients experience constipation that can be debilitating (see below). Failure to prevent constipation often results in noncompliance with opioid therapy. The preferred treatment is prevention. Cathartics (senna 2 tbsp qHS), stool softeners (docusate 100 mg PO qd), and/or laxatives (laxtulose 30 mL qd) are considered first-line treatment. For refractory cases, opioid antagonists or other therapies, such as lubiprostone, should be considered.

Methylnaltrexone is the best-studied opioid antagonist for use in refractory opioid-induced constipation. It reverses opioid-induced constipation by blocking peripheral opioid receptors, but not central receptors, for analgesia. In placebo-controlled trials, it has been shown to cause laxation within 24 h of administration. As with the use of opioids, about a third of patients using methylnaltrexone experience nausea and vomiting, but unlike with opioid usage, tolerance usually develops within a week. Therefore, when one is beginning opioids, an antiemetic such as metoclopramide or a serotonin antagonist is often prescribed prophylactically and stopped after 1 week. Olanzapine has also been shown to have antinausea properties and can be effective in countering delirium or anxiety, with the advantage of some weight gain.

Drowsiness, a common side effect of opioids, also usually abates within a week. For refractory or severe cases, pharmacologic therapy should be considered. The best-studied agents are the psychostimulants dextroamphetamine, methylphenidate, and modafinil, although evidence regarding their efficacy is weak. Modafinil has the advantage of once-a-day dosing compared to methyphenidate's twice daily dosing.

Seriously ill patients who require chronic pain relief rarely become addicted. Suspicion of addiction should not be a reason to withhold pain medications from terminally ill patients. Nonetheless, patients and families may withhold prescribed opioids for fear of addiction or dependence. Physicians and health care providers should reassure patients and families that the patient will not become addicted to opioids if they are used as prescribed for pain relief; this fear should not prevent the patient from taking the medications around the clock. However, diversion of drugs for use by other family members or illicit sale may occur. It may be necessary to advise the patient and caregiver about secure storage of opioids. Contract writing with the patient and family can help. If that fails, transfer to a safe facility may be necessary.

Tolerance describes the need to increase medication dosage for the same pain relief without a concurrent change in disease. In the case of patients with advanced disease, the need for increasing opioid dosage for pain relief usually is caused by disease progression rather than tolerance. Physical dependence is indicated by symptoms resulting from the abrupt withdrawal of opioids and should not be confused with addiction.

In recent years, the potential dangers of opioid drugs have become increasingly apparent. To help mitigate the risk of these powerful drugs, several strategies should be used to reduce the risk of aberrant drug use. To start, all patients should be assessed for their individual levels of risk. While there are multiple surveys available, including the Opioid Risk Tool, none have gained widespread use or validation. In general, however, it is important to screen for prior substance abuse and major psychiatric disorders.

For patients deemed to be high risk, a multidisciplinary effort should be pursued to reduce the risk of adverse consequences, such as addiction and diversion. Prescribing strategies include selecting opioids with longer durations of action and lower street values, such as methadone, and prescribing smaller quantities with more frequent follow-up. Monitoring options include periodic urine screening and referral to pain specialists. In some cases, it may also be reasonable to consider not offering short-acting opioids for breakthrough pain. In no situation, however, should adequate pain relief be withheld due to risk.

Adjuvant analgesic medications are nonopioids that potentiate the analgesic effects of opioids. They are especially important in the management of neuropathic pain. Gabapentin, an anticonvulsant initially studied in the setting of herpetic neuralgia, is now the first-line treatment for neuropathic pain resulting from a variety of causes. It is begun at 100–300 mg bid or tid, with 50–100% dose increments every 3 days. Usually 900–3600 mg/d in two or three doses is effective. The combination of gabapentin and nortriptyline may be more effective than gabapentin alone. Two potential side effects of gabapentin to be aware of are confusion and drowsiness, especially in the elderly. Other effective adjuvant medications include pregabalin, which has the same mechanism of action as gabapentin but is absorbed more efficiently from the GI tract. Lamotrigine is a novel agent whose mechanism of action is unknown but has been shown to be effective. It is recommended to begin at 25–50 mg/d, increasing to 100 mg/d. Carbamazepine, a first-generation agent, has been proven effective in randomized trials for neuropathic pain. Other potentially effective anticonvulsant adjuvants include topiramate (25–50 mg qd or bid, rising to 100–300 mg/d) and oxcarbazepine (75–300 mg bid, rising to 1200 mg bid).

Glucocorticoids, preferably dexamethasone given once a day, can be useful in reducing inflammation that causes pain, while also elevating mood, energy, and appetite. Its main side effects include confusion, sleep difficulties, and fluid retention. Glucocorticoids are especially effective for bone pain and abdominal pain from distention of the GI tract or liver. Other drugs, including clonidine and baclofen, can be effective in providing pain relief. These drugs are adjuvants and generally should be used in conjunction with—not instead of—opioids. Methadone, carefully dosed because of its unpredictable half-life in many patients, has activity at the *N*-methyl-D-aspartamate (NMDA) receptor and is useful for complex pain syndromes and neuropathic pain. It is generally reserved for cases in which first-line opioids (morphine, oxycodone, hydromorphone) are either ineffective or unavailable.

Radiation therapy can treat bone pain from single metastatic lesions. Bone pain from multiple metastases can be amenable to radiopharmaceuticals such as strontium-89 and samarium-153. Bisphosphonates, such as pamidronate (90 mg every 4 weeks) and calcitonin (200 IU intranasally once or twice a day), also provide relief from bone pain but have multiday onsets of action.

Constipation

FREQUENCY

Constipation is reported in up to 70–100% of patients requiring palliative care.

ETIOLOGY

Although hypercalcemia and other factors can cause constipation, it is most frequently a predictable consequence of the use of opioids for pain and dyspnea relief and of the anticholinergic effects of tricyclic antidepressants, as well as due to the inactivity and poor diets common among seriously ill patients. If left untreated, constipation can cause substantial pain and vomiting and also is associated with confusion and delirium. Whenever opioids and other medications known to cause constipation are used, preemptive treatment for constipation should be instituted.

ASSESSMENT

Assessing constipation can be difficult because people describe it differently. Four commonly used assessment scales are the Bristol Stool Form Scale, the Constipation Assessment Scale, the Constipation Visual Analogue Scale, and the Eton Scale Risk Assessment for Constipation. The Bowel Function Index can be used to quantify opioid-induced constipation. The physician should establish the patient's previous bowel habits, as well as any changes in subjective and objective qualities such as bloating or decreased frequency. Abdominal and rectal examinations should be performed to exclude impaction or an acute abdomen. Radiographic assessments beyond a simple flat plate of the abdomen in cases in which obstruction is suspected are rarely necessary.

INTERVENTION

Any measure to address constipation during end-of-life care should include interventions to reestablish comfortable bowel habits and to relieve pain or discomfort. Although physical activity, adequate hydration, and dietary treatments with fiber can be helpful, each is limited in its effectiveness for most seriously ill patients, and fiber may exacerbate problems in the setting of dehydration or if impaired motility is the etiology. Fiber is contraindicated in the presence of opioid use. Stimulant and osmotic laxatives, stool softeners, fluids, and enemas are the mainstays of therapy **(Table 12-5)**. To prevent constipation from opioids and other medications, a combination of a laxative and a stool softener (such as senna and docusate) should be used. If after several days of treatment a bowel movement has not occurred, a rectal examination to remove impacted stool and place a suppository is necessary. For patients with impending bowel obstruction or gastric stasis, octreotide to reduce secretions can be helpful. For patients in whom the suspected mechanism is dysmotility, metoclopramide can be helpful.

TABLE 12-5

Medications for the Management of Constipation

INTERVENTION	DOSE	COMMENT
Stimulant laxatives		These agents directly stimulate peristalsis and may reduce colonic absorption of water.
Prune juice	120–240 mL/d	Work in 6–12 h.
Senna (Senokot)	2–8 tablets PO bid	
Bisacodyl	5–15 mg/d PO, PR	
Osmotic laxatives		These agents are not absorbed. They attract and retain water in the gastrointestinal tract.
Lactulose	15–30 mL PO q4–8h	Lactulose may cause flatulence and bloating.
Magnesium hydroxide (Milk of Magnesia)	15–30 mL/d PO	Lactulose works in 1 day, magnesium products in 6 h.
Magnesium citrate	125–250 mL/d PO	
Stool softeners		These agents work by increasing water secretion and as detergents, increasing water penetration into the stool.
Sodium docusate (Colace)	300–600 mg/d PO	Work in 1–3 days.
Calcium docusate	300–600 mg/d PO	
Suppositories and enemas		
Bisacodyl	10–15 PR qd	
Sodium phosphate enema	PR qd	Fixed dose, 4.5 oz, Fleet's.

Nausea

FREQUENCY

Up to 70% of patients with advanced cancer have nausea, defined as the subjective sensation of wanting to vomit.

ETIOLOGY

Nausea and vomiting are both caused by stimulation at one of four sites: the GI tract, the vestibular system, the chemoreceptor trigger zone (CTZ), and

the cerebral cortex. Medical treatments for nausea are aimed at receptors at each of these sites: the GI tract contains mechanoreceptors, chemoreceptors, and 5-hydroxytryptamine type 3 (5-HT_3) receptors; the vestibular system probably contains histamine and acetylcholine receptors; and the CTZ contains chemoreceptors, dopamine type 2 receptors, and 5-HT3 receptors. An example of nausea that most likely is mediated by the cortex is anticipatory nausea before a dose of chemotherapy or other noxious stimuli.

Specific causes of nausea include metabolic changes (liver failure, uremia from renal failure, hypercalcemia), bowel obstruction, constipation, infection, GERD, vestibular disease, brain metastases, medications (including antibiotics, NSAIDs, proton pump inhibitors, opioids, and chemotherapy), and radiation therapy. Anxiety can also contribute to nausea.

INTERVENTION

Medical treatment of nausea is directed at the anatomic and receptor-mediated cause revealed by a careful history and physical examination. When no specific cause of nausea is identified, many advocate beginning treatment with metoclopramide; a serotonin type 3 (5-HT_3) receptor antagonist such as ondansetron, granisetron, palonosetron, dolasetron, tropisetron, or ramosetron; or a dopamine antagonist such as chlorpromazine, haloperidol, or prochlorperazine. When decreased motility is suspected, metoclopramide can be an effective treatment. When inflammation of the GI tract is suspected, glucocorticoids, such as dexamethasone, are an appropriate treatment. For nausea that follows chemotherapy and radiation therapy, one of the 5-HT_3 receptor antagonists or neurokinin-1 antagonists, such as aprepitant or fosaprepitant, is recommended. Clinicians should attempt prevention of postchemotherapy nausea, rather than simply providing treatment after the fact. Current clinical guidelines recommend tailoring the strength of treatments to the specific emetic risk posed by a specific chemotherapy drug. When a vestibular cause (such as “motion sickness” or labyrinthitis) is suspected, antihistamines, such as meclizine (whose primary side effect is drowsiness), or anticholinergics, such as scopolamine, can be effective. In anticipatory nausea, patients can benefit from nonpharmacologic interventions, such as biofeedback and hypnosis. The most common pharmacologic intervention for anticipatory nausea is a benzodiazepine, such as lorazepam. As with antihistamines, drowsiness and confusion are the main side effects.

The use of medical marijuana or oral cannabinoids for palliative treatment of nausea is controversial, as there are no controlled trials showing its effectiveness for patients at the end of life. A 2015 meta-analysis showed “low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy,” and such treatments are not as good as 5-HT_3 receptor antagonists and can sometimes even cause cannabis hyperemesis syndrome. Older patients, who compose the vast majority of dying patients, seem to tolerate cannabinoids poorly.

Dyspnea

FREQUENCY

Dyspnea is the subjective experience of being short of breath. Over 50%, and as many as 75%, of dying patients, especially those with lung cancer, metastases to the lung, CHF, and COPD, experience dyspnea at some point near the end of life. Dyspnea is among the most distressing of physical symptoms and can be even more distressing than pain.

ASSESSMENT

As with pain, dyspnea is a subjective experience that may not correlate with objective measures of P_{O_2}, P_{CO_2}, or respiratory rate. Consequently, measurements of oxygen saturation through pulse oximetry or blood gases are rarely helpful in guiding therapy. Despite the limitations of existing assessment methods, physicians should regularly assess and document patients’ experience of dyspnea and its intensity. Guidelines recommend visual analogue dyspnea scales to assess the severity of symptoms and the effects of treatment. Potentially reversible or treatable causes of dyspnea include infection, pleural effusions, pulmonary emboli, pulmonary edema, asthma, and tumor encroachment on the airway. However, the risk-versus-benefit ratio of the diagnostic and therapeutic interventions for patients with little time left to live must be considered carefully before undertaking diagnostic steps. Frequently, the specific etiology cannot be identified, and dyspnea is the consequence of progression of the underlying disease that cannot be treated. The anxiety caused by dyspnea and the choking sensation can significantly exacerbate the underlying dyspnea in a negatively reinforcing cycle.

INTERVENTIONS

When reversible or treatable etiologies are diagnosed, they should be treated as long as the side effects of treatment, such as repeated drainage of effusions or anticoagulants, are less burdensome than the dyspnea itself. More aggressive treatments such as stenting a bronchial lesion may be warranted if it is clear that the dyspnea is due to tumor invasion at that site and if the patient and family understand the risks of such a procedure.

Usually, treatment will be symptomatic **(Table 12-6)**. Supplemental oxygen does not appear to be effective. "A systematic review of the literature failed to demonstrate a consistent beneficial effect of oxygen inhalation over air inhalation for study participants with dyspnea due to end-stage cancer or cardiac failure." Therefore, oxygen may be no more than an expensive placebo. Low-dose opioids reduce the sensitivity of the central respiratory center and relieve the sensation of dyspnea. If patients are not receiving opioids, weak opioids can be initiated; if patients are already receiving opioids, morphine or other stronger opioids should be used. Controlled trials do not support the use of nebulized opioids for dyspnea at the end of life. Phenothiazines and chlorpromazine may be helpful when combined with opioids. Benzodiazepines can be helpful in treating dyspnea, but only if anxiety is present. Benzodiazepines should not be used as first-line therapy or if there is no anxiety. If the patient has a history of COPD or asthma, inhaled bronchodilators and glucocorticoids may be helpful. If the patient has pulmonary edema due to heart failure, diuresis with a medication such as furosemide is indicated. Excess secretions can be transdermally or intravenously dried with scopolamine. More general interventions that medical staff can perform include sitting the patient upright, removing smoke or other irritants like perfume, ensuring a supply of fresh air with sufficient humidity, and minimizing other factors that can increase anxiety.

TABLE 12-6

Medications for the Management of Dyspnea

INTERVENTION	DOSE	COMMENTS
Weak opioids		For patients with mild dyspnea
Codeine (or codeine with 325 mg acetaminophen)	30 mg PO q4h	For opioid-naïve patients
Hydrocodone	5 mg PO q4h	
Strong opioids		For opioid-naïve patients with moderate to severe dyspnea
Morphine	5–10 mg PO q4h	For patients already taking opioids for pain or other symptoms
	30–50% of baseline opioid dose q4h	
Oxycodone	5–10 mg PO q4h	
Hydromorphone	1–2 mg PO q4h	
Anxiolytics		Give a dose every hour until the patient is relaxed; then provide a dose for maintenance
Lorazepam	0.5–2.0 mg PO/SL/IV qh then q4–6h	
Clonazepam	0.25–2.0 mg PO q12h	
Midazolam	0.5 mg IV q15min	

Fatigue

FREQUENCY

Fatigue is one of the most commonly reported symptoms not only of cancer treatment but also of the palliative care of multiple sclerosis, COPD, heart failure, and HIV. More than 90% of terminally ill patients experience fatigue and/or weakness. Fatigue is frequently cited as one of the most distressing symptoms in these patients.

ETIOLOGY

The multiple causes of fatigue in the terminally ill can be categorized as resulting from the underlying disease; from disease-induced factors such as tumor necrosis factor and other cytokines; and from secondary factors such as dehydration, anemia, infection, hypothyroidism, and drug side effects. In addition to low caloric intake, loss of muscle mass and changes in muscle enzymes may play an important role in fatigue during terminal illness. The importance of changes in the CNS, especially the reticular activating system, have been hypothesized based on reports of fatigue in patients receiving cranial radiation, experiencing depression, or having chronic pain in the absence of cachexia or other physiologic changes. Finally, depression and other causes of psychological distress can contribute to fatigue.

ASSESSMENT

Like pain and dyspnea, fatigue is subjective, as it represents a patient's sense of tiredness and decreased capacity for physical work. Objective changes, even in body mass, may be absent. Consequently, assessment must rely on patient self-reporting. Scales used to measure fatigue, such as the Edmonton Functional Assessment Tool, the Fatigue Self-Report Scales, and the Rhoten Fatigue Scale, are usually appropriate for research but not clinical purposes. In clinical practice, a simple performance assessment such as the Karnofsky performance status or the Eastern Cooperative Oncology Group (ECOG)'s question "How much of the day does the patient spend in bed?" may be the best measure. In the ECOG 0–4 performance status assessment, 0 = normal activity; 1 = symptomatic without being bedridden; 2 = requiring some, but <50%, bed time; 3 = bedbound more than half the day; and 4 = bedbound all the time. Such a scale allows for assessment over time and correlates with overall disease severity and prognosis. A 2008 review by the European Association of Palliative Care also described several longer assessment tools that contained 9–20 items, including the Piper Fatigue Inventory, the Multidimensional Fatigue Inventory, and the Brief Fatigue Inventory (BFI).

INTERVENTIONS

Reversible causes of fatigue, such as anemia and infection, should be treated. However, at the end of life, it must be realistically acknowledged that fatigue will not be "cured." The goal is to ameliorate fatigue and help patients and families adjust expectations. Behavioral interventions should be utilized to avoid blaming the patient for inactivity and to educate both the family and the patient that the underlying disease causes physiologic changes that produce low energy levels. Understanding that the problem is physiologic and not psychological can help alter expectations regarding the patient's level of physical activity. Practically, this may mean reducing routine activities such as housework, cooking, and social events outside the house and making it acceptable to receive guests while lying on a couch. At the same time, the implementation of exercise regimens and physical therapy can raise endorphins, reduce muscle wasting, and decrease the risk of depression. In addition, ensuring good hydration without worsening edema may help reduce fatigue. Discontinuing medications that worsen fatigue may help, including cardiac medications, benzodiazepines, certain antidepressants, or opioids if the patient's pain is well-controlled. As end-of-life care proceeds into its final stages, fatigue may protect patients from further suffering, and continued treatment could be detrimental.

Only a few pharmacologic interventions target fatigue and weakness. Randomized controlled trials suggest glucocorticoids can increase energy and enhance mood. Dexamethasone (8 mg/d) is preferred for its once-a-day dosing and minimal mineralocorticoid activity. Benefit, if any, is usually seen within the first month. For fatigue related to anorexia, megestrol (480–800 mg) can be helpful. Psychostimulants such as dextroamphetamine (5–10 mg PO) and methylphenidate (2.5–5 mg PO) may enhance energy levels, although controlled trials have not shown these drugs to be effective for fatigue induced by mild to moderate cancer. Doses should be given in the morning and at noon to minimize the risk of counterproductive insomnia. Modafinil and armodafinil, developed for narcolepsy, have shown promise in the treatment of fatigue and have the advantage of once-daily dosing. Their precise role in fatigue at the end of life has not been documented but may be worth trying if other interventions are not beneficial. Anecdotal evidence suggests that L-carnitine may improve fatigue, depression, and sleep disruption.

PALLIATIVE SEDATION

Palliative sedation is used in distressing situations that cannot be addressed in other ways. When patients experience severe symptoms, such as pain or dyspnea, that cannot be relieved by conventional interventions or experience acute catastrophic symptoms, such as uncontrolled seizures, then palliative sedation should be considered as an intervention of last resort. It can be abused if done to hasten death (which it usually does not), when done at the request of the family rather than according to the patient's wishes, or when there are other interventions that could still be tried. The use of palliative sedation in cases of extreme existential or spiritual distress remains controversial. Typically, palliative sedation should be introduced only after the patient and family have been assured that all other interventions have been tried and after the patient and their loved ones have been able to "say goodbye."

Palliative sedation can be achieved by significantly increasing opioid doses until patients become unconscious and then putting them on a continuous infusion. Another commonly used medication for palliative sedation is midazolam at 1–5 mg IV every 5–15 min to calm the patient, followed by a continuous IV or subcutaneous infusion of 1 mg/h. In hospital settings, a continuous propofol infusion of 5 μg/kg per min can be used. There are also other, less commonly used medications for palliative sedation that include levomepromazine, chlorpromazine, and phenobarbital.

PSYCHOLOGICAL SYMPTOMS AND THEIR MANAGEMENT

Depression

FREQUENCY AND IMPACT

Depression at the end of life presents an apparently paradoxical situation. Many people believe that depression is normal among seriously ill patients because they are dying. People frequently say, "Wouldn't you be depressed?" Although sadness, anxiety, anger, and irritability are normal responses to a serious condition, they are typically of modest intensity and transient. Persistent sadness and anxiety and the physically disabling symptoms that they can lead to are abnormal and suggestive of major depression. The precise number of terminally ill patients who are depressed is uncertain, primarily due to a lack of consistent diagnostic criteria and screening. Careful follow-up of patients suggests that while as many as 75% of terminally ill patients experience depressive symptoms, ~25% of terminally ill patients have major depression. Depression at the end of life is concerning because it can decrease the quality of life, interfere with closure in relationships and other separation work, obstruct adherence to medical interventions, and amplify the suffering associated with pain and other symptoms.

ETIOLOGY

Previous history of depression, family history of depression or bipolar disorder, and prior suicide attempts are associated with increased risk for depression among terminally ill patients. Other symptoms, such as pain and fatigue, are associated with higher rates of depression; uncontrolled pain can exacerbate depression, and depression can cause patients to be more distressed by pain. Many medications used in the terminal stages, including glucocorticoids, and some anticancer agents, such as tamoxifen, interleukin 2, interferon α, and vincristine, also are associated with depression. Some terminal conditions, such as pancreatic cancer, certain strokes, and heart failure, have been reported to be associated with higher rates of depression, although this is controversial. Finally, depression may be attributable to grief over the loss of a role or function, social isolation, or loneliness.

ASSESSMENT

Unfortunately, many studies suggest that most depressed patients at the end of life are not diagnosed, or if they are diagnosed, they are not properly treated. Diagnosing depression among seriously ill patients is complicated, as many of the vegetative symptoms in the *DSM-V* (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*) criteria for clinical depression—insomnia, anorexia and weight loss, fatigue, decreased libido, and difficulty concentrating—are associated with the process of dying itself. The assessment of depression in seriously ill patients therefore should focus on the dysphoric mood, helplessness, hopelessness, and lack of interest, enjoyment, and concentration in normal activities. It is now recommended that patients near the end of life should be screened with either the PHQ-9 or the PHQ-2, which asks "Over the past 2 weeks, how often have you been bothered by any of the following problems? (1) Little interest or pleasure in doing things and (2) feeling down, depressed or hopeless." The answer categories are as follows: not at all, several days, more than half the days, nearly every day. Other possible diagnostic tools include the short form of the Beck Depression Index or a visual analogue scale.

Certain conditions may be confused with depression. Endocrinopathies, such as hypothyroidism and Cushing's syndrome, electrolyte abnormalities, such as hypercalcemia, and akathisia, especially from dopamine-blocking antiemetics such as metoclopramide and prochlorperazine, can mimic

depression and should be excluded.

INTERVENTIONS

Undertreatment of depressed, terminally ill patients is common. Physicians must treat any physical symptom, such as pain, that may be causing or exacerbating depression. Fostering adaptation to the many losses that the patient is experiencing can also be helpful. Unfortunately, there are few randomized trials to guide such interventions. Thus, treatment typically follows the treatment used for non–terminally ill depressed patients.

In the absence of randomized controlled trials, nonpharmacologic interventions, including group or individual psychological counseling, and behavioral therapies such as relaxation and imagery can be helpful, especially in combination with drug therapy.

Pharmacologic interventions remain at the core of therapy. The same medications are used to treat depression in terminally ill as in non–terminally ill patients. Psychostimulants may be preferred for patients with a poor prognosis or for those with fatigue or opioid-induced somnolence. Psychostimulants are comparatively fast-acting, working within a few days instead of the weeks required for selective serotonin reuptake inhibitors (SSRIs). Dextroamphetamine or methylphenidate should be started at 2.5–5.0 mg in the morning and at noon, the same starting doses used for treating fatigue. The doses can eventually be escalated up to 15 mg bid. Modafinil is started at 100 mg qd and can be increased to 200 mg if there is no effect at the lower dose. Pemoline is a nonamphetamine psychostimulant with minimal abuse potential. It is also effective as an antidepressant beginning at 18.75 mg in the morning and at noon. Because it can be absorbed through the buccal mucosa, it is preferred for patients with intestinal obstruction or dysphagia. If it is used for prolonged periods, liver function must be monitored. The psychostimulants can also be combined with more traditional antidepressants while waiting for the antidepressants to become effective, then tapered down after a few weeks if necessary. Psychostimulants have side effects, particularly initial anxiety, insomnia, and very rarely paranoia, which may necessitate lowering the dose or discontinuing treatment.

Mirtazapine, an antagonist at the postsynaptic serotonin receptors, is a promising psychostimulant. It should be started at 7.5 mg before bed and titrated up no more than once every 1–2 weeks to a maximal dose of 45 mg/d. It has sedating, antiemetic, and anxiolytic properties, with few drug interactions. Its side effect of weight gain may be beneficial for seriously ill patients; it is available in orally disintegrating tablets.

For patients with a prognosis of several months or longer, SSRIs, including fluoxetine, sertraline, paroxetine, escitalopram, and citalopram, and serotonin-noradrenaline reuptake inhibitors, such as venlafaxine and duloxetine, are the preferred treatments, due to their efficacy and comparatively few side effects. Because low doses of these medications may be effective for seriously ill patients, one should use half the usual starting dose as for healthy adults. The starting dose for fluoxetine is 10 mg once a day. In most cases, once-a-day dosing is possible. The choice of which SSRI to use should be driven by (1) the patient's past success or failure with the specific medication and (2) the most favorable side effect profile for that specific agent. For instance, for a patient in whom fatigue is a major symptom, a more activating SSRI (fluoxetine) would be appropriate. For a patient in whom anxiety and sleeplessness are major symptoms, a more sedating SSRI (paroxetine) would be appropriate. Importantly, it can take up to 4 weeks for these drugs to have an effect.

Atypical antidepressants are recommended only in select circumstances, usually with the assistance of a specialty consultation. Trazodone can be an effective antidepressant but is sedating and can cause orthostatic hypotension and, occasionally, priapism. Therefore, it should be used before bed and only when a sedating effect is desired and is often used for patients with insomnia at a dose starting at 25 mg. Bupropion can also be used. In addition to its antidepressant effects, bupropion is energizing, making it useful for depressed patients who experience fatigue. However, it can cause seizures, preventing its use for patients with a risk of CNS neoplasms or terminal delirium. Finally, alprazolam, a benzodiazepine, starting at 0.25–1.0 mg tid, can be effective in seriously ill patients who have a combination of anxiety and depression. Although it is potent and works quickly, it has many drug interactions and may cause delirium, especially among very ill patients, because of its strong binding to the benzodiazepine–γ-aminobutyric acid (GABA) receptor complex.

Unless used as adjuvants for the treatment of pain, tricyclic antidepressants are not recommended. While they can be effective, their therapeutic window and serious side effects typically limit their utility. Similarly, monoamine oxidase (MAO) inhibitors are not recommended because of their side effects and dangerous drug interactions.

Delirium

(See Chap. 27)

FREQUENCY

In the weeks or months before death, delirium is uncommon, although it may be significantly underdiagnosed. However, delirium becomes relatively common in the days and hours immediately before death. Up to 85% of patients dying from cancer may experience terminal delirium.

ETIOLOGY

Delirium is a global cerebral dysfunction characterized by alterations in cognition and consciousness. It is frequently preceded by anxiety, changes in sleep patterns (especially reversal of day and night), and decreased attention. In contrast to dementia, delirium has an acute onset, is characterized by fluctuating consciousness and inattention, and is reversible, although reversibility may be more theoretical than real for patients near death. Delirium may occur in a patient with dementia; indeed, patients with dementia are more vulnerable to delirium.

Causes of delirium include metabolic encephalopathy arising from liver or renal failure, hypoxemia, or infection; electrolyte imbalances such as hypercalcemia; paraneoplastic syndromes; dehydration; and primary brain tumors, brain metastases, or leptomeningeal spread of tumor. Among dying patients, delirium is commonly caused by side effects of treatments, including radiation for brain metastases and medications, such as opioids, glucocorticoids, anticholinergic drugs, antihistamines, antiemetics, benzodiazepines, and chemotherapeutic agents. The etiology may be multifactorial; e.g., dehydration may exacerbate opioid-induced delirium.

ASSESSMENT

Delirium should be recognized in any terminally ill patient exhibiting new onset of disorientation, impaired cognition, somnolence, fluctuating levels of consciousness, or delusions with or without agitation. Delirium must be distinguished from acute anxiety, depression, and dementia. The central distinguishing feature is altered consciousness, which usually is not noted in anxiety, depression, or dementia. Although “hyperactive” delirium, characterized by overt confusion and agitation, is probably more common, patients should also be assessed for “hypoactive” delirium, which is characterized by sleep-wake reversal and decreased alertness.

In some cases, use of formal assessment tools such as the Mini-Mental Status Examination (which does not distinguish delirium from dementia) and the Delirium Rating Scale (which does distinguish delirium from dementia) may be helpful in distinguishing delirium from other processes. The patient’s list of medications must be evaluated carefully. Nonetheless, a reversible etiologic factor for delirium is found in fewer than half of all terminally ill patients. Given that most terminally ill patients experiencing delirium are very close to death and often at home, extensive diagnostic evaluations such as lumbar punctures and neuroradiologic examinations are inappropriate.

INTERVENTIONS

One of the most important objectives of terminal care is to provide terminally ill patients the lucidity to say goodbye to the people they love. Delirium, especially when in combination with agitation during the final days, is distressing to family and caregivers. A strong determinant of bereavement difficulties is witnessing a difficult death. Thus, terminal delirium should be treated aggressively.

At the first sign of delirium, such as day-night reversal with slight changes in mentation, the physician should let the family members know that it is time to be sure that everything they want to say has been said. The family should be informed that delirium is common just before death.

If medications are suspected of being a cause of the delirium, unnecessary agents should be discontinued. Other potentially reversible causes, such as constipation, urinary retention, and metabolic abnormalities, should be treated. Supportive measures aimed at providing a familiar environment should be instituted, including restricting visits only to individuals with whom the patient is familiar and eliminating new experiences; orienting the patient, if possible, by providing a clock and calendar; and gently correcting the patient’s hallucinations or cognitive mistakes.

Pharmacologic management focuses on the use of neuroleptics and, in extreme cases, anesthetics **(Table 12-7)**. Haloperidol remains the first-line therapy. Usually, patients can be controlled with a low dose (1–3 mg/d), given every 6 h, although some may require as much as 20 mg/d. Haloperidol can be administered PO, SC, or IV. IM injections should not be used, except when this is the only way to address a patient’s delirium. Olanzapine, an atypical neuroleptic, has shown significant effectiveness in completely resolving delirium in cancer patients. It also has other beneficial effects for terminally ill patients, including antinausea, antianxiety, and weight gain. Olanzapine is useful for patients with longer anticipated life expectancies because it is less likely to cause dysphoria and has a lower risk of dystonic reactions. Additionally, because olanzapine is metabolized through multiple

pathways, it can be used in patients with hepatic and renal dysfunction. Olanzapine has the disadvantage that it is only available orally and takes a week to reach steady state. The usual dose is 2.5–5 mg PO bid. Chlorpromazine (10–25 mg every 4–6 h) can be useful if sedation is desired and can be administered IV or PR in addition to PO. Dystonic reactions resulting from dopamine blockade are a side effect of neuroleptics, although they are reported to be rare when these drugs are used to treat terminal delirium. If patients develop dystonic reactions, benztropine should be administered. Neuroleptics may be combined with lorazepam to reduce agitation when the delirium is the result of alcohol or sedative withdrawal.

TABLE 12-7

Medications for the Management of Delirium

INTERVENTIONS	DOSE
Neuroleptics	
Haloperidol	0.5–5 mg q2–12h, PO/IV/SC/IM
Thioridazine	10–75 mg q4–8h, PO
Chlorpromazine	12.5–50 mg q4–12h, PO/IV/IM
Atypical neuroleptics	
Olanzapine	2.5–5 mg qd or bid, PO
Risperidone	1–3 mg q12h, PO
Anxiolytics	
Lorazepam	0.5–2 mg q1–4h, PO/IV/IM
Midazolam	1–5 mg/h continuous infusion, IV/SC
Anesthetics	
Propofol	0.3–2.0 mg/h continuous infusion, IV

If no response to first-line therapy is observed, a specialty consultation should be obtained with a goal to change to a different medication. If the patient fails to improve after a second neuroleptic, sedation with either an anesthetic such as propofol or continuous-infusion midazolam may be necessary. By some estimates, as many as 25% of patients at the very end of life who experience delirium, especially restless delirium with myoclonus or convulsions, may require sedation.

Physical restraints should be used with great reluctance and only when patients' violence is threatening to themselves or others. If restraints are used, their appropriateness should be frequently reevaluated.

Insomnia

FREQUENCY

Sleep disorders, defined as difficulty initiating sleep or maintaining sleep, sleep difficulty at least 3 nights a week, or sleep difficulty that causes impairment of daytime functioning, occurs in 19–63% of patients with advanced cancer. Some 30–74% of patients with other end-stage conditions, including AIDS, heart disease, COPD, and renal disease, experience insomnia.

ETIOLOGY

Patients with cancer may experience changes in sleep efficiency, such as an increase in stage I sleep. Insomnia may also coexist with both physical illnesses, like thyroid disease, and psychological illnesses, like depression and anxiety. Medications, including antidepressants, psychostimulants, glucocorticoids, and β agonists, are significant contributors to sleep disorders, as are caffeine and alcohol. Multiple over-the-counter medications contain caffeine and antihistamines, which can contribute to sleep disorders.

ASSESSMENT

Assessments should include specific questions concerning sleep onset, sleep maintenance, and early-morning wakening, as these will provide clues to both the causative agents and management of insomnia. Patients should be asked about previous sleep problems, screened for depression and anxiety, and asked about symptoms of thyroid disease. Caffeine and alcohol are prominent causes of sleep problems, and a careful history of the use of these substances should be obtained. Both excessive use and withdrawal from alcohol can be causes of sleep problems.

INTERVENTIONS

The mainstays of any intervention include improvement of sleep hygiene (encouragement of regular time for sleep, decreased nighttime distractions, elimination of caffeine and other stimulants and alcohol), interventions to treat anxiety and depression, and treatment for the insomnia itself. For patients with depression who have insomnia and anxiety, a sedating antidepressant such as mirtazapine can be helpful. In the elderly, trazodone, beginning at 25 mg at nighttime, is an effective sleep aid at doses lower than those that cause its antidepressant effect. Zolpidem may have a decreased incidence of delirium in patients compared with traditional benzodiazepines, but this has not been clearly established. When benzodiazepines are prescribed, short-acting ones (such as lorazepam) are favored over longer-acting ones (such as diazepam). Patients who receive these medications should be observed for signs of increased confusion and delirium.

SOCIAL NEEDS AND THEIR MANAGEMENT

Financial Burdens

FREQUENCY

Dying can impose substantial economic strains on patients and families, potentially causing distress. This is known as financial toxicity. In the United States, which has the least comprehensive health insurance systems among wealthy countries, a quarter of families coping with end-stage cancer report that care was a major financial burden and a third used up most of their savings. Among Medicare beneficiaries, average out-of-pocket costs were >$8000. Between 10% and 30% of families are forced to sell assets, use savings, or take out a mortgage to pay for the patient's health care costs.

The patient is likely to reduce hours worked and eventually stop working altogether. In 20% of cases, a family member of the terminally ill patient also must stop working to provide care. The major underlying causes of economic burden are related to poor physical functioning and care needs, such as the need for housekeeping, nursing, and personal care. More debilitated patients and poor patients experience greater economic burdens.

INTERVENTION

The economic burden of end-of-life care should not be ignored as a private matter. It has been associated with a number of adverse health outcomes, including preferring comfort care over life-prolonging care, as well as consideration of euthanasia or physician-assisted suicide (PAS). Economic burdens increase the psychological distress of the families and caregivers of terminally ill patients, and poverty is associated with many adverse health outcomes. Importantly, studies have found that "patients with advanced cancer who reported having end-of-life conversations with physicians had significantly lower health care costs in their final week of life. Higher costs were associated with worse quality of death." Assistance from a social worker, early on if possible, to ensure access to all available benefits may be helpful. Many patients, families, and health care providers are unaware of options for long-term care insurance, respite care, the Family Medical Leave Act (FMLA), and other sources of assistance. Some of these options (such as respite care) may be part of a formal hospice program, but others (such as the FMLA) do not require enrollment in a hospice program.

Relationships

FREQUENCY

Settling personal issues and closing the narrative of lived relationships are universal needs. When asked if sudden death or death after an illness is preferable, respondents often initially select the former, but soon change to the latter as they reflect on the importance of saying goodbye. Bereaved family members who have not had the chance to say goodbye often have a more difficult grief process.

INTERVENTIONS

Care of seriously ill patients requires efforts to facilitate the types of encounters and time spent with family and friends that are necessary to meet those needs. Family and close friends may need to be accommodated in hospitals and other facilities with unrestricted visiting hours, which may include sleeping near the patient, even in otherwise regimented institutional settings. Physicians and other health care providers may be able to facilitate and resolve strained interactions between the patient and other family members. Assistance for patients and family members who are unsure about how to create or help preserve memories, whether by providing materials such as a scrapbook or memory box or by offering them suggestions and informational resources, can be deeply appreciated. Taking photographs and creating videos can be especially helpful to terminally ill patients who have younger children or grandchildren.

Family Caregivers

FREQUENCY

Caring for seriously ill patients places a heavy burden on families. Families are frequently required to provide transportation and homemaking, as well as other services. Typically, paid professionals, such as home health nurses and hospice workers, supplement family care; only about a quarter of all caregiving consists of exclusively paid professional assistance. Over the past 40 years, there has been a significant decline in the United States of deaths occurring in hospitals, with a simultaneous increase in deaths in other facilities and at home. Over a third of deaths occur in patients' homes. This increase in out-of-hospital deaths increases reliance on families for end-of-life care. Increasingly, family members are being called upon to provide physical care (such as moving and bathing patients) and medical care (such as assessing symptoms and giving medications) in addition to emotional care and support.

Three-quarters of family caregivers of terminally ill patients are women—wives, daughters, sisters, and even daughters-in-law. Since many are widowed, women tend to be able to rely less on family for caregiving assistance and may need more paid assistance. About 20% of terminally ill patients report substantial unmet needs for nursing and personal care. The impact of caregiving on family caregivers is substantial: both bereaved and current caregivers have a higher mortality rate than that of non-caregiving controls.

INTERVENTIONS

It is imperative to inquire about unmet needs and to try to ensure that those needs are met either through the family or by paid professional services when possible. Community assistance through houses of worship or other community groups often can be mobilized by telephone calls from the medical team to someone the patient or family identifies. Sources of support specifically for family caregivers should be identified through local sources or nationally through groups such as the National Family Caregivers Association (*www.nfcacares.org*), the American Cancer Society (*www.cancer.org*), and the Alzheimer's Association (*www.alz.org*).

EXISTENTIAL NEEDS AND THEIR MANAGEMENT

Frequency

Religion and spirituality are often important to dying patients. Nearly 70% of patients report becoming more religious or spiritual when they became terminally ill, and many find comfort in religious or spiritual practices such as prayer. However, ~20% of terminally ill patients become less religious, frequently feeling cheated or betrayed by becoming terminally ill. For other patients, the need is for existential meaning and purpose that is distinct from, and may even be antithetical to, religion or spirituality. When asked, patients and family caregivers frequently report wanting their professional caregivers to be more attentive to religion and spirituality.

Assessment

Health care providers are often hesitant about involving themselves in the religious, spiritual, and existential experiences of their patients because it

may seem private or not relevant to the current illness. But physicians and other members of the care team should be able at least to detect spiritual and existential needs. Screening questions have been developed for a physician's spiritual history taking. Spiritual distress can amplify other types of suffering and even masquerade as intractable physical pain, anxiety, or depression. The screening questions in the comprehensive assessment are usually sufficient. Deeper evaluation and intervention are rarely appropriate for the physician unless no other member of a care team is available or suitable. Pastoral care providers may be helpful, whether from the medical institution or from the patient's own community.

Interventions

Precisely how religious practices, spirituality, and existential explorations can be facilitated and improve end-of-life care is not well established. What is clear is that for physicians, one main intervention is to inquire about the role and importance of spirituality and religion in a patient's life. This will help a patient feel heard and help physicians identify specific needs. In one study, only 36% of respondents indicated that a clergy member would be comforting. Nevertheless, the increase in religious and spiritual interest among a substantial fraction of dying patients suggests inquiring of individual patients how this need can be addressed. Some evidence supports specific methods of addressing existential needs in patients, ranging from establishing a supportive group environment for terminal patients to individual treatments emphasizing a patient's dignity and sources of meaning.

MANAGING THE LAST STAGES

PALLIATIVE CARE SERVICES: HOW AND WHERE

Determining the best approach to providing palliative care to patients will depend on patient preferences, the availability of caregivers and specialized services in close proximity, institutional resources, and reimbursement. Hospice is a leading, but not the only, model of palliative care services. In the United States, slightly more than a third—35.7%—of hospice care is provided in private residential homes with 14.5% of hospice care in nursing homes. In the United States, Medicare pays for hospice services under Part A, the hospital insurance part of reimbursement. Two physicians must certify that the patient has a prognosis of ≤6 months if the disease runs its usual course. Prognoses are probabilistic by their nature; patients are not required to die within 6 months but rather to have a condition from which half the individuals with it would not be alive within 6 months. Patients sign a hospice enrollment form that states their intent to forgo curative services related to their terminal illness but can still receive medical services for other comorbid conditions. Patients also can withdraw enrollment and reenroll later; the hospice Medicare benefit can be revoked later to secure traditional Medicare benefits. Payments to the hospice are per diem (or capitated), not fee-for-service. Payments are intended to cover physician services for the medical direction of the care team; regular home care visits by registered nurses and licensed practical nurses; home health aide and homemaker services; chaplain services; social work services; bereavement counseling; and medical equipment, supplies, and medications. No specific therapy is excluded, and the goal is for each therapy to be considered for its symptomatic (as opposed to disease-modifying) effect. Additional clinical care, including services of the primary physician, is covered by Medicare Part B even while the hospice Medicare benefit is in place.

The Affordable Care Act directs the secretary of Health and Human Services to gather data on Medicare hospice reimbursement with the goal of reforming payment rates to account for resource use over an entire episode of care. The legislation also requires additional evaluations and reviews of eligibility for hospice care by hospice physicians or nurses. The Center for Medicare and Medicaid Innovation (CMMI) sponsors and carries out demonstration projects to test models and evaluate the potential of new methods. In 2016, CMMI started a 5-year test of concurrent hospice and palliative care services with curative treatment for terminally ill patients who have a life expectancy of ≤6 months. A 4-year test initiated in 2021 will examine the inclusion of hospice in Medicare Advantage covering 8% of the market and include important health plans.

By 2018, the average length of enrollment in a hospice for Medicare beneficiaries was 90 days. However, the median length of stay was just 18 days, suggesting most patients are in hospice for a short time. Such short stays create barriers to establishing high-quality palliative services in patients' homes and also place financial strains on hospice providers since the initial assessments are resource intensive. Physicians should initiate early referrals to the hospice to allow more time for patients to receive palliative care.

In the United States, hospice care has been the main method for securing palliative services for terminally ill patients. However, leading physicians have increasingly emphasized the need to introduce palliative care much earlier in patients' illness, and efforts are being made to develop palliative care services that can be provided before the last 6 months of life and across a variety of settings. Studies of terminally ill patients indicate that those who received in-home palliative care delivered by an interdisciplinary team compared to usual care were more satisfied, more likely to die at home, and had fewer visits to the emergency room and lower per-day costs. More companies and home health agencies are now offering nonhospice palliative care services in patients' homes in an effort to increase quality of life and forestall emergency room visits and hospitalizations. Similarly,

palliative care services are increasingly available via consultation, rather than being available only in hospital, day care, outpatient, and nursing home settings. Palliative care consultations for nonhospice patients can be billed as for other consultations under Medicare Part B. It is argued that using palliative care earlier in patients' illness allows patients and family members to become more acculturated to avoiding life-sustaining treatments, facilitating a smoother transition to hospice care closer to death.

WITHDRAWING AND WITHHOLDING LIFE-SUSTAINING TREATMENT

Legal Aspects

For centuries, it has been deemed ethical to withhold or withdraw life-sustaining interventions. The current legal consensus in the United States and most wealthy countries is that patients have a moral as well as legal right to refuse medical interventions. American courts also have held that incompetent patients have a right to refuse medical interventions. For patients who are incompetent and terminally ill and who have not completed an advance care directive, next of kin can exercise that right, although this may be restricted in some states, depending on how clear and convincing the evidence is of the patient's preferences. Courts have limited families' ability to terminate life-sustaining treatments in patients who are conscious and incompetent but not terminally ill. In theory, patients' right to refuse medical therapy can be limited by four countervailing interests: (1) preservation of life, (2) prevention of suicide, (3) protection of third parties such as children, and (4) preservation of the integrity of the medical profession. In practice, these interests almost never override the right of competent patients and incompetent patients who have left explicit wishes or advance care directives.

For incompetent patients who either appointed a proxy without specific indications of their wishes or never completed an advance care directive, three criteria have been suggested to guide the decision to terminate medical interventions. First, some commentators suggest that ordinary care should be administered but extraordinary care could be terminated. Because the ordinary/extraordinary distinction is too vague, courts and commentators widely agree that it should not be used to justify decisions about stopping treatment. Second, many courts have advocated the use of the substituted-judgment criterion, which holds that the proxy decision-makers should try to imagine what the incompetent patient would do if he or she were competent. However, multiple studies indicate that many proxies, even close family members, cannot accurately predict what the patient would have wanted. Therefore, substituted judgment becomes more of a guessing game than a way of fulfilling the patient's wishes. Finally, the best-interests criterion holds that proxies should evaluate treatments by balancing their benefits and risks and select those treatments where the benefits maximally outweigh the burdens of treatment. Clinicians have a clear and crucial role in this by carefully and dispassionately explaining the known benefits and burdens of specific treatments. Yet even when that information is as clear as possible, different individuals can have very different views of what is in the patient's best interests, and families may have disagreements or even overt conflicts. This criterion has been criticized because there is no single way to determine the balance between benefits and burdens; it depends on a patient's personal values. For instance, for some people, being alive even if mentally incapacitated is a benefit, whereas for others, it may be the worst possible existence. As a matter of practice, physicians rely on family members to make decisions that they feel are best and object only if those decisions seem to demand treatments that the physicians consider not beneficial.

Practices

Withholding and withdrawing acutely life-sustaining medical interventions from terminally ill patients are now standard practice. More than 90% of American patients die without cardiopulmonary resuscitation (CPR), and just as many forgo other potentially life-sustaining interventions. For instance, in ICUs in the period of 1987–1988, CPR was performed 49% of the time, but it was performed only 10% of the time in 1992–1993 and on just 1.8% of admissions from 2001 to 2008. On average, 3.8 interventions, such as vasopressors and transfusions, were stopped for each dying ICU patient. However, up to 19% of decedents in hospitals received interventions such as extubation, ventilation, and surgery in the 48 h preceding death. There is wide variation in practices among hospitals and ICUs, suggesting an important element of physician preferences rather than consistent adherence to professional society recommendations.

Mechanical ventilation may be the most challenging intervention to withdraw. The two approaches are *terminal extubation*, which is the removal of the endotracheal tube, and *terminal weaning*, which is the gradual reduction of the fraction of inspired oxygen (FIO_2) or ventilator rate. One-third of ICU physicians prefer to use the terminal weaning technique, and 13% extubate; the majority of physicians utilize both techniques. The American Thoracic Society's 2008 clinical policy guidelines note that there is no single correct process of ventilator withdrawal and that physicians use and should be proficient in both methods but that the chosen approach should carefully balance benefits and burdens as well as patient and caregiver preferences. Some recommend terminal weaning because patients do not develop upper airway obstruction and the distress caused by secretions or stridor;

however, terminal weaning can prolong the dying process and not allow a patient's family to be with the patient unencumbered by an endotracheal tube. To ensure comfort for conscious or semiconscious patients before withdrawal of the ventilator, neuromuscular blocking agents should be terminated and sedatives and analgesics administered. Removing the neuromuscular blocking agents permits patients to show discomfort, facilitating the titration of sedatives and analgesics; it also permits interactions between patients and their families. A common practice is to inject a bolus of midazolam (2–4 mg) or lorazepam (2–4 mg) before withdrawal, followed by a bolus of 5–10 mg of morphine and continuous infusion of morphine (50% of the bolus dose per hour) during weaning. In patients who have significant upper airway secretions, IV scopolamine at a rate of 100 μg/h can be administered. Additional boluses of morphine or increases in the infusion rate should be administered for respiratory distress or signs of pain. Higher doses will be needed for patients already receiving sedatives and opioids.

The median time to death after stopping of the ventilator is 1 h. However, up to 10% of patients unexpectedly survive for 1 day or more after mechanical ventilation is stopped. Women and older patients tend to survive longer after extubation. Families need to be reassured about both the continuations of treatments for common symptoms, such as dyspnea and agitation, after withdrawal of ventilatory support and the uncertainty of length of survival after withdrawal of ventilatory support.

FUTILE CARE

Beginning in the late 1980s, some commentators argued that physicians could terminate futile treatments demanded by the families of terminally ill patients. Although no objective definition or standard of futility exists, several categories have been proposed. Physiologic futility means that an intervention will have no physiologic effect. Some have defined qualitative futility as applying to procedures that "fail to end a patient's total dependence on intensive medical care." Quantitative futility occurs "when physicians conclude (through personal experience, experiences shared with colleagues, or consideration of reported empiric data) that in the last 100 cases, a medical treatment has been useless." The term conceals subjective value judgments about when a treatment is "not beneficial." Deciding whether a treatment that obtains an additional 6 weeks of life or a 1% survival advantage confers benefit depends on patients' preferences and goals. Furthermore, physicians' predictions of when treatments are futile deviate markedly from the quantitative definition. When residents thought CPR was quantitatively futile, more than one in five patients had a >10% chance of survival to hospital discharge. Most studies that purport to guide determinations of futility are based on insufficient data and therefore cannot provide statistical confidence for clinical decision-making. Quantitative futility rarely applies in ICU settings.

Many commentators reject using futility as a criterion for withdrawing care, preferring instead to consider futility situations as ones that represent conflict that calls for careful negotiation between families and health care providers. The American Medical Association and other professional societies have developed process-based approaches to resolving cases clinicians feel are futile. These process-based measures mainly suggest involving consultants and/or ethics committees when there are seemingly irresolvable differences. Some hospitals have enacted "unilateral do-not-resuscitate" policies to allow clinicians to provide a do-not-resuscitate order in cases in which consensus cannot be reached with families and medical opinion is that resuscitation would be futile if attempted. This type of a policy is not a replacement for careful and patient communication and negotiation but recognizes that agreement cannot always be reached.

In 1999, Texas enacted the so-called Futile Care Act. Other states, such as Virginia, Maryland, and California, have also enacted such laws that provide physicians a "safe harbor" from liability if they refuse a patient's or family's request for life-sustaining interventions. For instance, in Texas, when a disagreement about terminating interventions between the medical team and the family has not been resolved by an ethics consultation, the physician is tasked with trying to facilitate transfer of the patient to an institution willing to provide treatment. If this fails after 10 days, the hospital and physician may unilaterally withdraw treatments determined to be futile. The family may appeal to a state court. Early data suggest that the law increases futility consultations for the ethics committee and that, although most families concur with withdrawal, ~10–15% of families refuse to withdraw treatment. As of 2007, there had been 974 ethics committee consultations on medical futility cases and 65 in which committees ruled against families and gave notice that treatment would be terminated. In 2007, a survey of Texas hospitals showed that 30% of hospitals had used the futility law in 213 adult cases and 42 pediatric cases. Treatment was withdrawn for 27 of those patients, and the remainder were transferred to other facilities or died while awaiting transfer.

EUTHANASIA AND PHYSICIAN-ASSISTED SUICIDE

Euthanasia and PAS are defined in **Table 12-8**. Terminating life-sustaining care and providing opioid medications to manage symptoms such as pain or dyspnea have long been considered ethical by the medical profession and legal by courts and should not be conflated with euthanasia or PAS.

TABLE 12-8

Definitions of Physician-Assisted Suicide and Euthanasia

TERM	DEFINITION	LEGAL STATUS
Voluntary active euthanasia	Intentionally administering medications or other interventions to cause the patient's death with the patient's informed consent	Netherlands, Belgium, Luxembourg, Canada, Colombia, Spain, Western Australia, New Zealand
Involuntary active euthanasia	Intentionally administering medications or other interventions to cause the patient's death when the patient was competent to consent but did not—e.g., the patient may not have been asked	Nowhere
Passive euthanasia	Withholding or withdrawing life-sustaining medical treatments from a patient to let him or her die (terminating life-sustaining treatments)	Everywhere
Physician-assisted suicide	A physician provides medications or other interventions to a patient with the understanding that the patient can use them to commit suicide	Netherlands, Belgium, Luxembourg, Canada, Colombia, Germany, Switzerland, Oregon, Washington, Montana, Vermont, California, Colorado, District of Columbia, Hawaii, Maine, New Jersey, New Mexico

Legal Aspects

Euthanasia and PAS are legal in the Netherlands, Belgium, Luxembourg, Colombia, Canada, Spain, Western Australia, and New Zealand. Euthanasia was legalized in the Northern Territory of Australia in 1996, but that legislation was repealed 9 months later in 1997. Under certain conditions, a layperson in Switzerland or Germany can legally elect assisted suicide. In the United States, PAS is legal in Washington, D.C., and 10 states: Oregon, Washington State, Montana, Vermont, California, Colorado, Hawaii, Maine, New Jersey, and New Mexico. No state in the United States has legalized euthanasia. In the United States, multiple criteria must be met for PAS: the patient must have a terminal condition of <6 months and must be determined eligible through a process that includes a 15-day waiting period. In 2009, the state supreme court of Montana ruled that state law permits PAS for terminally ill patients. Many other countries, such as Portugal, are actively debating the legalization of euthanasia and/or PAS.

Practices

Fewer than 10–20% of terminally ill patients actually consider euthanasia and/or PAS for themselves. Use of euthanasia and PAS is increasing but remains relatively rare. In all countries, even the Netherlands and Belgium where these practices have been tolerated and legal for many years, <5% of death occur by euthanasia or PAS. As of the most recent data, 4.7% of all deaths were by euthanasia or PAS in the Netherlands (2015) and 4.6% in Belgium (2013). Just 0.50% of all deaths in Oregon in 2019 (188 of 37,397 deaths) and 0.36% of all deaths in Washington State in 2018 (203 of 56,913 deaths) were reported to be by PAS, although these may be underestimates since the cause of some deaths of patients who received medications could not be verified.

In Belgium, the Netherlands, Oregon, and Washington, >70% of patients utilizing these interventions are dying of cancer; <10% of deaths by euthanasia or PAS involve patients with AIDS or amyotrophic lateral sclerosis. While the numbers are small, in the Netherlands, the numbers of euthanasia or PAS cases in patients with psychiatric disorders, dementia, and the accumulation of health issues are increasing.

Pain is not the primary motivator for patients' requests for or interest in euthanasia and/or PAS. Among the first patients to receive PAS in Oregon, only 1 of the 15 patients had inadequate pain control, compared with 15 of the 43 patients in a control group who experienced inadequate pain relief. About 33% of patients in Oregon seeking PAS currently cite pain or fear of pain as their main reason for doing so. Conversely, depression and hopelessness are strongly associated with patient interest in euthanasia and PAS. Concerns about loss of dignity or autonomy or being a burden on

family members appear to be more important factors motivating a desire for euthanasia or PAS. Losing autonomy (87% Oregon [OR], 85% Washington [WA]), not being able to enjoy activities (90% OR, 84% WA), and fear of losing dignity (72% OR, 69% WA) are the most-cited end-of-life concerns in both states. A high percentage of patients seeking PAS note being a burden on family (59% OR, 51% WA). A study from the Netherlands showed that depressed terminally ill cancer patients were four times more likely to request euthanasia and confirmed that uncontrolled pain was not associated with greater interest in euthanasia.

Euthanasia and PAS are no guarantee of a painless, quick death. Data from the Netherlands indicate that in as many as 20% of euthanasia and PAS cases technical and other problems arose, including patients waking from coma, not becoming comatose, regurgitating medications, and experiencing a prolonged time to death. Data from Oregon between 1998 and 2017 and Washington between 2009 and 2017 indicate that of patients who received PAS prescriptions, 81% died at home and prescribers were present in 9.7% of cases. The time between drug intake and coma ranged from 1 min to 11 h, and the time from drug intake to death ranged from 1 min to 104 h. The median time from ingestion to coma was 5 min and from ingestion to death was 25 min. In Oregon between 1998 and 2015, 53% of patients had no complications, 44% of patients had no data on complications, and 2.4% of patients had regurgitation after taking the prescribed medicine as the only complication. In addition, six patients awakened. In Washington State between 2014 and 2015, 1.4% of patients had regurgitation, one patient had a seizure, and the reported range of time to death extended to 30 h. In the Netherlands, problems were significantly more common in PAS, sometimes requiring the physician to intervene and provide euthanasia.

Regardless of whether they practice in a setting where euthanasia is legal or not, many physicians over the course of their careers will receive a patient request for euthanasia or PAS. In the United States, 18% of physicians have received a request for PAS and 11% have received a request for euthanasia. Three percent complied with a request for PAS, while 5% complied with a request for euthanasia. In the Netherlands, where the practices are legal, 77% of physicians have received a request for PAS or euthanasia and 60% have performed these interventions.

Competency in dealing with such a request is crucial. Although challenging, the request can also provide a chance to address intense suffering. After receiving a request for euthanasia and/or PAS, health care providers should carefully clarify the request with empathic, open-ended questions to help elucidate the underlying cause for the request, such as, “What makes you want to consider this option?” Endorsing either moral opposition or moral support for the act tends to be counterproductive, giving an impression of being judgmental or of endorsing the idea that the patient’s life is worthless. Health care providers must reassure the patient of continued care and commitment. The patient should be educated about alternative, less laden options, such as symptom management and withdrawing any unwanted treatments, and the reality of euthanasia and/or PAS, since the patient may have misconceptions about their effectiveness as well as the legal implications of the choice. Depression, hopelessness, and other symptoms of psychological distress, as well as physical suffering and economic burdens, are likely factors motivating the request, and such factors should be assessed and treated aggressively. After these interventions and clarification of options, most patients proceed with another approach, declining life-sustaining interventions, possibly including refusal of nutrition and hydration.

CARE DURING THE LAST HOURS

Most laypersons have limited experiences with the actual dying process and death. They frequently do not know what to expect of the final hours and afterward. The family and other caregivers must be prepared, especially if the plan is for the patient to die at home.

Patients in the last days of life typically experience extreme weakness and fatigue and become bedbound; this can lead to pressure sores. The issue of turning patients who are near the end of life, however, must be balanced against the potential discomfort that movement may cause. Patients stop eating and drinking with drying of mucosal membranes and dysphagia. Careful attention to oral swabbing, lubricants for lips, and use of artificial tears can provide a form of care to substitute for attempts at feeding the patient. With loss of the gag reflex and dysphagia, patients may also experience accumulation of oral secretions, producing noises during respiration sometimes called “the death rattle.” Scopolamine can reduce the secretions. Patients also experience changes in respiration with periods of apnea or Cheyne-Stokes breathing. Decreased intravascular volume and cardiac output cause tachycardia, hypotension, peripheral coolness, and livedo reticularis (skin mottling). Patients can have urinary and, less frequently, fecal incontinence. Changes in consciousness and neurologic function generally lead to two different paths to death.

Each of these terminal changes can cause patients and families distress, requiring reassurance and targeted interventions **(Table 12-9)**. Informing families that these changes might occur and providing them with an information sheet can help preempt problems and minimize distress. Understanding that patients stop eating because they are dying, not dying because they have stopped eating, can reduce family and caregiver anxiety. Similarly, informing the family and caregivers that the “death rattle” may occur and that it is not indicative of suffocation, choking, or pain can reduce their worry from the breathing sounds.

TABLE 12-9

Managing Changes in the Patient's Condition during the Final Days and Hours

CHANGES IN THE PATIENT'S CONDITION	POTENTIAL COMPLICATION	FAMILY'S POSSIBLE REACTION AND CONCERN	ADVICE AND INTERVENTION
Profound fatigue	Bedbound with development of pressure ulcers that are prone to infection, malodor, and pain, and joint pain	Patient is lazy and giving up.	Reassure family and caregivers that terminal fatigue will not respond to interventions and should not be resisted. Use an air mattress if necessary.
Anorexia	None	Patient is giving up; patient will suffer from hunger and will starve to death.	Reassure family and caregivers that the patient is not eating because he or she is dying; not eating at the end of life does not cause suffering or death. Forced feeding, whether oral, parenteral, or enteral, does not reduce symptoms or prolong life.
Dehydration	Dry mucosal membranes (see below)	Patient will suffer from thirst and die of dehydration.	Reassure family and caregivers that dehydration at the end of life does not cause suffering because patients lose consciousness before any symptom distress. Intravenous hydration can worsen symptoms of dyspnea by pulmonary edema and peripheral edema as well as prolong the dying process.
Dysphagia	Inability to swallow oral medications needed for palliative care		Do not force oral intake. Discontinue unnecessary medications that may have been continued, including antibiotics, diuretics, antidepressants, and laxatives. If swallowing pills is difficult, convert essential medications (analgesics, antiemetics, anxiolytics, and psychotropics) to oral solutions, buccal, sublingual, or rectal administration.
"Death rattle"—noisy breathing		Patient is choking and suffocating.	Reassure the family and caregivers that this is caused by secretions in the oropharynx and the patient is not choking. Reduce secretions with scopolamine (0.2–0.4 mg SC q4h or 1–3 patches q3d). Reposition patient to permit drainage of secretions. Do not suction. Suction can cause patient and family discomfort and is usually ineffective.
Apnea, Cheyne-Stokes respirations, dyspnea		Patient is suffocating.	Reassure family and caregivers that unconscious patients do not experience suffocation or air hunger. Apneic episodes are frequently a premorbid change. Opioids or anxiolytics may be used for dyspnea. Oxygen is unlikely to relieve dyspneic symptoms and may prolong the dying process.

Urinary or fecal incontinence	Skin breakdown if days until death Potential transmission of infectious agents to caregivers	Patient is dirty, malodorous, and physically repellent.	Remind family and caregivers to use universal precautions. Frequent changes of bedclothes and bedding. Use diapers, urinary catheter, or rectal tube if diarrhea or high urine output.
Agitation or delirium	Day/night reversal Hurt self or caregivers	Patient is in horrible pain and going to have a horrible death.	Reassure family and caregivers that agitation and delirium do not necessarily connote physical pain. Depending on the prognosis and goals of treatment, consider evaluating for causes of delirium and modifying medications. Manage symptoms with haloperidol, chlorpromazine, diazepam, or midazolam.
Dry mucosal membranes	Cracked lips, mouth sores, and candidiasis can also cause pain. Odor	Patient may be malodorous, physically repellent.	Use baking soda mouthwash or saliva preparation q15–30 min. Use topical nystatin for candidiasis. Coat lips and nasal mucosa with petroleum jelly q60–90 min. Use ophthalmic lubricants q4h or artificial tears q30 min.

Families and caregivers may also feel guilty about stopping treatments, fearing that they are “killing” the patient. This may lead to demands for interventions, such as feeding tubes, that may be ineffective. In such cases, the physician should remind the family and caregivers about the inevitability of events and the palliative goals. Interventions may prolong the dying process and cause discomfort. Physicians also should emphasize that withholding treatments is both legal and ethical and that the family members are not the cause of the patient’s death. This reassurance may have to be provided multiple times.

Hearing and touch are said to be the last senses to stop functioning. Whether this is the case or not, families and caregivers can be encouraged to communicate with the dying patient. Encouraging them to talk directly to the patient, even if he or she is unconscious, and hold the patient’s hand or demonstrate affection in other ways can be an effective way to channel their urge “to do something” for the patient.

When the plan is for the patient to die at home, the physician must inform the family and caregivers how to determine that the patient has died. The cardinal signs are cessation of cardiac function and respiration; the pupils become fixed; the body becomes cool; muscles relax; and incontinence may occur. Remind the family and caregivers that the eyes may remain open even after the patient has died.

The physician should establish a plan for who the family or caregivers will contact when the patient is dying or has died. Without a plan, family members may panic and call 911, unleashing a cascade of unwanted events, from arrival of emergency personnel and resuscitation to hospital admission. The family and caregivers should be instructed to contact the hospice (if one is involved), the covering physician, or the on-call member of the palliative care team. They should also be told that the medical examiner need not be called unless the state requires it for all deaths. Unless foul play is suspected, the health care team need not contact the medical examiner either.

Just after the patient dies, even the best-prepared family may experience shock and loss and be emotionally distraught. They need time to assimilate the event and be comforted. Health care providers are likely to find it meaningful to write a bereavement card or letter to the family. The purpose is to communicate about the patient, perhaps emphasizing the patient’s virtues and the honor it was to care for the patient, and to express concern for the family’s hardship. Some physicians attend the funerals of their patients. Although this is beyond any medical obligation, the presence of the physician can be a source of support to the grieving family and provides an opportunity for closure for the physician.

Death of a spouse is a strong predictor of poor health, and even mortality, for the surviving spouse. It may be important to alert the spouse’s physician about the death so that he or she is aware of symptoms that might require professional attention.

FURTHER READING

Emanuel E et al: Attitudes and practices of euthanasia and physician-assisted suicide in the United States, Canada, and Europe. JAMA 316:79, 2016. [PubMed: 27380345]

Kelley AS, Meier DE: Palliative care—A shifting paradigm. N Engl J Med 363:781, 2010. [PubMed: 20818881]

Kelley AS et al: Hospice enrollment saves money for Medicare and improves care quality across a number of different lengths-of-stay. Health Aff 32:552, 2012.

Kelley AS et al: Palliative care for the seriously ill. N Engl J Med 373:747, 2015. [PubMed: 26287850]

Mack JW et al: Associations between end-of-life discussion characteristics and care received near death: A prospective cohort study. J Clin Oncol 30:4387, 2012. [PubMed: 23150700]

Murray SA et al: Illness trajectories and palliative care. BMJ 330:1007, 2005. [PubMed: 15860828]

Neuman P et al: Medicare per capita spending by age and service: New data highlights oldest beneficiaries. Health Aff (Millwood) 34:335, 2015. [PubMed: 25588646]

Nicholas LH et al: Regional variation in the association between advance directives and end-of-life Medicare expenditures. JAMA 306:1447, 2011. [PubMed: 21972306]

Ornstein KA et al: Evaluation of racial disparities in hospice use and end-of-life treatment intensity in the REGARDS cohort. JAMA Netw Open 3(8):e2014639, 2020. [PubMed: 32833020]

Quinn KL et al: Association of receipt of palliative care interventions with health care use, quality of life, and symptom burden among adults with chronic noncancer illness: A systematic review and meta-analysis. JAMA 324:1439, 2020. [PubMed: 33048152]

Teno JM et al: Change in end-of-life care for medicare beneficiaries: Site of death, place of care, and health transitions in 2000, 2005, and 2009. JAMA 309:470, 2013. [PubMed: 23385273]

Teno JM et al: Site of death, place of care, and health care transitions among US Medicare beneficiaries, 2000-2015. JAMA 320:264, 2018. [PubMed: 29946682]

Van Den Beuken-VanEverdingen MH et al: Update on prevalence of pain in patients with cancer: Systematic review and meta-analysis. J Pain Symptom Manage 51:1070, 2016. [PubMed: 27112310]

WEBSITES

American Academy of Hospice and Palliative Medicine: *www.aahpm.org*

Center to Advance Palliative Care: *http://www.capc.org*

Education in Palliative and End of Life Care (EPEC): *http://www.epec.net*

Family Caregiver Alliance: *http://www.caregiver.org*

National Hospice and Palliative Care Organization (including state-specific advance directives): *http://www.nhpco.org*

NCCN: The National Comprehensive Cancer Network palliative care guidelines: *http://www.nccn.org*

Our Care Wishes Advance Care Planning Tool: *https://www.ourcarewishes.org*