TABLE 10-4 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	

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. 54 and 99, Chap. 38, and Chap. 55, respectively.**

Pain • ***FREQUENCY*** The frequency of pain among terminally ill patients varies widely. Substantial pain occurs in 36–90% of patients with advanced cancer. In the SUPPORT study of hospitalized patients with diverse conditions and an estimated survival ≤6 months, 22% reported moderate to severe pain, and caregivers of those patients noted that 50% had similar levels of pain during the last few days of life. A meta-analysis found pain prevalence of 58–69% in studies that included patients characterized as having advanced, metastatic, or terminal cancer; 44–73% in studies that included patients characterized as undergoing cancer treatment; and 21–46% in studies that included posttreatment individuals.

ETIOLOGY *Nociceptive 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, 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 shocklike pain. Classic examples are poststroke 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, such as the Visual Analogue Scale, the Brief Pain Inventory, and the pain component of one of the more comprehensive symptom assessment instruments. Frequent reassessments are essential to assess the effects of 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. Pain medications are the cornerstone of management. 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.

Pharmacologic interventions follow the World Health Organization three-step approach involving nonopioid analgesics, mild opioids, and strong opioids, with or without adjuvants **(Chap. 18)**. 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 also may have central nervous system (CNS) effects. They have a ceiling effect. Ibuprofen, up to a total dose of 1600 mg/d given in four doses of 400 mg each, has a minimal risk of causing bleeding and renal impairment and is a good initial choice. In patients with a history of severe gastrointestinal (GI) or other bleeding, it 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 given in four doses of 1 g each. 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. They work by interacting with μ opioid receptors in the CNS to activate pain-inhibitory neurons; most are receptor antagonists. The mixed agonist/antagonist opioids useful for postacute pain should not be used for the chronic pain in end-of-life care. Weak opioids such as codeine can be used initially. However, if they are escalated and fail to relieve pain, strong opioids such as morphine, 5–10 mg every 4 h, should be used. Nonopioid analgesics should be combined with opioids because they potentiate the effect of opioids.

For continuous pain, opioids should be administered on a regular, around-the-clock basis consistent with their duration of analgesia. They should not be provided only when the patient experiences pain; the goal is to prevent patients from experiencing pain. Patients also should 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 after 24 h the patient's pain remains uncontrolled and recurs before the next dose, requiring the patient to use the rescue medication, the daily opioid dose can be increased by the total dose of rescue medications used by the patient, or by 50% for moderate pain and 100% for severe pain of the standing opioid daily dose.

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 with short-acting preparations, one should switch to extended-release preparations. Even with a stable extended-release preparation regimen, the patient may have 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.

Because of 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.