Approach to symptom assessment in palliative care

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INTRODUCTION — Palliative care is an interdisciplinary medical specialty that focuses on preventing and relieving suffering, and on supporting the best possible quality of life for patients who are facing a serious and/or life-threatening illness and their families [1]. Palliative care aims to relieve suffering in all stages of disease, and is not limited to end of life care. Within an integrated model of medical care, palliative care is provided at the same time as curative or life-prolonging treatments (algorithm 1). (See "Palliative care: Benefits, services, and models of care".)

Patients in the advanced stage of a serious and/or life threatening illness typically experience multiple symptoms, the most common of which are pain, depression, anxiety, confusion, fatigue, breathlessness, insomnia, nausea, constipation, diarrhea, and anorexia (table 1) [2-4]. These symptoms may result from a number of factors. Among patients with advanced cancer, for example, symptoms may result from the disease (eg, bone pain from metastases, dyspnea from pleural effusions), from treatment (eg, esophagitis with thoracic radiation therapy), or from other concurrent conditions (eg, osteoarthritis).

This topic review provides a suggested approach to assessment for the most common physical and psychological symptoms that arise in patients receiving palliative care for an advanced serious and/or life-threatening illness. The principles underlying the comprehensive palliative care assessment (which include domains other than physical and psychologic symptoms), and an overview of treatment for symptoms commonly encountered in a palliative care population are provided elsewhere. (See "Overview of comprehensive patient assessment in palliative care" and "Overview of managing common non-pain symptoms in palliative care".)

GENERAL PRINCIPLES — Patient descriptions of physical symptoms and their severity are the primary data for symptom assessment in palliative care. Exploring patients' reports of symptoms requires thoroughness, persistence, and patience; this is a fundamental aspect of patient-centered care.

It is important to assess mental status and stamina before starting to elicit information as to the nature and severity of symptoms. Seriously fatigued patients may only be able to answer a few questions briefly, and more than one visit may be necessary. Patients who are confused or delirious will not be able to cooperate fully, making symptom identification and assessment difficult; failure to recognize delirium may lead to inaccurate assessments and inappropriate therapies [5]. (See "Diagnosis of delirium and confusional states".)

Patients with advanced illnesses typically have multiple symptoms, and systematic assessment is preferable to relying on spontaneously described symptoms. A study of patients referred to a palliative medicine program found that there were 10 symptoms for every one symptom that was volunteered by a patient [6]. A careful review of symptoms with a focus on common problems in palliative care practice is required. Comprehensive symptom assessment can contribute to significant symptom improvement and better quality of life [7,8].

Each identified symptom should be investigated in regard to its Onset, Palliating and Provoking factors, Quality, Response to previous treatments, Related factors/symptoms, Severity, and Temporality (the OPQRST historical structure for evaluating medical complaints). Of comparable importance, but less emphasized, is understanding the personal meaning of a symptom to the patient and how the symptom affects their psychosocial well-being (the MOPQRST mnemonic (table 2)). Sample questions to explore the meaning of specific symptoms include:

- Of the symptoms that have been bothering you, which symptom bothers you the most [9]?
- How do the symptoms affect you? How much do they interfere with your life (eg, sleep? daily activities? your sense of well-being?)
- What ideas do you have about the meaning of these symptoms?
- Do they make you worry about your health/illness? What are your concerns?
- How are these symptoms affecting your family and friends?

Discussing symptoms with the patient's caregivers may also be informative and provide opportunities to be supportive and educate family and friends [10].

Following initial assessment, periodic symptom reassessment is valuable for identifying or modifying treatment goals, monitoring the response to specific symptomatic interventions, and for communicating between members of the health care team and with caregivers.

Dimensions of symptom assessment — Dimensions are different aspects of symptoms, such as severity, frequency, level of interference with activities, and level of distress associated with the symptom.

Symptom severity is a useful guide to treatment (eg, pain) and it may also provide some prognostic information (eg, dyspnea). (See 'Performance status, symptoms, and prognosis' below.)

The use of rating instruments that are completed by patients themselves represents a major change in symptom assessment over the last 30 years. In evaluating symptoms, it is helpful to obtain the patient's rating of severity within a given time frame, such as the last 24 hours. The approach to rating pain relies exclusively on how the patient reports pain, using a verbal or numerical scale. The patient can be asked to make a mark on a 10 cm straight line (Visual Analog Scale or VAS, (figure 1)) or rate severity on a scale of 0 to 10, where 10 is worst. These approaches are based upon psychophysical studies in the field of subjective sensory physiology, where it has been shown that perception of a stimulus is closely related to the strength of the stimulus [11].

Some patients are unable to rate their symptom severity on a numerical scale [12]. An alternative approach is to ask patients for their rating of symptom distress rather than severity, and to give them categories of response (eg, bothered not at all, a little bit, somewhat, quite a bit, very much). Some symptoms, such as fatigue, may be rated by patients as mild in severity, but severe in distress. The amount and type of interference with daily activities caused by a symptom also can illustrate symptom severity and provide another means of determining therapeutic success.

Symptom change — The patient's assessment of symptom relief is also important since it drives the therapeutic plan. The definition of the minimum clinically significant differences in symptom instruments for pain, fatigue, and dyspnea has been an important advance in the interpretation of symptom ratings, and can be considered to be a 2 point change on an 11 point scale (eg, 0 to 10, (figure 1)) or any change in categories of a Likert scale, such as the faces pain scale (form 1) [13-17].

Challenges in symptom assessment — A number of situations raise particular challenges for symptom assessment in palliative care patients:

- Patient's assessment of symptoms may differ from that of the health professional. In general, clinicians (and caregivers) have greater discordance with patients in assessing the severity of subjective symptoms than for objective states, such as the presence of vomiting. Clinicians tend to rate the severity of symptoms lower than do patients and family members, and to tolerate levels of symptom-related distress and suffering that patients find unacceptable [18-22]. In contrast, family members tend to over-rate symptoms as well [23-25]. However, where pain is concerned, older family members tend to over-rate while younger family members tend to under-rate pain [23].
- Patients may downplay or not report symptoms (particularly pain) because of fears that worsening symptoms reflect disease progression. Underreporting may also occur if a patient feels that a symptom such as pain is an inevitable consequence of the disease, its treatment, or of dying. In addition, if patients do not receive attention to oft-voiced complaints, they may stop communicating about distress related to that specific complaint.
- Many symptoms are multifactorial in origin. A comprehensive assessment process will help define all the possible factors that may be causing a specific symptom. (See 'Approach to specific symptoms' below.)
- Patients and/or their families may have suffered harm in the health care system and lost trust in the system and/or care providers. This may make them particularly reluctant to discuss psychological symptoms. Particularly in these cases, the assessment interview with the patient and family may itself have therapeutic value in enhancing the care provider relationships with patient and family, eliciting care preferences and developing trust. (See "The initial interview in palliative care consultation".)
- Cultural factors may affect symptom assessment. Cultural factors may determine which symptoms are acceptable for discussion between patients and physicians, and how patients perceive their symptoms [26]. As an example, in some cultures, women may not be comfortable sharing gynecologic complaints with a male physician.
- Patients may have difficulty communicating. Examples include intubated patients in the intensive care unit, patients who are withdrawn or who have cognitive impairment, and those who are just too ill to voice complaints. As patients near death, symptom assessment becomes more difficult because the majority of patients become noncommunicative and other symptoms, such as restlessness and confusion, may interfere with effective communication. The study of behavioral changes as clues to the presence of pain (eg, grimacing) is an area of ongoing research, and forms the basis for observer-based rating instruments such as the Pain Assessment in Advanced Dementia [PAINAD] tool. (See 'Patients unable to self-report' below.)

  Involved family members and caregivers may be asked by health professionals to assess and rate symptoms (proxy ratings). However, there may be disparities between patient and caregiver symptom assessments or ratings [23,27,28]. For patients with impaired communication, the palliative care consultant may have to balance multiple assessments by family, caregivers, and health care personnel. (See 'Patients unable to self-report' below.)
- Care providers (physicians and nurses alike) may not be aware of the high prevalence of symptoms in these patients, may not have symptom assessment incorporated into their conversations with patients, and may lack knowledge about symptom identification and management. The average number of symptoms ranges from 11 to 18 in a wide variety of illnesses [29-31].

ASSESSMENT AND RATING INSTRUMENTS FOR SYMPTOMS — Formal multiple symptom assessment tools, especially those that are symptom inventories like the revised Edmonton Symptom Assessment Scale, provide a good overview of symptoms in individual patients (figure 2). In particular, multiple symptom assessment tools are highly effective in the recognition of unreported symptoms, when combined with further patient interviewing to delineate the details of positive responses. When a specific tool has been chosen, it should be used consistently to ensure reliability in the clinical setting.

Many of these symptom assessment tools have been tested for reliability and validity. However, like any other measurement of health outcomes, there are potential errors in assessment [32]. The possibilities for assessment errors include:

- Motor, hearing, and visual impairments may impede the usefulness of symptom assessment tools in the elderly [33]. (See "Palliative care: Issues specific to geriatric patients", section on 'Symptom assessment'.)
- Cognitive dysfunction may lead to misleading responses and inaccurate assessment, even when paired with behavioral indicators [5]. The cognitive dysfunction may be quite subtle. (See 'Patients unable to self-report' below.)
- Shorter tools may miss symptoms that are important to the patient, and longer tools may be too tiring for patients to complete. (See 'Challenges in symptom assessment' above.)
- As the patient's condition changes, symptom ratings may change as he or she accommodates to the new condition, even if the symptom has not changed. This is referred to as the phenomenon of response shift. Ratings may also be influenced by other symptoms, especially anxiety and other emotional reactions, which may change over time. (See 'Symptom change' above.)
- Interpretation of the "anchors" (0 and 10 on the numerical 0 to 10 scale) may vary between patients, depending upon their previous experience. Caregivers and health care personnel may also interpret the anchors differently. It may be necessary to repeat the definitions of the anchors when asking patients to give a rating.
- For numerical scales, the "cut point" is a number that identifies how to categorize severity. Studies have identified cut points of 4 out of 10 (mild versus moderate) and 7 out of 10 (moderate versus severe) for pain [34]; work is ongoing to determine optimal cut points for other symptoms [35,36].

Despite these limitations, a number of validated multiple symptom assessment tools are in wide usage in palliative and end of life care settings, including:

- The Edmonton Symptom Assessment Scale, which is available as a nine-item (figure 2) and a 15-item scale (table 3) [37,38]. A revised version is available online that reorders the symptoms into physical first, psychosocial second, and overall well-being last (ESAS-r). A Spanish language version has also been developed [39].

- Memorial Symptom Assessment Scale-Short (MSAS) Form (figure 3) and Condensed MSAS [40-42]
- MD Anderson Brief Symptom Inventory [43,44]
- Rotterdam Symptom Checklist [45]
- Symptom Distress Scale [46]
- Patient-Reported Outcomes Measurement Information System (PROMIS, www.nihpromis.org [47]), as developed by the US National Institutes of Health (see "Evaluation of health-related quality of life", section on 'Combined instruments for patient-reported outcomes')
- The Interactive Symptom Assessment and Collection (ISAAC) tool, developed and hosted by Cancer Care Ontario
- The National Comprehensive Cancer Network (NCCN) Distress thermometer

Instruments are available that focus on one symptom, such as dyspnea or pain. One example is the Brief Pain Inventory, a patient self-rating scale that assesses pain intensity and pain interference in various areas of function [48,49]; a short-form version is available online (BPI-SF). (See 'History' below.)

However, detailed instruments such as these are not available for all symptoms, and patients may not be able to answer the multiple questions from many instruments.

PERFORMANCE STATUS, SYMPTOMS, AND PROGNOSIS — Performance status is a critical aspect of patient assessment in palliative care. As a general rule, performance status, as assessed by the Karnofsky or ECOG performance status scales (table 4 and table 5) is a key indicator of prognosis in individuals with advanced terminal disease [50]. The Palliative Performance Scale (PPS) is gaining wide acceptance as a tool for assessing functional levels and as a method of estimating prognosis in patients with advanced cancer [51,52]. The PPS [52,53] may be a better indicator of functional status than other types of performance status scales, including Karnofsky and ECOG, in this population. Comparisons suggest there is considerable overlap [54]. (See "Survival estimates in advanced terminal cancer", section on 'Patients receiving supportive care only' and "Survival estimates in advanced terminal cancer", section on 'Performance status'.)

Less well recognized is the relationship between symptoms, performance status, and prognosis. As an example, symptom number and intensity correlate significantly with performance status and prognosis [55]. As a terminal disease progresses, there is often a continual decline in function that is accompanied by increasing fatigue and cachexia.

Other specific clinical signs and symptoms may represent independent prognostic factors in patients with advanced serious or life-threatening disease. As an example, in a systematic review of survival prediction in terminal cancer, the strongest evidence after performance status for an independent association with death was for dyspnea, dysphagia, weight loss, xerostomia, anorexia, and cognitive impairment (delirium) [56]. The following table shows the range of median survivals in patients with various signs and symptoms in univariate analyses from this and other studies (table 6). These findings suggest that for patients with advanced life threatening diseases, such as those referred to palliative care programs, the presence of these symptoms may help physicians estimate patient survival.

Dyspnea is a particularly important indicator of shortened survival in a variety of diseases, but especially in terminally ill cancer patients [3,6,37,40-42,57]. In one study, the presence of dyspnea was associated with a median survival of less than 30 days [57]. The impact of dyspnea and other symptoms on prognostic estimates in advanced cancer, and assessment of dyspnea in palliative care patients are discussed in more detail elsewhere. (See "Survival estimates in advanced terminal cancer", section on 'Clinical signs and symptoms' and "Assessment and management of dyspnea in palliative care", section on 'Assessment of dyspnea'.)

Among dyspneic patients, other findings may help to predict the likelihood of imminent death. As an example, in a retrospective sample of 122 patients with cancer who presented to an emergency room with acute dyspnea, a respiratory rate greater than 28/min, heart rate greater than 110 beats per minute, uncontrolled disease, and the presence of metastases were all predictive of death within two weeks; the relative risk for imminent death among patients with a respiratory rate above 28/min, compared to the overall group, was 12.7 (95% CI 3.1-52.8) [58].

Noisy breathing, also known as the "death rattle", refers to gurgling breath sounds and is usually a preterminal finding, with death likely in hours to days [59]. (See "Overview of managing common non-pain symptoms in palliative care", section on 'Last hours of life'.)

APPROACH TO SPECIFIC SYMPTOMS — The following is a brief discussion about assessing highly prevalent symptoms in the palliative care patient. More detailed discussions of some of these symptoms are available in related topic reviews.

Pain — The purpose of pain assessment is to obtain a rating of severity and to make a diagnosis of the likely cause. The identification of a specific pain syndrome in cancer patients may lead to a specific management plan. (See "Overview of cancer pain syndromes".)

The first step is to ask the patient about the presence of pain and its severity and to believe the answers. As noted above, there is a great divergence between how patients and professionals evaluate pain severity. In a study of 103 cancer patients, a comparison of Visual Analogue Scale (VAS) pain ratings by health professionals with those of patients showed lower ratings of severe pain by health care professionals more than 70 percent of the time [18].

Pain does not occur just in patients with cancer, however. It is also experienced by a large percentage of patients with end stage heart failure [60,61], chronic obstructive pulmonary disease (COPD), and cirrhosis [62,63], and is particularly associated with arthritis [64].

The following sections will briefly summarize the components of the pain evaluation. A more detailed discussion is available elsewhere. (See "Assessment of cancer pain".)

History — In eliciting a pain history, initial questions should include site, nature and severity, interference, and relief. In addition, patients may have had (untreated) chronic pains, such as that related to arthritis, that predate the advanced illness [64].

- **Site** — It is always wise to have the patient point to the site of pain to avoid a misunderstanding of anatomical terms.
- **Type of pain** — Among patients with cancer, the specific type of pain may help to elucidate the specific pathophysiology. As examples (see "Assessment of cancer pain", section on 'Inferred pathophysiology (types of cancer pain)'):
    - Nociceptive pain is sustained predominantly by ongoing tissue injury. Somatic nociceptive pain involves injury to somatic structures like skin, bone,

joints, or muscles. It is usually well localized, and often described by patients as "aching", "stabbing" or "throbbing", in quality. Visceral nociceptive pain results from distension, injury to, or inflammation of visceral organs. It is usually poorly localized, and characterized as "gnawing" or "crampy" when arising from the obstruction of a hollow viscus (eg, the bowel lumen), or as "aching" or "stabbing" when arising from other somatically innervated visceral structures, such as organ capsules or parietal pleura. Visceral pain can be referred to somatic structures. Further evaluation often yields an abnormal finding that can be identified on physical examination (such as localized tenderness to palpation) or radiographic scans to explain the symptoms.

- Neuropathic pain is sustained by abnormal somatosensory processing in the peripheral or central nervous system, or direct damage to nerves. Examples include postherpetic neuralgia, postchemotherapy neuropathy, and phantom pain. Patients may describe unpredictable shooting, burning, numbness, or pruritus. The sensory examination is often helpful if abnormalities such as lack of sensation, increased sensitivity (hyperesthesia), or pain with nonpainful stimuli (allodynia) can be demonstrated.

Depending on the location of the mass, neuropathic pain may be present with nociceptive pain, and may not have its signature features of sensory disturbance or shooting pain, but may be gnawing or constant.

- **Severity and QOL impact** — Pain severity guides medication choice and dosage. (See "Cancer pain management: General principles and risk management for patients receiving opioids" and "Cancer pain management with opioids: Optimizing analgesia" and "Pain assessment and management in the last weeks of life".)

  There are a number of simple ways to assess pain severity, including a Faces scale (form 1), a VAS (figure 1), or a categorical Likert scale (none, a little, somewhat, quite a bit, very much).

  Formal instruments have also been developed to rate pain severity in multiple dimensions. These include the Brief Pain Inventory (BPI; a short-form version of which is available online (BPI-SF)) [48,49], the McGill Pain Questionnaire [65] (a shortened version is available [66]), and the Memorial Pain Assessment Card [67]. Both the McGill Pain Questionnaire and the BPI have been translated into several languages. Although many of these tools were developed for patients with cancer, they are equally applicable to patients with other serious and/or life threatening conditions. (See "Assessment of cancer pain", section on 'Intensity'.)

  Another way to evaluate severity is through assessment of the impact of pain on physical and psychological function and quality of life (QOL). Family members may be able to provide important information in this regard. Pain can interfere with QOL by interfering with daily activities, walking, and sleep, and by affecting mood. Severe pain may engender a sense of hopelessness and anxiety. Anxiety, in turn, may increase reactions to pain, while fear can decrease pain reactivity [68].

- **Aggravating and alleviating factors** – This includes response to prior treatment(s)

- **Associated symptoms** – This includes paresthesias, weakness, nausea

- **Temporal patterns** – Temporal assessment of the pain may include information about onset, duration, and fluctuation. Both the extent and duration of relief provided by interventions should be determined.

  Pseudoaddiction describes a situation in which a patient's legitimate chronic pain condition is undertreated with pain medication, leading the patient to act in a way that resembles addictive behavior (requesting extra medications and demanding attention); such patients are often labeled as demonstrating "drug seeking behaviors". A careful pain history that emphasizes perceived pain relief will help clarify the issue.

  Most patients with chronic cancer pain experience periodic flares, often referred to as "breakthrough pain". Breakthrough pain can be caused by inadequate dosing, an unprovoked flare of the underlying pain syndrome, or be provoked by a procedure or activity (incident pain). Especially for inpatients, procedural pain is an experience that is often overlooked. Breakthrough pain may result from such routine procedures as dressing changes for pressure ulcers or wounds, positioning for change of bed sheets, or movement in bed for a radiographic study [69]. (See "Assessment of cancer pain", section on 'Pain characteristics' and "Cancer pain management with opioids: Optimizing analgesia", section on 'Management of breakthrough pain'.)

- **Patient and family perspective** – Patients and their family members should be asked about the meaning of the pain, their understanding of its cause, worries about relief, personal and cultural attitudes, concerns about opioid tolerance and addiction, diversion, and expense. Inquiring about personal experiences with pain earlier in the course of the disease, or in friends and family members can dispel hidden anxieties and misunderstandings.

Special circumstances

Patients with a history of substance abuse — Opioids are widely used for treatment of pain in patients with cancer because of their safety, multiple routes of administration, ease of titration, reliability, and effectiveness for all types of pain (ie, somatic, visceral, neuropathic). However, opioids are also potentially abusable drugs. The public health consequences of opioid abuse drive the imperative that all physicians assume responsibility for risk management when these drugs are prescribed for legitimate medical purposes. These issues are discussed elsewhere. (See "Cancer pain management: General principles and risk management for patients receiving opioids", section on 'Risk assessment and management for patients receiving opioids'.)

Assessing and managing pain is difficult in patients who have a history of substance abuse. Patients with a history of substance abuse who complain of pain can cause considerable apprehension for their care providers because of fears about the potential for deception, drug abuse, addiction, and diversion [70].

Patients with a remote history of substance use and who have a stable support system are less likely to abuse opioids [71]. In our own experience, these patients appreciate a careful and objective pain evaluation and are generally responsible and appropriate in their use of opioids as a component of their medical treatment. Further inquiry into the circumstances of past substance use is helpful. Sometimes they and their family members are even more concerned about addiction to pain medications than are professional staff.

Patients who are actively using "street drugs" at the time of initial evaluation should have a careful and objective pain evaluation. The possibility that they are using street drugs to obtain pain relief should be considered. Even if they have an addiction, their pain is real and assessment needs to focus on ways to both treat their pain and help with their addiction. The initial encounter with the patient is most important, as failure to establish a relationship will make it nearly

impossible to obtain an accurate pain history and render trials of medications impossible to interpret.

Principles of risk management in these patients are outlined in the table (table 7). Psychologic evaluation may be helpful in evaluating underlying psychiatric or personality disorders. Assessment and recognition of substance abuse disorders and risk assessment in patients receiving opioids for management of cancer pain are all discussed in more detail elsewhere. (See "Substance use disorder: Principles for recognition and assessment in general medical care" and "Cancer pain management: General principles and risk management for patients receiving opioids", section on 'Risk assessment and management for patients receiving opioids'.)

Patients unable to self-report — Assessment of pain in patients who are unable to self-report is a challenging problem in symptom assessment. The spectrum of patients who have impaired communication includes patients with permanent deficits such as dementia, and those with more temporary cognitive impairments such as delirium, sedation, or trauma. Patients with impaired ability to self-report pain present across the continuum of care, from intensive care units to clinics, home, and long term care settings. Individuals who are unable to communicate their pain are at greater risk for underrecognition and undertreatment of pain.

Patients with mild dementia are often able to give a description and rating of their pain. Patients with advanced dementia may express pain by distress behaviors such as restlessness, grimacing, moaning, guarding, and changes in daily activity, but these behaviors are not specific for pain. When such behaviors occur, a physical examination should be performed with attention to the association of the pain behavior with movement, pressure, toileting, hunger, fear, loneliness, or visual impairment.

A hierarchical approach has been proposed for this set of patients, whereby multiple sources of information are integrated by the examiner, starting with patient report, and including reports from observers (proxy reporting of pain), observation of patient behavior, use of behavioral pain assessment tools, and search for potential causes of pain [72]. A number of instruments have been developed to systematically assess pain-related behaviors in non-verbal adults [73-76]. A review of tools to assess pain in non-verbal adults is available [77]. Sufficient evidence has accumulated to support the use of the Pain Assessment in Advanced Dementia (PAINAD) tool [76].

An empiric trial of analgesics may be warranted if, after the initial assessment, questions remain as to whether a distress behavior is indicative of pain in a patient with cognitive dysfunction.

Dyspnea — Dyspnea is a particularly common symptom in patients who have advanced COPD, heart failure, primary lung cancer, or intrathoracic metastatic disease. However, for unclear reasons, it is also a common symptom in patients with no direct lung pathology [78]. As an example, a National Hospice Study found that 24 percent of terminally-ill cancer patients had dyspnea in the absence of known cardiopulmonary pathology [79]. (See "Assessment and management of dyspnea in palliative care", section on 'Prevalence'.)

As with pain, dyspnea is defined solely by patient self-report. Attention to the words that patients use in describing their breathing discomfort may provide insight into the underlying clinical condition as well as the basic physiologic mechanisms producing dyspnea. (See "Assessment and management of dyspnea in palliative care", section on 'Assessment of dyspnea'.)

Objective measures, such as respiratory rate, oxygen saturation, and arterial blood gas determination may not correlate with, nor provide a quantitative measure of the degree of dyspnea [80,81]. Physical examination, pulse oximetry, and chest x-ray do not clarify whether the patient has dyspnea, but may help the clinician to identify likely causes for the symptom (table 8). (See "Assessment and management of dyspnea in palliative care", section on 'Role of investigations'.)

Many methods for assessing the severity of dyspnea are based upon functional assessment (ie, studies of tasks and effort) and quantify the amount of exertion required to cause dyspnea. Breathless patients inevitably reduce their activity level to accommodate dyspnea, so questions about limitations in performing specific activities can be used to assess the impact of dyspnea. As an example, the Oxygen Cost Diagram (figure 4) [82] asks patients to identify the level of activity they are unable to perform due to dyspnea, giving clinicians valuable information regarding the functional impact of the symptom. (See "Assessment and management of dyspnea in palliative care", section on 'Functional impact'.)

Patient rated scales of dyspnea intensity have been based upon psychophysical descriptions of the relationship between work and perceived exertion. As an example, the Borg scale (table 9) measures the severity of dyspnea using a scale from 0 to 10, anchored by descriptive words; it may be used in conjunction with an exertional test [83]. The most common exertional tests involve having the patient walk for 6 or 12 minutes and then rate their dyspnea afterwards. (See "Assessment and management of dyspnea in palliative care", section on 'Intensity'.)

For patients with COPD, the frequency and severity of dyspnea can be assessed using validated questionnaires such as the Clinical COPD Questionnaire (table 10) or the Chronic Respiratory Questionnaire (CRQ), a shortened version of which is available [84]. Although these approaches are useful for evaluating symptom severity in patients with COPD, neither is appropriate for patients with advanced serious life-threatening illness and severe dyspnea at rest. (See "Chronic obstructive pulmonary disease: Definition, clinical manifestations, diagnosis, and staging".)

None of these tools adequately measure the multidimensionality of dyspnea. A Cancer Dyspnea Scale has been developed in Japan for use in patients with lung cancer and translated into English [85]. Although it appears to reliably measure the sensation and psychologic components of dyspnea, further validation in other palliative care populations is needed.

The prognostic implications of dyspnea, particularly in patients with cancer, are discussed above. (See 'Performance status, symptoms, and prognosis' above.)

Fatigue — In the past, the terms “asthenia” and “weakness” were used to describe a subjective sensation of tiredness, while the specific term “fatigue” was used to describe a symptom of tiredness precipitated by effort. However, the terms are currently often used in the same context, and this broad sense of the term “fatigue” has gained widespread acceptance in the medical literature. (See "Palliative care: Overview of fatigue, weakness, and asthenia", section on 'Definition'.)

Fatigue is a highly prevalent and poorly understood symptom in patients with advanced serious and/or life-threatening illness. It is reported by 80 percent of cancer patients overall, and by up to 99 percent of patients following radiotherapy or chemotherapy [86]. Fatigue is also prevalent in palliative care patients with advanced life threatening illness other than cancer, including those with HIV, multiple sclerosis, COPD, and heart failure. (See "Cancer-related fatigue: Prevalence, screening and clinical assessment" and "End of life considerations for heart failure patients" and "Palliative care: Overview of fatigue, weakness, and asthenia", section on 'Prevalence'.)

The assessment of fatigue in palliative care patients can be complex given its subjective and multidimensional nature. As such, there is a trend towards

multidimensional assessment (ie, asking about different aspects of fatigue, such as muscular weakness of tiredness associated with a sleep disturbance) rather than asking a single question "are you tired?". (See "Palliative care: Overview of fatigue, weakness, and asthenia", section on 'Clinical assessment'.)

Instruments have been developed for assessment of fatigue in cancer patients which assess both severity and functional impact (eg, the Brief Fatigue Inventory (table 11) [87]), and this subject is addressed in more detail elsewhere. (See "Cancer-related fatigue: Prevalence, screening and clinical assessment", section on 'Clinical assessment'.)

A listing of assessment tools for fatigue in patients with cancer as well as other serious life-threatening illnesses is available in the table (table 12). Questions about fatigue are also present in some symptom assessment instruments for patients with COPD and heart failure. However, in such patients, it can be difficult to separate out fatigue from dyspnea [88]. A combined dyspnea/fatigue instrument has been developed for patients with heart failure [89]. (See "End of life considerations for heart failure patients".)

Fatigue severity can also be quantified using a 0 to 10 visual analog scale such as provided in the Edmonton Symptom Assessment Scale (figure 2). Ratings of fatigue severity have been shown to be clinically meaningful in patients with cancer in terms of interference with function [90]. (See "Cancer-related fatigue: Prevalence, screening and clinical assessment", section on 'Clinical assessment' and "Palliative care: Overview of fatigue, weakness, and asthenia", section on 'Clinical assessment'.)

The cause of fatigue in palliative care patients is typically multifactorial; acute fatigue, which may be caused by acute illness such as infection or cardiac decompensation, must be distinguished from more chronic fatigue, which is more typically (particularly for cancer patients) related to the underlying illness or its treatment. A comprehensive history and physical examination should be undertaken to ascertain the various organ systems affected by the underlying disease and the impact of fatigue on activities of daily living and quality of life, to search for potentially reversible or treatable contributory factors, and to direct the diagnostic work-up. Review of all medications (both prescribed and over the counter, including complementary/alternative therapies) is important. (See "Palliative care: Overview of fatigue, weakness, and asthenia", section on 'Causes and pathophysiology'.)

Factors that are often causally related to fatigue should be specifically assessed, including anemia, uncontrolled pain, emotional distress, sleep disturbance, weight loss and malnutrition, electrolyte disturbances (table 13), and the presence of other comorbidities (eg, infection, cardiopulmonary, renal, hepatic, neurologic, or endocrine dysfunction). (See "Cancer-related fatigue: Prevalence, screening and clinical assessment", section on 'Main contributory factors' and "Cancer-related fatigue: Prevalence, screening and clinical assessment", section on 'Assess for potentially remediable contributing factors'.)

Dry mouth — Xerostomia, the feeling of a dry mouth, is a highly prevalent symptom in palliative care. Risk factors include medications, mouth breathing, advanced age, and in cancer patients, a previous history of radiation to the head and neck. A number of medical conditions such as Sjögren's syndrome, diabetes mellitus, and anxiety states can contribute to this symptom. Dehydration from reduced oral intake may be associated with a dry mouth. Medications are a significant cause of xerostomia in palliative care; in one survey, hospice patients were on a median number of four drugs that were associated with xerostomia [91]. (See "Clinical manifestations of Sjögren's syndrome: Exocrine gland disease", section on 'Xerostomia' and "Management of late complications of head and neck cancer and its treatment", section on 'Salivary gland damage and xerostomia' and "Normal aging", section on 'Oropharynx' and "Stopping artificial nutrition and hydration at the end of life", section on 'Fluid deficits at the end of life'.)

A dry mouth can alter taste and make it difficult for patients to eat and swallow. Patients with xerostomia may also complain of mouth pain and difficulty with speaking [92].

On examination, the presence of dry lips, dry mucosa, dental caries, a coated tongue, and ropy saliva helps confirm the impression of xerostomia. Associated findings of relevance include the presence of thrush, periodontal disease, and herpetic infection. Patients with erythematous candidiasis may have patchy erythema of the dorsal tongue and other mucosal surfaces and angular cheilitis.

While there are objective tests to confirm the presence of xerostomia (eg, measures of saliva production, such as the unstimulated and stimulated [after eating] whole salivary flow rates), these tests are used primarily for research purposes.

Dysphagia — Dysphagia, which is sometimes associated with odynophagia and/or aspiration, occurs regularly in patients with advanced illness, especially in the setting of neurologic disorders (including amyotrophic lateral sclerosis [ALS] and other motor neuron diseases, brain metastases, and leptomeningeal carcinomatosis), as well as cancers of the head and neck and esophagus. (See "Oropharyngeal dysphagia: Etiology and pathogenesis" and "Epidemiology, pathobiology, and clinical manifestations of esophageal cancer", section on 'Clinical manifestations' and "Overview of the diagnosis and staging of head and neck cancer", section on 'Clinical presentation' and "Clinical features of amyotrophic lateral sclerosis and other forms of motor neuron disease", section on 'Upper motor neuron symptoms' and "Speech and swallowing rehabilitation of the patient with head and neck cancer", section on 'Aspiration'.)

In dysphagia, patients will complain of a bolus getting “stuck” after swallowing and often can point to a site. Aspiration should be suspected when patients start coughing after drinking liquids, with accompanying hoarseness.

Dysphagia may be classified as oropharyngeal or esophageal and patients may have difficulty with ONE OR BOTH phases of the swallowing mechanism (see "Oropharyngeal dysphagia: Etiology and pathogenesis", section on 'Physiology of swallowing'):

- Oropharyngeal dysphagia, also called transfer dysphagia, arises from disorders that affect the function of the oropharynx, larynx, and upper esophageal sphincter. Neurogenic and myogenic disorders as well as oropharyngeal tumors are the most common underlying mechanisms for oropharyngeal dysphagia.
- Esophageal dysphagia arises within the body of the esophagus, the lower esophageal sphincter, or cardia, and is most commonly due to mechanical causes or a motility disturbance.

An overview of the many causes of oropharyngeal dysphagia is provided in the table (table 14). The differential diagnosis of esophageal dysphagia is presented elsewhere. (See "Oropharyngeal dysphagia: Etiology and pathogenesis", section on 'Etiology and pathogenesis' and "Overview of dysphagia in adults", section on 'Differential diagnosis of esophageal dysphagia'.)

A separate but related problem, pain upon swallowing (odynophagia), can result from inflammation, infection, or neoplasia. (See "Deep neck space infections" and "Medication-induced esophagitis" and "Clinical manifestations of oropharyngeal and esophageal candidiasis" and "Herpes simplex virus infection of the esophagus" and "Epidemiology, pathobiology, and clinical manifestations of esophageal cancer", section on 'Clinical manifestations' and "Evaluation of the HIV-infected patient with odynophagia and dysphagia", section on 'Etiology'.)

Algorithmic approaches to the differential diagnosis of dysphagia and suggested workup for patients with esophageal dysphagia and oropharyngeal dysphagia

are presented in the algorithms (algorithm 2 and algorithm 3 and algorithm 4). (See "Overview of dysphagia in adults", section on 'Differential diagnosis of esophageal dysphagia' and "Overview of dysphagia in adults", section on 'Diagnostic testing' and "Oropharyngeal dysphagia: Clinical features, diagnosis, and management", section on 'Determining the etiology'.)

Aspiration — A disordered swallowing mechanism predisposes to aspiration. In addition to dysphagia, other factors that predispose to aspiration include reduced consciousness which compromises the cough reflex, mechanical disruption of the upper airway or gastrointestinal tract, and recumbent patients who receive large volume tube feedings and feeding gastrostomy. All patients with these conditions should be asked about and observed for cough after swallowing. A history of coughing while eating or drinking is likely to indicate aspiration, but aspiration may also be clinically silent. (See "Aspiration pneumonia in adults".)

When aspiration is suspected, bedside assessment includes observation of the patient after swallowing a sample of thin liquids, thick liquids, and solids. In addition to cough, helpful signs include drooling after swallowing, wet or hoarse vocal quality after swallowing, head or neck repositioning while swallowing, and multiple attempts to swallow a bolus. When evaluated with formal swallowing studies, some of these patients will be found to have laryngeal penetration. In such cases, a balance has to be struck between quality of life issues (ie, continue eating despite the high risk for aspiration) and safety considerations (mechanical soft or pureed diets, nasogastric tube, gastrostomy tube, or nothing by mouth). Interestingly, many patients who aspirate when swallowing still are able to swallow small pills without difficulty. (See "Aspiration pneumonia in adults", section on 'Evaluation of dysphagia' and "Aspiration pneumonia in adults", section on 'Prevention'.)

Lack of appetite — Lack of appetite is frequently seen in patients with many kinds of advanced illnesses (eg, heart failure, cancer, COPD, frail elderly), and is often a foremost concern of patients and their families.

Although the reliability of subjective assessments of appetite is debated, they are probably the simplest and most practical measures available. Patient-rated assessment measures have been developed in the setting of trials of megestrol acetate for cancer or HIV-related anorexia (eg, Functional Assessment of Anorexia/Cachexia Therapy, FAACT [93]). Another instrument, the Subjective Global Assessment of Nutrition instrument, has been correlated with nutritional status and caloric intake, but requires further validation [94]. A simple vertical VAS measurement has been shown to correlate with nutritional intake in cancer patients in the last few weeks of life [95]. Simply asking about what the patient eats and drinks in a typical day can allow the clinician to estimate caloric intake.

Lack of appetite can be a consequence of chronic fatigue or associated with barely noticeable nausea; depression, pain, xerostomia, and constipation can also contribute. An important and treatable etiology is early satiety due to disorders of gastric motility. Lack of appetite does not always lead to weight loss, but recognition of weight loss should lead to questions about lack of appetite. It is helpful to determine whether the patient is distressed by lack of appetite (ie, whether or not they feel hunger) in prioritizing symptoms for treatment. (See "Malignancy-associated gastroparesis: Pathophysiology and management" and "Gastroparesis: Etiology, clinical manifestations, and diagnosis" and "Diabetic autonomic neuropathy of the gastrointestinal tract".)

Other common considerations include medications (amphetamines, antibiotics, antihistamines, digoxin, ranolazine), depression, taste disturbances, and food aversions. Decreased appetite is a component of the “failure to thrive” (FTT) syndrome, which is described by The National Institute of Aging as "syndrome of weight loss, decreased appetite and poor nutrition, and inactivity, often accompanied by dehydration, depressive symptoms, impaired immune function, and low cholesterol" [96]. In geriatric practice, FTT describes a point further along a geriatric functional continuum that is closer to full dependence and death, with “frailty as a mid-point between independence and pre-death” [97]. (See "Failure to thrive in elderly adults: Evaluation".)

Weight loss — Among patients with advanced illness, weight loss may occur even in the setting of a good appetite and adequate caloric intake, as typified by cachexia associated with advanced heart and lung disease, cancer, and HIV and other chronic infections. Weight loss of greater than 5 percent of baseline is generally accepted as significant. Determining whether patients feel they “look like themselves” may lead to a discussion of weight loss. Cachexia is a hypercatabolic state that is characterized by an accelerated loss of skeletal muscle in the context of a chronic inflammatory response, and should be distinguished from sarcopenia, loss of muscle. In advanced illness, weight loss is not remedied by nutritional supplementation. Important physical findings that support the suspicion of cachexia are temporal wasting, thenar wasting, and dorsal interosseous wasting. (See "Pathogenesis, clinical features, and assessment of cancer cachexia" and "End of life considerations for heart failure patients", section on 'Anorexia and cachexia'.)

While cachexia in advanced illness typically reflects a metabolic disorder of uncertain cause and for which treatment is largely ineffective, the usual causes of weight loss, such as loss of appetite, inadequate nutritional intake, and malabsorption, should not be overlooked. In some cases, cancer treatment (eg, androgen deprivation therapy for advanced prostate cancer, tyrosine kinase inhibitors such as sorafenib) may contribute to loss of lean body mass. (See "Pathogenesis, clinical features, and assessment of cancer cachexia", section on 'Contribution from cancer treatment' and "Toxicity of molecularly targeted antiangiogenic agents: Non-cardiovascular effects", section on 'Muscle wasting/sarcopenia'.)

Nausea with or without vomiting — Nausea and vomiting are symptoms that are common near the end of life, and they can cause substantial physical and psychological distress for patients and their families [98]. Although vomiting is more easily quantified, nausea has been routinely measured using a visual analog scale in clinical trials of antiemetics in patients with chemotherapy-induced nausea and vomiting. (See "Approach to the adult with nausea and vomiting" and "Prevention and treatment of chemotherapy-induced nausea and vomiting".)

A thorough history and physical examination are essential first steps in the management of these patients to define the severity of the symptoms and identify clues to the underlying etiology. Among patients receiving chemotherapy, nausea and vomiting should not be automatically assumed to represent breakthrough chemotherapy-induced nausea and vomiting (CINV), particularly if symptoms develop at a time point that is not consistent with CINV. (See "Prevention and treatment of chemotherapy-induced nausea and vomiting".)

From a pathophysiologic standpoint, nausea and vomiting can be vagally mediated through the emesis center in the medulla, systemically mediated through the chemoreceptor trigger zone (CTZ), vestibular, or centrally mediated (figure 5). The differential diagnosis of nausea and vomiting in the adult is broad, and includes medications and toxic etiologies (including chemotherapy and opioids), disorders of the gut and peritoneum (including gastroparesis), central nervous system disorders (brain metastases, cranial irradiation), vestibular disorders, and endocrinologic/metabolic causes. (See "Approach to the adult with nausea and vomiting", section on 'Differential diagnosis'.)

The most common causes of nausea and vomiting in palliative care patients are outlined in the table (table 15). Most palliative care patients who are nauseated have more than one contributory factor. This subject is discussed in detail elsewhere. (See "Palliative care: Assessment and management of nausea and vomiting", section on 'Patient assessment'.)

Constipation — Determining the presence of constipation can be difficult as the term has varied meanings for different people. For some, it may mean that stools are too hard or too small, or that defecation is too difficult or infrequent. The first three complaints are difficult to quantify in clinical practice; the last can

be measured and compared to the general population. (See "Etiology and evaluation of chronic constipation in adults", section on 'Definition of constipation'.)

Definitions of constipation used in different publications have been variable [99]. Formal criteria are available to define functional constipation (the Rome III criteria) [100], but they are not useful in palliative care as the criteria must be fulfilled for at least three months. (See "Constipation in the older adult", section on 'Definition of constipation'.) Some have suggested that four domains are pivotal to making a diagnosis of constipation in palliative care [99]:

- Any life-long history of constipation (using the Rome criteria)
- Evaluation of physical dysfunction that may impede normal defecation
- Subjective sensations (eg, feelings of incomplete defecation or bloating or fullness)
- Objective changes (eg, frequency or consistency of stools)

A patient with constipation should be asked when he or she last had a bowel movement, and for any associated symptoms. In the palliative care setting, patients with constipation may present with abdominal pain, nausea, vomiting, diarrhea, or difficulty with a bowel movement. Consistency of stool (soft or hard) is a helpful detail.

Risk factors for constipation in patients with a serious or life-threatening illness include advanced disease, older age, decreased physical activity, low fiber diet, depression, and cognitive impairment. Medications which can cause or exacerbate constipation include opioids, calcium channel blockers, diuretics, anticholinergic drugs, iron, serotonin antagonists, and chemotherapy (vinca alkaloids, thalidomide, vandetanib). There are also neural (eg, epidural spinal cord compression) and metabolic causes of constipation (eg, hypercalcemia and hypothyroidism).

A comprehensive physical examination should be performed that includes a rectal exam to palpate for hard stool, assess for masses, anal fissures, hemorrhoids, sphincter tone, push effort during attempted defecation, prostatic hypertrophy in males, and posterior vaginal masses in females. Rectal examination may demonstrate impaction, or the rectal vault may be empty. (See "Etiology and evaluation of chronic constipation in adults", section on 'Physical examination'.)

If the rectal vault is empty and a diagnosis of malignant bowel obstruction is suspected, radiographic imaging with abdominal x-ray or CT scan is indicated. (See "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults".)

For patients without clinical suspicion of bowel obstruction, abdominal plain films can be used to estimate the degree of retention of stool which may be difficult to determine from history and physical exam. Some have proposed scoring systems for assessing the severity of constipation in terminal cancer patients based upon the amount and distribution of stool in different quadrants of the large bowel [101,102]. Each abdominal quadrant on plain films can be assessed for stool content and ranked for 0 to 3, resulting in a severity score from 0 to 12. A clinical constipation assessment scale also has been developed and validated (table 16) [103,104].

Swelling in the arms and legs — Peripheral edema, palpable swelling that is produced by expansion of the interstitial fluid volume, is a common complication in patients with advanced organ dysfunction. When massive and generalized, the excess fluid accumulation is called anasarca. Anasarca or just lower extremity edema can interfere with ambulation and is often a source of pain from stretching of the skin. It may also directly affect the patient's sense of body image. (See "Clinical manifestations and diagnosis of edema in adults".)

Assessment of edema starts with the history which should include questions about area(s) of involvement, associated symptoms (eg, pain), use of medications that may be associated with edematous states (eg, nonsteroidal antiinflammatory agents) or that are being used to treat edema (eg, diuretics), progression of symptoms, and history of medical conditions associated with lymphedema, including surgery and prior radiation therapy, travel, or infection. (See "Pathophysiology and etiology of edema in adults", section on 'Drug-induced edema'.)

The physical examination should be aimed at establishing the pattern of edema (pulmonary, peripheral, ascites, localized) and an assessment of the central venous pressure. The results can indicate the likely cause of edema (table 17). (See "Clinical manifestations and diagnosis of lymphedema", section on 'Diagnosis' and "Pathophysiology and etiology of edema in adults", section on 'Etiology'.)

For patients with lymphedema, clinical measurements of girth or estimates of lymphedema volume are necessary to establish baseline and to track changes during treatment. Methods to obtain clinical measurements are described in detail elsewhere. (See "Clinical manifestations and diagnosis of lymphedema", section on 'Clinical measurements'.)

A variety of clinical conditions are associated with the development of edema, including heart failure, cirrhosis, hypothyroidism, and the nephrotic syndrome, as well as local conditions such as venous and lymphatic disease or malignant ascites (table 18). Among patients who are terminally ill with a serious and/or life-threatening illness, the most common causes of chronic lower extremity edema are venous obstruction, hypoalbuminemia, decreased mobility, fluid retention and medications including corticosteroids. (See "Pathophysiology and etiology of edema in adults".)

Lymphedema, a specific type of peripheral edema that is usually (but not always) nonpitting, may represent a complication of a cancer or its treatment. Lymphedema occurs when the lymphatic load exceeds the transport capacity of the lymphatic system, which causes filtered protein-rich fluid to accumulate in the interstitium [105]. Lymphedema is generally due to disruption of lymphatic flow which may be secondary to injury, surgery, radiotherapy, infection, or malignancy. As compared to generalized edematous states, the rate of capillary filtration is normal in patients with lymphedema. (See "Clinical manifestations and diagnosis of lymphedema", section on 'Physiologic basis of lymphedema'.)

Chronic lymphedema affects both physical and psychological wellbeing as a result of interruption of normal daily activities. Cancer patients with lymphedema are more likely to experience greater disability, poorer quality of life, and greater psychological distress as compared to cancer patients without lymphedema [106]. It may cause patients to feel mental suffering, discomfort, and reduce mobility as well as function [107,108]. (See "Clinical manifestations and diagnosis of lymphedema".)

Psychological and cognitive symptoms — The key psychological symptoms requiring assessment in palliative care patients are depression (as distinct from adjustment reaction and grief), anxiety, and delirium. Clinicians should screen for the multiple factors that increase the prevalence and/or severity of psychological distress (rapidly advancing disease, medications such as interferon or glucocorticoids, metabolic abnormalities, uncontrolled pain, impaired cognition, financial distress) and address them, if possible. Psychological distress frequently lessens with adequate pain relief [109].

Sadness, grief, and depression — The spectrum of mood disorders and conditions seen in palliative care patients includes sadness, normal grief reaction

(including anticipatory grief), pathologic grief, adjustment disorder with depressed features, and minor as well as major depression. Grief, a natural and expected reaction to having a life-limiting illness and loss, can and should be distinguished from major depression [110].

A summary of some of the contrasting characteristics of normal grief versus depression in terminally-ill patients is provided in a table (table 19), and this subject is discussed in detail elsewhere. (See "Assessment and management of depression in palliative care", section on 'Assessment and diagnosis' and "Grief and bereavement", section on 'Normal bereavement' and "Grief and bereavement", section on 'Abnormal bereavement'.)

There is a high frequency of mood disorders in patients with a serious and/or life-threatening illness. As an example, in a meta-analysis, there was a 25 percent combined prevalence of all types of depression, and 38 percent prevalence of mood disorders among palliative care patients [111].

Unfortunately, depression is frequently unrecognized and undiagnosed [19,112]. The prevalence, burden, and challenges in recognizing and treating depression in palliative care patients are addressed in detail elsewhere. (See "Assessment and management of depression in palliative care", section on 'Prevalence of depression in palliative care' and "Assessment and management of depression in palliative care", section on 'Burden of depression'.)

Patients with advanced illness may display many of the vegetative signs of depression (sleep disorder, poor concentration, fatigue, lack of appetite) without being depressed, since such symptoms can be caused by the medical condition or its treatment. Patients facing the end of life may also demonstrate significant guilt and preoccupation with death without being depressed. Nevertheless, the presence of these markers in the absence of other causes should lead to the suspicion of depression. Indicators of poor emotional well being, such as a sense of pervasive hopelessness, helplessness, worthlessness, or guilt, may be more useful in making the diagnosis and in assessing suicide risk. Unrelieved symptoms, particularly pain, may contribute to a sense of hopelessness and lead to depression. Among patients with severe pain or other symptoms, a diagnosis of depression should not be made until symptoms are controlled.

The impact of mood disorders in palliative care is underscored by one study which found that mortality rates in cancer patients are up to 25 percent higher in those who experience depressive symptoms [113]. In addition, individuals who suffer from depression are at increased risk of suicide. Passive suicidal ideation (I'd be better off dead) should be distinguished from active suicidal ideation (I'd be better off dead and this is how I'm going to do it). An expressed desire for a hastened death should not be considered a request for euthanasia, but as a marker for intense distress which requires further exploration [114]. (See "Assessment and management of depression in palliative care", section on 'Burden of depression' and "Euthanasia and physician assisted suicide".)

A variety of screening tools for symptoms of depression are available:

- Abbreviated screening instruments (table 20) appear to be as effective as longer instruments to screen for depression. As an example, screening using a simple one question assessment ("Are you depressed?" or "Have you been depressed most of the time for the past two weeks?") has a negative predictive value (NPV) of 94 percent [115,116] in identifying patients in whom a diagnosis of depression would be excluded on the basis of a full psychiatric interview. Adding a second question that addresses anhedonia ("Have you experienced loss of interest in things or activities that you would normally enjoy?") increases the NPV to 98 percent [116].
- Another simple screening strategy for mood disorder and psychosocial distress utilizes the Distress and Impact Thermometer [117] or other ultra-short methods [118].

Importantly, these brief tools are designed for screening patients who may subsequently need a full diagnostic evaluation for depression. The subject of screening for depression in palliative care patients is discussed in more detail elsewhere. (See "Assessment and management of depression in palliative care", section on 'Simple screening instruments'.)

Anxiety — Anxiety is common in patients with an advanced serious or life-threatening illness. As an example, the reported prevalence of anxiety among advanced cancer patients is 18 percent [119]. (See "Overview of anxiety in palliative care".)

Anxiety may also be related to a preexisting anxiety disorder, substance abuse, delirium, or under-treated symptoms, most commonly pain. A single aggregate question ("Have you felt anxious, nervous, uneasy, tense, or frightened in the recent days") can be utilized to screen for symptoms of anxiety.

Delirium — Delirium and confusional states are among the most common neuropsychiatric disorders encountered in patients with medical illness, particularly the elderly. The American Psychiatric Association's Diagnostic and Statistical Manual, 4th edition (DSM-IV) lists four key features that characterize delirium [120] (see "Diagnosis of delirium and confusional states"):

- Disturbance of consciousness with reduced ability to focus, sustain, or shift attention.
- A change in cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia.
- The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a medical condition, substance intoxication, or medication side effect.

Additional features that may accompany delirium and confusion include the following:

- Psychomotor behavioral disturbances such as hypoactivity, hyperactivity with increased sympathetic activity, and impairment in sleep duration and architecture.
- Variable emotional disturbances, including fear, depression, euphoria, or perplexity.

The mnemonic FACT provides a summary of the diagnostic criteria of delirium:

- Fluctuating cognitive deficit(s) with acute onset
- Attention deficits, and either
- Consciousness level disturbance, or
- Thought disorganization

Delirium is the most common neuropsychiatric complication seen in patients with advanced cancer nearing the end of life and can result in distress for patients, family members, and healthcare providers. It is also a marker for shortened survival in hospitalized and institutionalized patients [67,121]. (See 'Performance status, symptoms, and prognosis' above.)

For many terminally ill patients with COPD, end-stage renal disease, heart failure, and other serious life-threatening diseases, global cerebral dysfunction without a definable reversible cause, manifested as delirium, is the final common complication that precedes death. However, for many palliative care patients,

a number of factors may contribute to the development of delirium, many of which are potentially reversible [122]. Some of the most frequent contributors are [123]:

- Opioid-induced toxicity (see "Cancer pain management with opioids: Prevention and management of side effects", section on 'Somnolence and mental clouding')
- Brain tumor/metastases/cerebral edema
- Cancer treatment (chemotherapy, radiation therapy) (see "Overview of neurologic complications of non-platinum cancer chemotherapy" and "Diagnosis of psychiatric disorders in patients with cancer")
- Psychotropic drugs (tricyclic antidepressants, benzodiazepines)
- Metabolic (increased calcium, decreased sodium, renal failure) (see "Hypercalcemia of malignancy" and "Clinical manifestations of hypercalcemia" and "Overview of the treatment of hyponatremia" and "Evaluation of adults with hyponatremia")
- Disturbed sleep (in the ICU setting), and other causes of sleep deprivation
- Sepsis
- Paraneoplastic neurologic syndromes (see "Overview of paraneoplastic syndromes of the nervous system" and "Paraneoplastic and autoimmune encephalitis")

Many of the risk factors for delirium are already present in patients with advanced terminal illnesses, although many patients improve with treatment of specific causes. (See "Overview of managing common non-pain symptoms in palliative care", section on 'Delirium'.)

The fact that delirium may be reversible in up to 50 percent of cases [122] underscores the importance of early recognition and aggressive evaluation and management.

Multiple instruments have been developed for assessing delirium, which are based upon the criteria for delirium in the DSM-IV [124]:

- The Confusion Assessment Method (CAM, (table 21)) has become a standard screening device in clinical studies of delirium, conducted across multiple settings including emergency rooms and long-term care [125]; a version is available (CAM-ICU) that is validated in patients in the intensive care unit [126,127]. (See "Diagnosis of delirium and confusional states".)
- The MDAS (form 2A-B) is a 10-item, four-point (0 to 3) observer-rated scale that was designed to quantify the severity of delirium in medically ill patients with serial observations [128,129]. It includes assessment of disturbances in awareness, orientation, short-term memory, digit span, attention capacity, organized thinking, perception, delusions, psychomotor activity, and arousal in a way that reflects all the main diagnostic criteria according to the Diagnostic and Statistical Manual for Mental Illness.

  The MDAS has been used and validated for screening and diagnosis of delirium in cancer patients [129] and is able to distinguish patients with delirium from those with other cognitive or noncognitive psychiatric disorders. In one study, a cutoff score of 7/30 on the MDAS yielded the highest sensitivity (98 percent) and specificity (96 percent) for the diagnosis of delirium [129]. In many institutions, this tool has replaced the mini-mental status examination for assessment and monitoring of delirium.
- The bedside confusion scale (ability to recite the 12 months in reverse order and assessment of consciousness state) is another excellent tool to screen and longitudinally follow delirium in palliative care [130]. Serial-sevens and spelling a word such as “farm” or “world” backward are other simple tests of attention. Another bedside test of attention is outlined in the table (table 22). (See "Diagnosis of delirium and confusional states" and "Diagnosis of psychiatric disorders in patients with cancer".)

PHYSICAL EXAMINATION AND INVESTIGATIONS — Both physical examination and investigations may be important in characterizing a symptom and for definitive diagnosis.

When considering new investigations on palliative care patients who may be quite ill (particularly if they are at the end of life), an important consideration is that if the result is not expected to change management of a symptom complex, the investigation should NOT be done. Sometimes, even necessary investigations may have to be eliminated or postponed because of patient frailty.

SUMMARY

- Frequently encountered symptoms in patients with an advanced serious and/or life-threatening illness include pain, dyspnea, fatigue, dry mouth, dysphagia and aspiration, loss of appetite and weight, nausea/vomiting, constipation, edema, depression, anxiety, and delirium. An approach to assessment of these symptoms is outlined in the sections above (see 'Approach to specific symptoms' above). In palliative care populations, symptom etiology is commonly multifactorial. As an example, among patients with advanced cancer, symptoms may result from the disease, from treatment for the disease, or from other concurrent unrelated conditions. (See 'Introduction' above.)
- Patient descriptions and symptom ratings are the primary data for overall assessment. The use of different dimensions (severity, frequency, distress, interference) may help when patients and families get stuck on trying to describe the impact of a symptom.
- Once a symptom is identified, timely reevaluation is necessary to determine whether it has improved after a specific therapeutic intervention.
- Clinician, caregiver, and patient assessments of symptoms may differ; clinicians tend to rate the severity of symptoms lower than patients.
- The patient's assessment of symptom relief is important, and may differ from that of the health professional. (See 'General principles' above.)
- Performance status (table 4 and table 5) is a key indicator of prognosis in individuals with advanced terminal disease, and is associated with symptom severity. For patients with advanced serious life threatening diseases, such as those referred to palliative care programs, the presence or absence of certain symptoms, particularly dyspnea, may help physicians provide a more refined estimate of patient survival. (See 'Performance status, symptoms, and prognosis' above.)
- A number of validated symptom assessment tools may be useful in palliative care settings, including those that evaluate multiple symptoms such as the

Edmonton Symptom Assessment Scale, and symptom-specific tools such as the Brief Pain Inventory. Multisymptom assessment tools definitely yield a higher number of symptoms, and can be used as checklists.

All of these tools (which often address both severity and how much a specific symptom is bothering or impairing the patient) are most effective combined with careful patient interviews to delineate the details of each symptom. Furthermore, when a specific tool has been chosen, it should be used consistently. (See 'Assessment and rating instruments for symptoms' above.)

- New investigations on palliative care patients who may be quite ill (particularly if they are at the end of life), should not be pursued unless the result is expected to change management of a symptom complex. (See 'Physical examination and investigations' above.)

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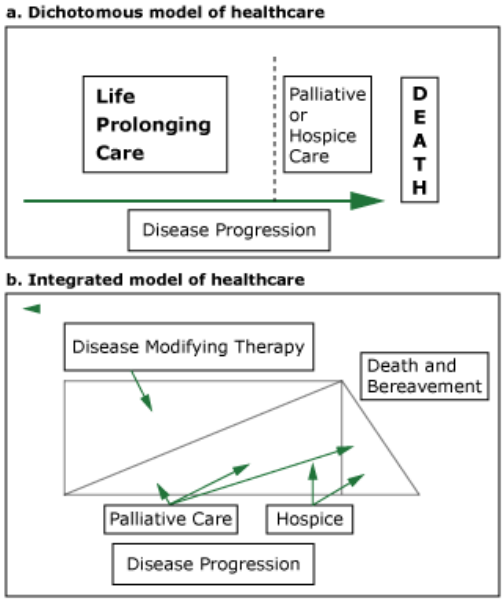
Topic 2196 Version 32.0

GRAPHICS

Models of healthcare delivery



Adapted from National Consensus Project for Quality Palliative Care (2004). Clinical practice guidelines for quality palliative care. http://www.nationalconsensusproject.org.

Graphic 64252 Version 1.0

Symptom prevalence in palliative care patients

Symptom	Cancer		AIDS		Heart disease		Chronic obstructive pulmonary disease (COPD)		Renal disease	
	Number of patients	Percentage with symptom	Number of patients	Percentage with symptom	Number of patients	Percentage with symptom	Number of patients	Percentage with symptom	Number of patients	Percentage with symptom
Pain	10,379	35 to 96	942	63 to 80	882	41 to 77	372	34 to 77	370	47 to 50
Depression	4378	3 to 77	616	10 to 82	80	9 to 36	150	37 to 71	956	5 to 60
Anxiety	3274	13 to 79	346	8 to 34	80	49	1008	51 to 75	72	39 to 70
Confusion	9154	6 to 93	?	30 to 65	343	18 to 32	309	18 to 33		
Fatigue	2888	32 to 90	1435	54 to 85	409	69 to 82	285	68 to 80	116	73 to 87
Breathlessness	10,029	10 to 70	504	11 to 62	948	60 to 88	372	90 to 95	334	11 to 62
Insomnia	5606	9 to 69	504	74	146	36 to 48	150	55 to 65	351	31 to 71
Nausea	9140	6 to 68	689	43 to 49	146	17 to 48			362	30 to 43
Constipation	7602	23 to 65	689	34 to 35	80	38 to 42	150	27 to 44	483	29 to 70
Diarrhea	3392	3 to 29	504	30 to 90	80	12			19	21
Anorexia	9113	30 to 92	504	51	146	21 to 41	150	35 to 67	395	25 to 64

Original figure modified for this publication. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 2006; 31:58. Table used with the permission of Elsevier Inc. All rights reserved.

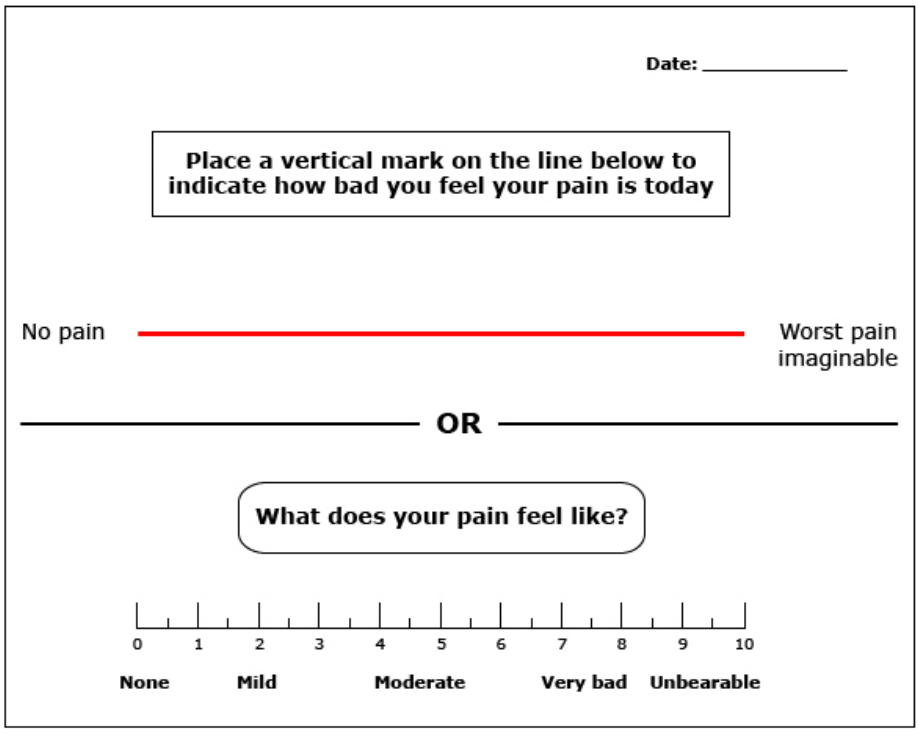
Graphic 87163 Version 1.0

MOPQRST mnemonic for assessment of patient symptoms in palliative care

M	Meaning of the symptom
O	Onset of the symptom
P	Palliating and provoking factors
Q	Quality of the symptom
R	Related factors/symptoms
	Region and radiation
S	Severity of the symptom
T	Temporality of the symptom

Graphic 87818 Version 2.0

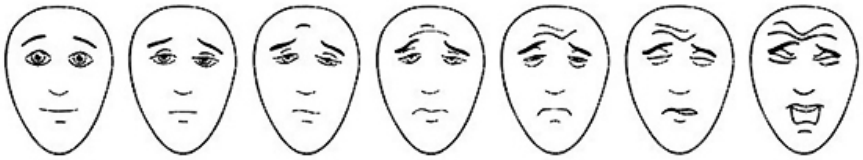
Visual analog scale



Visual Analog Scale (VAS) (10 cm line).
[Score = 0 to 100 mm] - measuring in millimeters from the left hand end of the line to the point that the patient marks.

Graphic 62346 Version 3.0

Faces pain scale



Schematic representation of the faces pain scale, rated from 0 to 6 left to right.

Bieri, D, Reeve, RA, Champion, GD, et al. Pain 1990; 41:139. Copyright © 1990 with permission from Elsevier Science.

Graphic 67351 Version 4.0

Edmonton symptom assessment system: numeric scale

Please circle the number that best describes:

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst possible pain
Not tired	0	1	2	3	4	5	6	7	8	9	10	Worst possible tiredness
Not nauseated	0	1	2	3	4	5	6	7	8	9	10	Worst possible nausea
Not depressed	0	1	2	3	4	5	6	7	8	9	10	Worst possible depression
Not anxious	0	1	2	3	4	5	6	7	8	9	10	Worst possible anxiety
Not drowsy	0	1	2	3	4	5	6	7	8	9	10	Worst possible drowsiness
Best appetite	0	1	2	3	4	5	6	7	8	9	10	Worst possible appetite
Best feeling of wellbeing	0	1	2	3	4	5	6	7	8	9	10	Worst possible feeling of wellbeing
No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Worst possible shortness of breath
Other problem	0	1	2	3	4	5	6	7	8	9	10	

Graphic 65702 Version 1.0

Domains of the supplemented Edmonton Symptom Assessment Scale (ESAS)

Limited activity
Fatigue
Physical discomfort
Shortness of breath
Pain
Lack of well-being
Problems with appetite
Feelings of depression
Anxiety
Nausea
Difficulty sleeping
Weakness
Dizziness
Difficulty thinking
Constipation

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Bruera, E, Kuehn, N, Miller, MJ, et al. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. J Palliat Care 1991; 7:6.
Walke, LM, Byers, AL, McCorkle, R, Fried, TR. Symptom assessment in community-dwelling older adults with advanced chronic disease. J Pain Symptom Manage. 2006; 31:31.

Graphic 56065 Version 1.0

Memorial Symptom Assessment Scale - Short Form [MSAS-SF]

Patient's Name _____ Date ____/____/____ ID#_____

Instructions:
I. Below is a list of symptoms. If you had the symptom DURING THE PAST WEEK, please check Yes. If you did have the symptom, please check the box that tells us how much the symptom DISTRESSED or BOTHERED you.

Check all the symptoms you have had during the PAST WEEK.	Yes [✓]	» IF YES: How much did it DISTRESS or BOTHER you? Not at all [0]	A little bit [1]	Some-what [2]	Quite a bit [3]	Very much [4]
Difficulty concentrating						
Pain						
Lack of energy						
Cough						
Changes in skin						
Dry mouth						
Nausea						
Feeling drowsy						
Numbness/tingling in hands and feet						
Difficulty sleeping						
Feeling bloated						
Problems with urination						
Vomiting						
Shortness of breath						
Diarrhea						
Sweats						
Mouth sores						
Problems with sexual interest or activity						
Itching						
Lack of appetite						
Dizziness						
Difficulty swallowing						
Change in the way food tastes						
Weight loss						
Hair loss						
Constipation						
Swelling of arms or legs						
"I don't look like myself"						
If you had any other symptoms during the PAST WEEK, please list them below, indicating how much the symptom DISTRESSED or BOTHERED you.						
1.						
2.						

II. Below are other commonly listed symptoms. Please indicate if you had the symptom DURING THE PAST WEEK, and is so, how OFTEN it occurred.

Check all the symptoms you have had during the PAST WEEK.	Yes [✓]	» IF YES: How OFTEN did it occur? Rarely [1]	Occasionally [2]	Frequently [3]	Almost constantly [4]
Feeling sad					
Worrying					
Feeling irritable					
Feeling nervous					

Graphic 60205 Version 1.0

Karnofsky performance status scale

Value	Level of functional capacity	Definition
100	Normal, no complaints, no evidence of disease	Able to carry on normal activity and to work; no special care needed
90	Able to carry on normal activity, minor signs or symptoms of disease	
80	Normal activity with effort, some signs or symptoms of disease	
70	Cares for self, unable to carry on normal activity or to do active work	Unable to work; able to live at home and care for most personal needs; various degrees of assistance needed
60	Requires occasional assistance, but is able to care for most needs	
50	Requires considerable assistance and frequent medical care	
40	Disabled, requires special care and assistance	Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly
30	Severely disabled, hospitalization is indicated although death is not imminent	
20	Hospitalization is necessary, very sick, active supportive treatment necessary	
10	Moribund, fatal processes progressing rapidly	
0	Dead	

Graphic 58785 Version 4.0

Eastern Cooperative Oncology Group (ECOG, Zubrod, WHO) performance scale

Performance status	Definition
0	Fully active; no performance restrictions
1	Strenuous physical activity restricted; fully ambulatory and able to carry out light work
2	Capable of all selfcare but unable to carry out any work activities. Up and about >50 percent of waking hours.
3	Capable of only limited selfcare; confined to bed or chair >50 percent of waking hours
4	Completely disabled; cannot carry out any selfcare; totally confined to bed or chair

Excerpted from: Oken MM, et al. Am J Clin Oncol 1982; 5:649.

Graphic 72901 Version 4.0

Predictors of survival in patients with advanced cancer under palliative care

Index Survival	Value	Median	References
Karnofsky Performance Status	10 to 20	7 to 16 days	Evans 1985, Maltoni 1994, Maltoni 1995; Reuben 1998, Morita 1999, Llobera 2000, Bruera 1992
	30 to 40	8 to 50 days	
	>50	50 to 90 days	
Anorexia	Present	<58 days	Maltoni 1995, Llobera 2000, Bruera 1992
Confusion	Present	<38 days	Llobera 2000, Bruera 1992
Dysphagia	Present	<30 days	Maltoni 1995
Dyspnea	Present	<30 days	Maltoni 1995
Xerostomia	Present	<50 days	Bruera 1992
Physician estimate	3 mos	30 days	Parkes 1972, Heyse-Moore 1987, Christakis 2000

Graphic 56650 Version 1.0

Principles of risk management during opioid treatment for pain

	Goals	Strategies	Comments
Stratification of risk	To clarify the likelihood of future aberrant drug-related behavior	**Regard as high risk if:** ▪ History of alcohol or drug misuse ▪ Family history of alcohol or drug misuse ▪ Major psychiatric disorder **Other factors that suggest risk:** ▪ Cancer associated with heavy alcohol use or smoking ▪ Current heavy smoking ▪ Young age ▪ History of automobile accidents, chronic unemployment, poor support system **Factors that can mitigate risk:** ▪ Poor performance status ▪ Restricted prognosis ▪ Active recovery program	All patients should undergo risk assessment and stratification; although many questionnaires have been developed to predict aberrant behavior or addiction, the clinical assessment is generally used in practice.
Structuring of treatment commensurate with risk	Practices to match monitoring with risk, and when needed to help patients maintain control	**Strategies include:** ▪ Use of drug monitoring (eg, urine drug testing) ▪ Small amounts prescribed ▪ No use of short-acting drugs ▪ Use of one pharmacy ▪ Pill counts at time of visit ▪ Compulsory consultations	The decision to implement one or more of these strategies is a matter of clinical judgment.
Assessment of drug-related behaviors over time	Track drug use in tandem with all relevant outcomes	**Monitor:** ▪ Drug-related behavior - eg, need for early refills, obtaining several prescriptions, etc ▪ Pain relief ▪ Adverse drug effects ▪ Effect of drug on other outcomes	Broad monitoring of outcomes is consistent with integration of pain management into a palliative care model.
Response to aberrant drug-related behaviors	Clinician compliance with laws and regulations; identification of patients needing additional management	**If the patient engages in aberrant drug-related behavior:** ▪ Reassess and diagnose (addiction, other psychiatric disorder, pseudoaddiction, family issues, criminal intent) ▪ If diversion into the illicit marketplace is	Even advanced illness does not free the clinician from the requirement of compliance with laws and regulations.

		discovered, stop prescribing ▪ Otherwise, restructure treatment to improve control and obtain consultative help as needed	
Documentation and communication	Risk assessment and management should be viewed as integral to safe and effective prescribing	**Document:** ▪ Plan for monitoring and education of patient and family ▪ Monitoring of drug-related behavior on a regular basis ▪ Response should aberrant behavior occur	Open discussion of the need for universal risk management with other clinicians is valuable to reduce the risk of stigmatizing patients.

Reproduced from: Portenoy RK. Treatment of cancer pain. Lancet 2011; 377:2236. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 50477 Version 2.0

Causes of dyspnea in palliative care and potential treatments

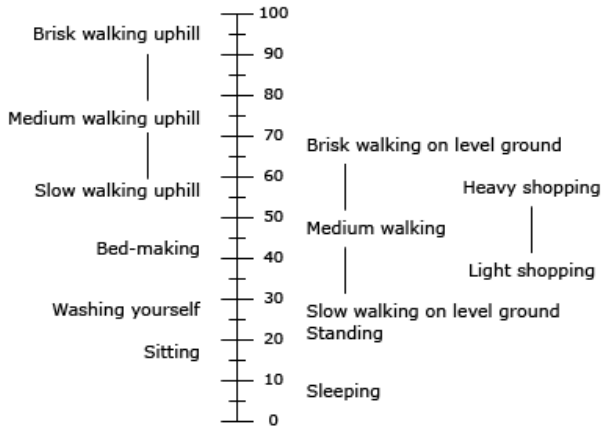
Disease process	Potential interventions
Airway obstruction	
Airway obstruction by tumor or by lymphadenopathy	Airway laser/cautery*, stent*, radiation therapy (RT)*, resection*, glucocorticoids
Bronchoconstriction (COPD, asthma)	Bronchodilators, glucocorticoids
Retained or excess secretions	Anticholinergic agents
Vocal cord paralysis	
Obstructive sleep apnea	Continuous positive airway pressure (CPAP) at night
Pulmonary parenchymal	
Widespread tumor metastases	RT*, chemotherapy*, glucocorticoids
Pneumonia, aspiration	Antibiotics, pulmonary toilet, aspiration precautions
Heart failure	Diuretics, ACE inhibitors, etc
Pericardial disease, tamponade	Pericardiocentesis*
Lymphangitic tumor	Diuretics, glucocorticoids, chemotherapy*
Lung resection (eg, lobectomy, pneumonectomy)	
Pneumonitis caused by antineoplastic therapy	Glucocorticoids
Radiation pneumonitis and fibrosis	Glucocorticoids
Interstitial lung disease	Glucocorticoids
Pulmonary vascular	
Venous thromboembolism	Anticoagulation*, thrombolysis*, inferior vena cava filter*
Sinusoidal obstruction syndrome (veno-occlusive disease)	
Tumor thromboembolism	
Pulmonary hypertension	
Superior vena cava syndrome	Glucocorticoids, RT*, chemotherapy*, stent*
Pleural	
Pleural effusion (eg, malignant, drug-induced)	Indwelling pleural catheter with intermittent drainage; pleurodesis
Pleural tumor	RT*, chemotherapy*
Pneumothorax	Chest tube
Pleural effusion due to lung entrapment by tumor	Indwelling pleural catheter with intermittent drainage as guided by symptoms*
Inspiratory muscle weakness	
Cachexia	
Electrolyte imbalance	Adjust electrolytes
Neuromuscular disease, including paraneoplastic syndromes	Noninvasive positive pressure ventilation (NPPV)*
Steroid myopathy	Physical therapy, reduce dose of glucocorticoids
Diaphragmatic paralysis, phrenic nerve paralysis	NPPV*, diaphragmatic pacing*
Decreased chest wall compliance	
Restriction post thoracotomy	
Restriction due to advanced chest wall tumor (eg, inflammatory breast cancer)	RT*, chemotherapy*
Massive ascites	Drainage*, including indwelling catheter with intermittent drainage
Massive abdominal organomegaly	
Obesity	
Systemic	
Anemia	Red blood cell transfusion*

Acidosis	Correct metabolic abnormalities
Arrhythmias	Usual treatments
Neuropsychiatric	
Pain	Opioids
Depression	Antidepressants, cognitive behavioral therapy
Anxiety, including hyperventilation	Anxiolytic medication, cognitive behavioral therapy
Respiratory panic	Anxiolytics, antidepressants, cognitive behavioral therapy

RT: radiation therapy; COPD: chronic obstructive pulmonary disease; ACE: angiotensin converting enzyme; NPPV: noninvasive positive pressure ventilation.
* Decisions regarding all therapies and disease-modifying treatments must be made in light of the expected burdens and benefits and be consistent with the patient's long-term and short-term goals of care.

Graphic 83934 Version 2.0

The Oxygen Cost Diagram



Values for oxygen expenditure

Brisk walking uphill	95	Light shopping	36
Medium walking uphill	75	Washing yourself	27
Brisk walking on level ground	69	Slow walking on level ground	27
Heavy shopping	58	Standing	21
Slow walking uphill	57	Sitting	17
Medium walking	47	Sleeping	7
Bed-making	42		

Patients are asked to identify the level of activity they are unable to perform due to dyspnea.

Graphic 64769 Version 1.0

The modified Borg Scale for assessing the intensity of dyspnea or fatigue

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

This Borg scale should be printed on heavy paper (11 inches high and perhaps laminated) in 20-point type size. At the beginning of the 6-minute exercise, show the scale to the patient and ask the patient this: "Please grade your level of shortness of breath using this scale." Then ask this: "Please grade your level of fatigue using this scale." At the end of the exercise, remind the patient of the breathing number that they chose before the exercise and ask the patient to grade their breathing level again. Then ask the patient to grade their level of fatigue, after reminding them of their grade before the exercise.

Sources:

1. *Reproduced with permission from: Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14:377. Copyright © 1982 Lippincott Williams & Wilkins.*
2. *Reproduced with permission from: the American Thoracic Society. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166:111.*

Graphic 63981 Version 3.0

Clinical COPD Questionnaire

Please *circle* the number of the response that best describes how you have been feeling during the *past week*.
(Only *one* response for each question)

On average, **during the past week**, how often did you feel:	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
1. Short of breath **at rest**?	0	1	2	3	4	5	6
2. Short of breath **doing physical activities**?	0	1	2	3	4	5	6
3. **Concerned** about getting a cold or your breathing getting worse?	0	1	2	3	4	5	6
4. **Depressed (down)** because of your breathing problems?	0	1	2	3	4	5	6
In general, **during the past week**, how much of the time:							
5. Did you **cough**?	0	1	2	3	4	5	6
6. Did you **produce phlegm**?	0	1	2	3	4	5	6
On average, **during the past week**, how limited were you in these activities **because of your breathing problems**:	Not limited at all	Very slightly limited	Slightly limited	Moderately limited	Very limited	Extremely limited	Totally limited/or unable to do
7. **Strenuous physical activities** (such as climbing stairs, hurrying, doing sports)?	0	1	2	3	4	5	6
8. **Moderate physical activities** (such as walking, housework, carrying things)?	0	1	2	3	4	5	6
9. **Daily activities at home** (such as dressing, washing yourself)?	0	1	2	3	4	5	6
10. **Social activities** (such as talking, being with children, visiting friends/relatives)?	0	1	2	3	4	5	6

CCQ Questionnaire calculation of scores:

- CCQ total score = (item 1 + 2 + 3 + 4 + 5 + 6 + 7 + 8 + 9 + 10)/10
- Symptom = (item 1 + 2 + 5 + 6)/4
- Functional state = (item 7 + 8 + 9 + 10)/4
- Mental state = (item 3 + 4)/2.

Graphic 86308 Version 2.0

Components of a Brief Fatigue Inventory (BFI)

1. Throughout our lives, most of us have times when we feel very tired or fatigued. Have you felt unusually tired or fatigued in the last week?	**Yes/No**
2. Please answer the following questions by rating your fatigue (weariness, tiredness) on a scale from 0 to 10, with 0 representing "no fatigue" and 10 representing "the worst fatigue you can imagine".	
A) Which number best represents your fatigue right **now?**	
B) Which number best describes your **usual** level of fatigue within the past 24 hours?	
C) Which number best describes your **worst** level of fatigue within the past 24 hours?	
3. Please use a scale from 0 to 10 to answer the following questions that describe how, during the past 24 hours, your fatigue has interfered with aspects of your life. 0 represents "no interference" and 10 represents "complete interference".	
A) General activity	
B) Mood	
C) Walking ability	
D) Normal work (including both work outside the home and daily chores)	
E) Relations with other people	
F) Enjoyment of life	

Modified from: Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. Cancer 1999; 85:1186.

Graphic 54810 Version 2.0

Assessment tools for fatigue in patients with cancer and/or other serious life-threatening conditions

1. Fatigue severity scale
2. Fatigue questionnaire
3. Multidimensional fatigue inventory
4. Multidimensional fatigue symptom inventory
5. Revised Piper fatigue scale
6. Revised Schwartz cancer fatigue scale
7. Brief fatigue inventory
8. Multidimensional assessment of fatigue
9. Fatigue symptom inventory
10. Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)
11. Functional Assessment of Cancer Therapy-Fatigue (FACT-F)
12. Edmonton Symptom Assessment Scale (ESAS)

Graphic 86228 Version 2.0

Cancer-related fatigue: Initial diagnostic work-up

Test
Electrolytes (sodium, potassium, chloride, bicarbonate)
Chemistry panel (creatinine, blood urea nitrogen, glucose, magnesium, calcium, phosphorus, total bilirubin, serum transaminases, alkaline phosphatase, lactic dehydrogenase, albumin, total protein)
Thyroid stimulating hormone (TSH)
Complete blood count (CBC) with differential and platelet count
Serum testosterone, in men if the clinical history suggestive of hypogonadism

Reproduced with permission from: Escalante CP, Manzullo MD, Valdrez R. A cancer-related fatigue clinic: Opportunities and challenges. J Nat Canc Inst 2003; 1:333. Copyright ©2003 Jones and Bartlett Publishers.

Graphic 64018 Version 5.0

Representative causes of oropharyngeal dysphagia

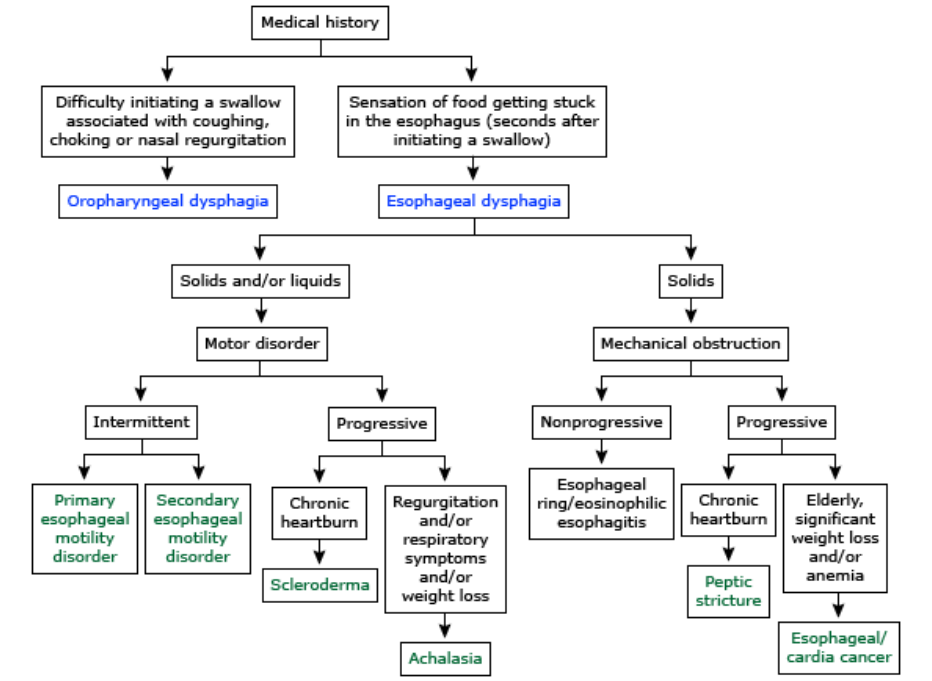
Iatrogenic
Medication side effects (chemotherapy, neuroleptics, etc)
Postsurgical muscular or neurogenic
Radiation
Corrosive (pill injury, intentional)
Infectious
Mucositis (herpes, cytomegalovirus, Candida, etc)
Diptheria
Botulism
Lyme disease
Syphilis
Metabolic
Amyloidosis
Cushing's syndrome
Thyrotoxicosis
Wilson disease
Myopathic
Connective tissue disease (overlap syndrome)
Dermatomyositis
Myasthenia gravis
Myotonic dystrophy
Oculopharyngeal dystrophy
Polymyositis
Sarcoidosis
Paraneoplastic syndromes

Neurological
Brainstem tumors
Head trauma
Stroke
Cerebral palsy
Guillain-Barré syndrome
Huntington disease
Multiple sclerosis
Polio
Postpolio syndrome
Tardive dyskinesia
Metabolic encephalopathies
Amyotrophic lateral sclerosis
Parkinson disease
Dementia
Structural
Cricopharyngeal bar
Zenker's diverticulum
Cervical webs
Oropharyngeal tumors
Osteophytes and skeletal abnormalities
Congenital (cleft palate, diverticula, pouches, etc)

Adapted from: Cook IJ, Kahrilas PJ. AGA: Technical review: Management of oropharyngeal dysphagia. Gastroenterology 1999; 116:455.

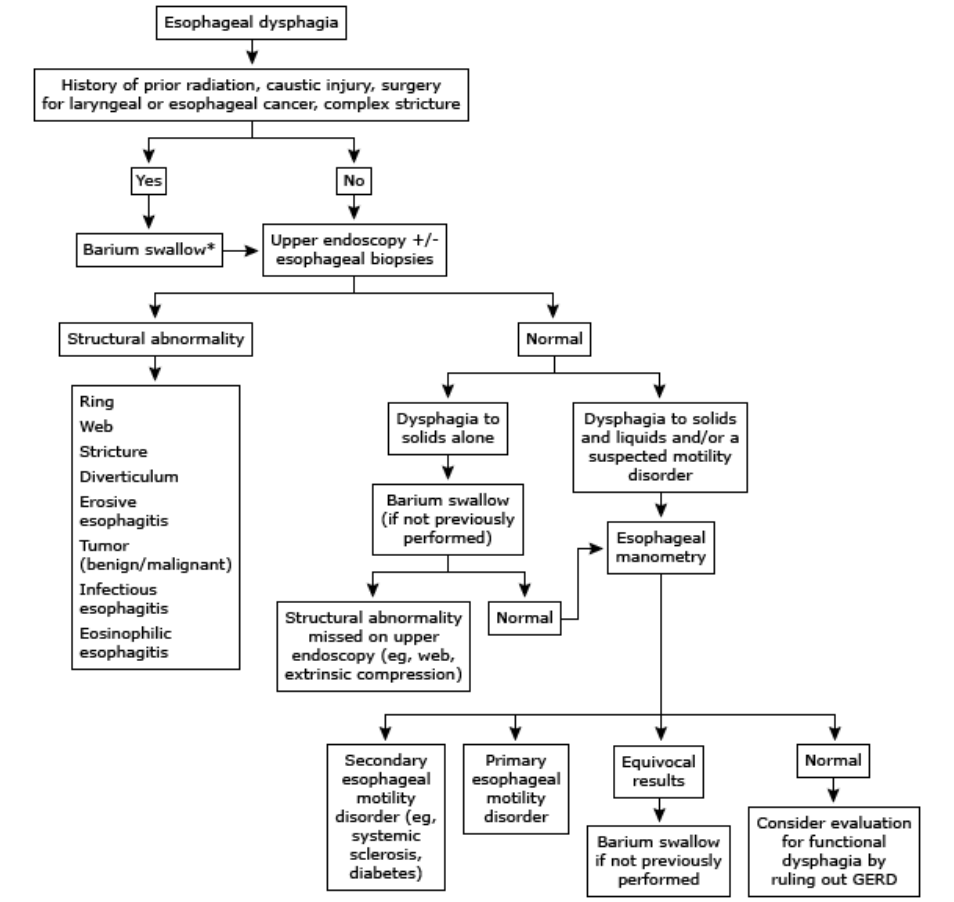
Graphic 52707 Version 6.0

Diagnosis of dysphagia



Graphic 70866 Version 3.0

Approach to the patient with esophageal dysphagia

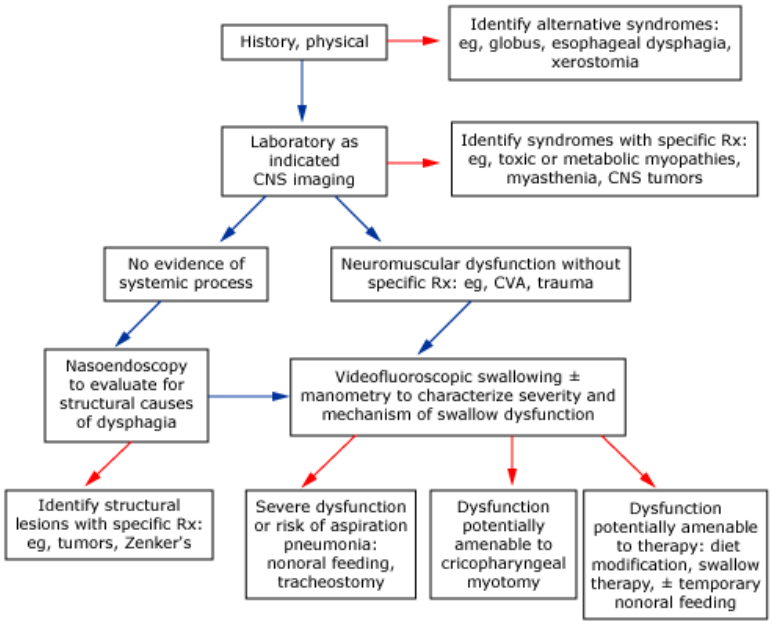


GERD: gastroesophageal reflux disease.

* Performing a barium swallow prior to an upper endoscopy is controversial.

Graphic 81108 Version 3.0

Evaluation and management of oropharyngeal dysphagia



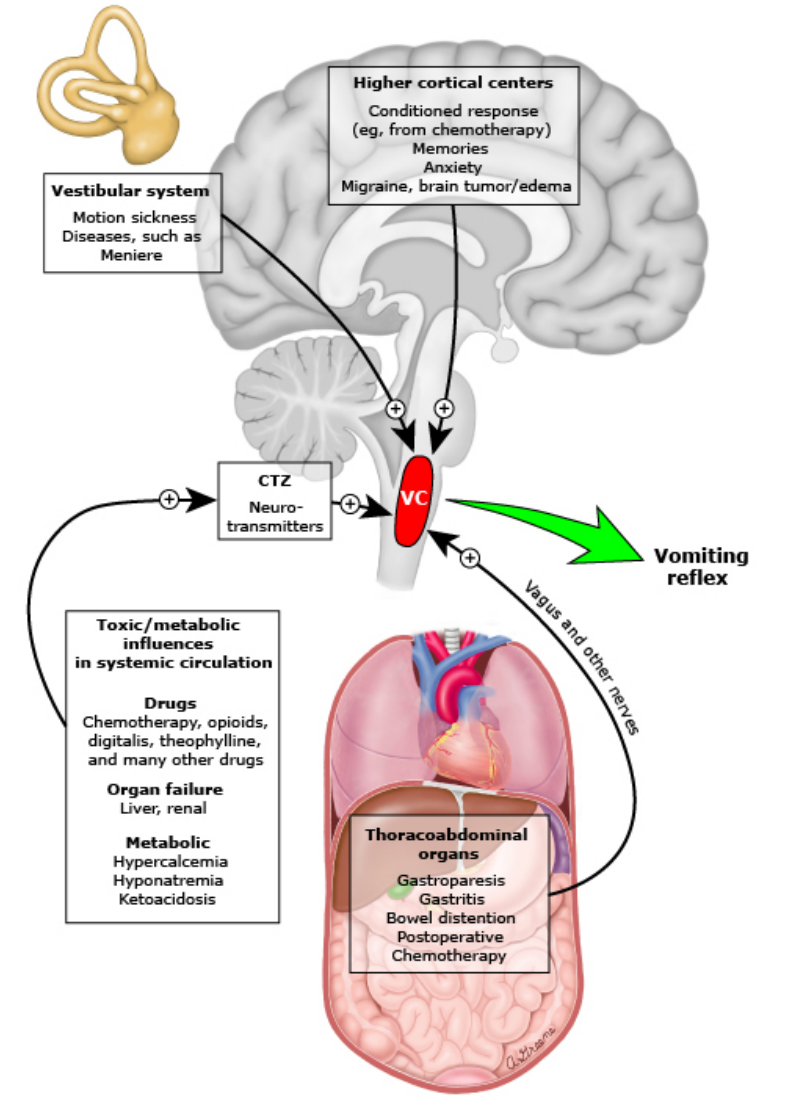
Summary of the clinical approach and key objectives in the management of oropharyngeal dysphagia. The objective is to reach a box targeted by a red arrow, which equates to a specific management strategy. Blue-headed arrows indicate a suggested pathway to proceed with the evaluation.

CNS: central nervous system; Rx: therapy; CVA: cerebrovascular accident.

Adapted from: Cook IJ, Kahrilas PJ. AGA: Technical review: Management of oropharyngeal dysphagia. Gastroenterology 1999; 116:455.

Graphic 54485 Version 2.0

Pathophysiologic pathways involved in emesis



Emesis is mediated centrally by two separate "centers". The chemoreceptor trigger zone (CTZ) is localized to the area postrema in the floor of the fourth ventricle where chemosensitive nerve cell projections are bathed by cerebrospinal fluid that is in equilibrium with blood in the fenestrated local capillaries. Neural pathways project from the CTZ to the nucleus tractus solitarius and the reticular formation of the medulla oblongata, which is the location of the vomiting center (VC). The VC is a diffuse, interconnecting neural network that integrates emetogenic stimuli with parasympathetic and motor efferent activity to produce the vomiting reflex. It receives afferents from the cerebral cortex and higher brainstem, thalamus and hypothalamus, the vestibular system, and via the vagus and splanchnic nerves, the pharynx, gastrointestinal tract, serosae, and other thoracoabdominal organs.

Graphic 87723 Version 1.0

Common causes of nausea and vomiting in palliative care

Toxic/metabolic	Disorders of viscera	CNS causes
Drugs	**Obstruction**	**Increased intracranial pressure**
Cytotoxic chemotherapy	Gastric outlet	Malignancy
Opioids, tramadol	Small bowel	Hemorrhage
NSAIDs, aspirin	Biliary/pancreatic duct	Cranial irradiation
Digitalis	**Constipation**	Abscess
Iron	**Gastroparesis**	**Vestibular**
Antibiotics	**Inflammation/irritation**	Drug effects
Theophylline	NSAID	Labyrinthitis
SSRIs and bupropion	Chemotherapy: (direct GI effects)	**Anxiety**
Anticonvulsants	Radiation	Anticipatory nausea and vomiting
Many other drugs	Gastritis	
Organ failure	Gastroenteritis	
Liver, renal	Hepatitis	
Metabolic	Cholecystitis	
Hypercalcemia	Pancreatitis	
Hyponatremia	**Tumors of the gastrointestinal tract and thorax**	
Ketoacidosis		
Poisoning, substance abuse		

SSRI: selective serotonin reuptake inhibitor.

Graphic 87625 Version 4.0

Constipation assessment scale

Directions:			
Circle the appropriate number to indicate whether, during the past three days, you have had NO PROBLEM, SOME PROBLEM, or a SEVERE PROBLEM with each of the items listed below.			
Item	**No problem**	**Some problem**	**Severe problem**
1. Abdominal distention or bloating	0	1	2
2. Change in amount of gas passed rectally	0	1	2
3. Less frequent bowel movements	0	1	2
4. Oozing liquid stool	0	1	2
5. Rectal fullness or pressure	0	1	2
6. Rectal pain with bowel movement	0	1	2
7. Small stool size	0	1	2
8. Urge but inability to pass stool	0	1	2

Adapted from: McMillan, SC, Williams, F. Validity and reliability of the constipation assessment scale. Cancer Nursing 1989; 12:183; and McMillan, SC, Levy, D. Reassessment of the validity and reliability of the CAS (and unpublished study).

Graphic 62148 Version 1.0

Major physical findings in edematous states

Disorder	Pulmonary edema	Central venous pressure	Ascites and/or pedal edema
Left-sided heart failure	+	Variable	-
Right-sided heart failure	-	↑	+
Cirrhosis	-	↓-Normal	+
Renal disease	Variable	↑	+
Nephrotic syndrome	-	Variable	+
Idiopathic edema	-	↓-Normal	+
Venous insufficiency	-	Normal	+, edema may be asymmetric

Graphic 72002 Version 1.0

Major causes of edema by primary mechanism

Increased capillary hydraulic pressure
Increased plasma volume due to renal sodium retention
Heart failure, including cor pulmonale
Primary renal sodium retention
• Renal disease, including the nephrotic syndrome
• Drugs*: Nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, fludrocortisone, thiazolidinediones (glitazones), insulins, estrogens, progestins, androgens, testosterone, aromatase inhibitors, tamoxifen; and by multiple mechanisms: vasodilators (hydralazine, minoxidil, diazoxide) and calcium channel blockers (particularly dihydropyridines, ie, amlodipine, nifedipine); also see "Arteriolar vasodilation" below
• Refeeding edema
• Early hepatic cirrhosis
Pregnancy and premenstrual edema
Idiopathic edema, when diuretic induced
Sodium or fluid overload: Parenteral antibiotics or other drugs with large amounts of sodium, sodium bicarbonate, or excessive or overly rapid fluid replacement
Venous obstruction
Cirrhosis or hepatic venous obstruction
Acute pulmonary edema
Local venous obstruction
Arteriolar vasodilation
Drugs*: Frequent - vasodilators (hydralazine, minoxidil, diazoxide), dihydropyridine calcium channel blockers; less frequent - alpha1 blockers, sympatholytics (ie, methyldopa), nondihydropyridine calcium channel blockers [1]
Idiopathic edema (?)
Hypoalbuminemia
Protein loss
Nephrotic syndrome
Protein-losing enteropathy
Reduced albumin synthesis
Liver disease
Malnutrition
Increased capillary permeability
Idiopathic edema (?)
Burns
Trauma
Inflammation or sepsis
Allergic reactions, including certain forms of angioedema
Adult respiratory distress syndrome
Diabetes mellitus
Interleukin-2 therapy
Malignant ascites
Lymphatic obstruction or increased interstitial oncotic pressure
Lymph node dissection
Nodal enlargement due to malignancy
Hypothyroidism
Malignant ascites
Other drugs* (uncertain mechanism)
Anticonvulsant: Gabapentin, pregabalin
Antineoplastic: Docetaxel, cisplatin

Antiparkinson: Pramipexole, ropinirole

* Patients with decreased cardiac output, preexisting renal insufficiency, and/or receiving higher doses are more likely to experience edema and edema-associated adverse events. This is not a complete list of drugs associated with edema. For additional information, refer to the Lexicomp individual drug monographs included with UpToDate.

Reference:

1. *Messerli FH. Vasodilatory edema: A common side effect of antihypertensive therapy. Curr Cardiol Rep 2002; 4(6):479.*

Graphic 53550 Version 7.0

Characteristics of grief versus depression

	Grief	Depression
Definition	Feelings and behaviors that result from a particular loss	Depressed mood, decreased interest and pleasure, appetite and sleep disturbance, psychomotor agitation or retardation, decreased concentration, loss of energy, feelings of worthlessness, guilt, hopelessness, helplessness, and thoughts of death with impairment of functioning lasting at least two weeks
Symptoms and signs	Somatic distress, sleep and appetite disturbance, diminished concentration, social withdrawal, sighing	Hopelessness, helplessness, anhedonia, worthlessness, guilt, suicidal ideation most useful diagnostic clues
		Somatic distress, sleep and appetite disturbance, diminished concentration, social withdrawal, sighing are also common
Other differentiating factors	Patient retains capacity for pleasure	Nothing is enjoyable
	Comes in waves	Constant
	Passive wishes for death	Intense, persistent suicidal thoughts
	Able to look forward to the future	No sense of anything to look forward to

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Graphic 53062 Version 2.0

Abbreviated screening methods for the assessment of depression in cancer patients

Single-item interview assessing depressed mood (adapted from SADS)[1]
Two-item interview assessing depressed mood and loss of interest in activities (adapted from SADS)[1]
Visual analog scale for depressed mood (adapted from Memorial Pain Assessment Card)[2]
13-item Beck Depression Inventory (adapted from 21-item Beck Depression Inventory)[3]
Brief Case-Find for Depression (BCD)[4]
Four-question algorithm for screening depression (energy level, anhedonia, depressive feelings, psychomotor agitation/retardation)[5]
Single-item interview assessing psychological distress in the MOS SF36 (36-item short-form) health survey[6]

SADS: Schedule for Affective Disorders and Schizophrenia.

1. Chochinov, HM, et al. Am J Psych 1997; 154:674.
2. Fishman, B, et al. Cancer 1987; 60:1151.
3. Beck, AT, et al. Postgrad Med 1972; 52:81.
4. Jefford, M, et al. Br J Cancer 2004; 91:900.
5. Robinson, J. Palliat Med 2005; 19:278.
6. Ware, JE. Med Care 1992; 30:473.

Graphic 61549 Version 1.0

Confusion assessment method (CAM) for the diagnosis of delirium*

Feature	Assessment
1. Acute onset and fluctuating course	Usually obtained from a family member or nurse and shown by positive responses to the following questions: "Is there evidence of an acute change in mental status from the patient's baseline?"; "Did the abnormal behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?"
2. Inattention	Shown by a positive response to the following: "Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said?"
3. Disorganized thinking	Shown by a positive response to the following: "Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?"
4. Altered level of consciousness	Shown by any answer other than "alert" to the following:
	"Overall, how would you rate this patient's level ofconsciousness?"
	Normal = alert
	Hyperalert = vigilant
	Drowsy, easily aroused = lethargic
	Difficult to arouse = stupor
	Unarousable = coma

*The diagnosis of delirium requires the presence of features 1 AND 2 plus either 3 OR 4.

Graphic 69489 Version 1.0

Memorial Delirium Assessment Scale (MDAS)

INSTRUCTIONS: Rate the severity of the following symptoms of delirium based on current interaction with subject or assessment of his/her behavior or experience over past several hours (as indicated in each time).

ITEM 1-REDUCED LEVEL OF CONSCIOUSNESS (AWARENESS): Rate the patient's current awareness of and interaction with the environment (interviewer, other people/objects in the room; for example, ask patients to describe their surroundings).

- ☐ 0: none (patient spontaneously fully aware of environment and interacts appropriately)
- ☐ 1: mild (patient is unaware of some elements in the environment, or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded strongly; interview is prolonged but not seriously disrupted)
- ☐ 2: moderate (patient is unaware of some or all elements in the environment, or not spontaneously interacting with the interviewer; becomes incompletely aware and inappropriately interactive when prodded strongly; interview is prolonged but not seriously disrupted)
- ☐ 3: severe (patient is unaware of all elements in the environment with no spontaneous interaction or awareness of the interviewer, so that the interview is difficult-to-impossible, even with maximal prodding)

ITEM 2-DISORIENTATION: Rate current state by asking the following 10 orientation items: date, month, day, year, season, floor, name of hospital, city, state, and country.

- ☐ 0: none (patient knows 9-10 items)
- ☐ 1: mild (patient knows 7-8 items)
- ☐ 2: moderate (patient knows 5-6 items)
- ☐ 3: severe (patient knows no more than 4 items)

ITEM 3-SHORT-TERM MEMORY IMPAIRMENT: Rate current state by using repetition and delayed recall of 3 words [patient must immediately repeat and recall words 5 mins later after an intervening task. Use alternate sets of 3 words for successive evaluations (for example, apple, table, tomorrow; sky cigar, justice)].

- ☐ 0: none (all 3 words repeated and recalled)
- ☐ 1: mild (all 3 repeated, patient fails to recall 1)
- ☐ 2: moderate (all 3 repeated, patient fails to recall 2 or 3)
- ☐ 3: severe (patient fails to repeat 1 or more words)

ITEM 4-IMPAIRED DIGIT SPAN: Rate current performance by asking subjects to repeat first 3, 4, then 5 digits forward and then 3, then 4 backwards; continue to the next step only if patient succeeds at the previous one.

- ☐ 0: none (patient can do at least 5 numbers forward and 4 backward)
- ☐ 1: mild (patient can do at least 5 numbers forward, 3 backward)
- ☐ 2: moderate (patient can do 4-5 numbers forward, cannot do 3 backward)
- ☐ 3: severe (patient can do no more than 3 numbers forward)

ITEM 5-REDUCED ABILITY TO MAINTAIN AND SHIFT ATTENTION: As indicated during the interview by questions needing to be rephrased and/or repeated because patient's attention wanders, patient loses track, patient is distracted by outside stimuli or over-absorbed in a task.

- ☐ 0: none (none of the above; patient maintains and shifts attention normally)
- ☐ 1: mild (above attentional problems occur once or twice without prolonging the interview)
- ☐ 2: moderate (above attentional problems occur often, prolonging the interview without seriously disrupting it)
- ☐ 3: severe (above attentional problems occur constantly, disrupting and making the interview difficult-to-impossible)

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Graphic 56787 Version 2.0

Memorial Delirium Assessment Scale (MDAS) cont.

ITEM 6-DISORGANIZED THINKING: As indicated during the interview by rambling, irrelevant, or incoherent speech, or by tangential, circumstantial, or faulty reasoning. Ask patient a somewhat complex question (for example, "Describe your current medical condition.").

- ☐ 0: none (patient's speech is coherent and goal-directed)
- ☐ 1: mild (patient's speech is slightly difficult to follow; responses to questions are slightly off target but not so much as to prolong the interview)
- ☐ 2: moderate (disorganized thoughts or speech are clearly present, such that the interview is prolonged but not disrupted)
- ☐ 3: severe (examination is very difficult or impossible due to disorganized thinking or speech)

ITEM 7-PERCEPTUAL DISTURBANCE: Misperceptions, illusions, hallucinations inferred from inappropriate behavior during the interview or admitted by subject, as well as those elicited from nurse/family/chart accounts of the past several hours or of the time since last examination.

- ☐ 0: none (no misperceptions, illusions, or hallucinations)
- ☐ 1: mild (misperceptions or illusions related to sleep, fleeting hallucinations on 1 to 2 occasions without inappropriate behavior)
- ☐ 2: moderate (hallucinations or frequent illusions on several occasions with minimal inappropriate behavior that does not disrupt the interview)
- ☐ 3: severe (frequent or intense illusions or hallucinations with persistent inappropriate behavior that disrupts the interview or interferes with medical care)

ITEM 8-DELUSIONS: Rate delusions inferred from inappropriate behavior during the interview or admitted by the patient, as well as delusions elicited from nurse/family/chart accounts of the past several hours or of the time since the previous examination.

- ☐ 0: none (no evidence of misinterpretations or delusions)
- ☐ 1: mild (misinterpretations or suspiciousness without clear delusional ideas or inappropriate behavior)
- ☐ 2: moderate (delusions admitted by the patient or evidenced by his/her behavior that do not or only marginally disrupt the interview or interfere with medical care)
- ☐ 3: severe (persistent and/or intense delusions resulting in inappropriate behavior, disrupting the interview or seriously interfering with medical care)

ITEM 9-DECREASED OR INCREASED PSYCHOMOTOR ACTIVITY: Rate activity over past several hours, as well as activity during interview, by circling (a) hypoactive, (b) hyperactive, or (c) elements of both present.

- ☐ 0: none (normal psychomotor activity)
- ☐ 1: mild a b c (Hypoactivity is barely noticeable, expressed as slightly slowing of movement. Hyperactivity is barely noticeable or appears as simple restlessness.)
- ☐ 2: moderate a b c (Hypoactivity is undeniable, with marked reduction in the number of movements or marked slowness of movement; subject rarely spontaneously moves or speaks. Hyperactivity is undeniable, subject moves almost constantly; in both cases, exam is prolonged as a consequence.)
- ☐ 3: severe a b c (Hypoactivity is severe; patient does not move or speak without prodding or is catatonic. Hyperactivity is severe; patient is constantly moving, overreacts to stimuli, requires surveillance and/or restraint; getting through the exam is difficult or impossible.)

ITEM 10-SLEEP-WAKE CYCLE DISTURBANCE (DISORDER OR AROUSAL): Rate patient's ability to either sleep or stay awake at the appropriate times. Utilize direct observation during the interview, as well as reports from nurses, family, patient, or charts describing sleep-wake cycle disturbance over the past several hours or since last examination. Use observations of the previous night for morning evaluations only.

- ☐ 0: none (at night, sleeps well; during the day, has no trouble staying awake)
- ☐ 1: mild (mild deviation from appropriate sleepfulness and wakefulness states: at night, difficulty falling asleep or transient night awakenings, needs medication to sleep well; during the day, reports periods of drowsiness or, during the interview, is drowsy but can easily fully awaken him/herself)
- ☐ 2: moderate (moderate deviations from appropriate sleepfulness and wakefulness states: at night, repeated and prolonged night awakening; during the day, reports of frequent and prolonged napping or, during the interview, can only be roused to complete wakefulness by strong stimuli)
- ☐ 3: severe (severe deviations from appropriate sleepfulness and wakefulness states: at night, sleeplessness; during the day, patient spends most of the time sleeping or, during the interview, cannot be roused to full wakefulness by any stimuli)

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Bedside tests of attention

Test	Directions	Scoring
Digit span	Ask the subject to listen carefully and repeat a series of random numbers. Begin with a string of 2 digits, then increase. Read each number in a normal tone of voice at a rate of one digit per second, taking care not to group digits in pairs or sequences that could aid repetition; eg, 3 - 52 - 8 - 18 - 4 - 9 - 36 - 3 - 8 - 5 - 15 - 7 - 2 - 9 - 4 - 68 - 1 - 9 - 2 - 7 - 5 - 6	Inability to repeat a string of at least five digits indicates probable impairment.
Vigilance "A" test	Read a list of 60 letters, among which the letter "A" appears with greater than random frequency. The subject is required to indicate (eg, by tapping on the desk) whenever the target letter is spoken by the examiner. The letter list is read in a normal tone at a rate of one letter per second; eg, L T P E A O A I C T D A L A A N I A B F S A M R A E O Z D P A K A L U C J T A E O	Count errors of omission and commission. More than two errors is considered abnormal.

Graphic 59119 Version 1.0

Disclosures

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