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FAST FACTS AND CONCEPTS #1
DIAGNOSIS AND TREATMENT OF TERMINAL DELIRIUM

David E Weissman MD and Drew A Rosielle MD

**Background** Some degree of loss of cognitive function occurs in most patients in the week or two before death. The typical scenario presented to housestaff is a late-night call from a ward nurse saying, “Mr. Jones is confused, what should we do?” This Fast Fact reviews assessment and management issues in terminal delirium. See Fast Fact #60 for a discussion of newer pharmacological treatments.

**Key teaching points:**
1. The term “confusion” is not an accurate descriptive term—it can mean anything from delirium, dementia, psychosis, obtundation, etc. Patients need a focused assessment, including a brief mini-mental examination. Clinicians should use one of several validated delirium assessment tools to help quantify and document cognitive function.
2. “Terminal delirium” is not a distinct diagnosis, although it is a commonly used phrase. It implies delirium in a patient in the final days/weeks of life, where treatment of the underlying cause is impossible, impractical, or not consistent with the goals of care.
3. Delirium can be either a hyperactive/agitated delirium or a hypoactive delirium. The hallmark of delirium is an acute change in the level of arousal; supporting features include altered sleep/wake cycle, mumbling speech, disturbance of memory and attention, and perceptual disturbances with delusions and hallucinations.
4. The most common identifiable cause of delirium in the hospital setting is drugs: anti-cholinergics (e.g. anti-secretion drugs, anti-emetics, anti-histamines, tricyclic anti-depressants, etc.), sedative-hypnotics (e.g. benzodiazepines), and opioids. Other common causes include metabolic derangements (elevated sodium or calcium, low glucose or oxygen); infections; CNS pathology; or drug/alcohol withdrawal.
5. The degree of work-up to seek the cause of delirium is determined by understanding the disease trajectory and overall goals of care (see Fast Fact #65).
6. The drug of choice for most patients is a neuroleptic. There is one controlled clinical trial of haloperidol versus lorazepam in HIV patients; haloperidol was the superior agent. Haloperidol is administered in a dose escalation process similar to treating pain. Start haloperidol 0.5-2 mg PO or
IV q1hour PRN. Atypical antipsychotics have also been studied for delirium are probably as efficacious as haloperidol. There are insufficient data to make a strong recommendation about the best drug or dosing of antipsychotics for delirium.

7. It is best to think of benzodiazepines as sedatives and anxiolytics but not as therapy for underlying delirium. On the rare occasion one wants to actually sedate a delirious patient a benzodiazepine may be indicated. If anxiety is a prominent part of a patient’s delirium, a benzodiazepine may help. Generally, however, benzodiazepines should be avoided as they can cause paradoxical worsening of the delirium and agitation.

8. Non-pharmacological treatments should always be used in delirium management: reduce or increase the sensory stimulation in the environment as needed; ask relatives/friends to stay by the patient; frequent reminders of time/place.

References


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Background  Diagnosing and providing treatment for a major depressive episode in patients with advanced cancer can improve quality of life. However, diagnosing major depression in an advanced cancer can be complicated by the fact that many cancer symptoms overlap with the somatic symptoms of depression. Furthermore, although depressive thoughts and symptoms may be present in up to 15-50% of cancer patients, only 5% to 20% will meet diagnostic criteria for major depressive disorder. This may create a clinical dilemma in determining when it is appropriate to add pharmacotherapies for depressive symptoms or whether reflective listening and exploration of the patient’s concerns may be the only needed intervention.

Assessment  Clinicians often rely more on the psychological or cognitive symptoms of depression (worthlessness, hopelessness, excessive guilt, and suicidal ideation) than the physical/somatic signs (weight loss, sleep disturbance) when making a diagnosis of major depressive disorder in advanced cancer patients. Endicott has proposed substituting somatic criteria with affective criteria when evaluating depression in advanced cancer patients:

Physical/somatic symptoms…
1. Change in appetite/weight
2. Sleep disturbance
3. Fatigue, loss of energy
4. Diminished ability to think or concentrate

…are replaced by psychological symptoms
1. Tearfulness, depressed appearance
2. Social withdrawal, decreased talkativeness
3. Brooding, self-pity, pessimism
4. Lack of reactivity, blunting

Screening Tools  The Association of Palliative Medicine Science Committee performed a thorough assessment of available screening tools and rating scales for depression in palliative care. While they found that commonly used tools such as the Edinburgh Depression Scale and the Hospital Anxiety and Depression Scale have validated cut-off thresholds for palliative care patients, the depression screening
tool with the highest sensitivity, specificity and positive predictive value was the single question: “Are you feeling down, depressed, or hopeless most of the time over the last two weeks?”

Other Etiologies  Medication side effects from commonly used therapeutics in this patient population, like chemotherapeutic agents, opioids, benzodiazepines or glucocorticoritcoids, can mimic the symptoms and signs of depression. Clinicians should be especially aware of hypoactive delirium in the differential diagnosis of depressive symptoms in cancer patients. Delirium is a particularly important consideration in the final days of life as its prevalence may reach up to 90% during this critical time.

Teaching Point: The key indicators of depression in the terminally ill are persistent feelings of hopelessness and worthless and/or suicidal ideation. Symptoms of depression can overlap with those of anticipatory grief, a normal aspect of the dying process. See Fast Fact # 43 for a complete description of anticipatory grief and how to differentiate from major depression. See Fast Fact #146 on screening for depression in palliative care.

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FAST FACT AND CONCEPT #32
GRIEF AND BEREAVEMENT

James Hallenbeck MD

Introduction  Grief is a normal response to loss, any loss: a job, a limb, a life. Clinicians have an important role in facilitating healthy grieving, and observing for signs of complicated grief. Grief experienced by dying patients and loved-ones prior to and in anticipation of death is called anticipatory grief (or mourning); grief of loved-ones following a death is termed bereavement. This Fast Fact provides an overview of grief and bereavement.

What is Grief?  Grief is a normal response to loss that involves processes and tasks at emotional, cognitive and behavioral levels. The initial shock of learning of impending or actual loss evolves into a process of creating a new relationship between the grieving person and the person (or object) of loss. Grief tends to be experienced in waves, triggered predictably by new losses (such as a loss of functional status) or unpredictably, by seemingly trivial events. Over time the intensity of these waves tends to decrease. Grief does not have a set schedule; individuals progress through the grief process at different speeds. However, no progress, getting stuck in one phase of grief, can be cause for concern.

What is Anticipatory Grief?  Anticipatory grief for patients involves reviewing one's life; for families/friends it means looking to a future without the dying person. Byock has suggested that patients and families may wish to say to each other, in some way, "Forgive me, I forgive you, thank you, I love you and good-bye." People from different cultural backgrounds may differ in terms of how and what they want to say or do in preparation for death. Not knowing or acknowledging that a person is dying will likely delay or interfere with normal anticipatory grief. Grief reactions in dying patients may be confused with pain, depression, and even imminent death (e.g. social withdrawal may imply pain, depression, or anticipatory grief).

Distinguishing Grief from Depression  Neither pain nor depression are normal aspects of the dying experience, they should be carefully evaluated as both are treatable (See Fast Fact #43). Grief tends to be experienced as sadness, whereas depression is associated with lack of self-worth. The question, "Are you sad or are you feeling depressed?" may help begin a dialog to help you distinguish between grief and clinical depression.

What is Complicated Grief?  About 10-20% of the bereaved can experience a persistent or prolonged period of intense loss. There is debate regarding the precise diagnostic criteria for complicated grief and duration of symptoms (see Fast Fact # 254 for further information). However, insecure attachment styles, weak parental bonding in childhood, childhood abuse and neglect, female gender, low perceived social support, supportive marital relationships, and low preparation for the loss are all felt to be risk factors.

What can the physician do to facilitate normal grieving?

6
Be honest when discussing prognosis, goals and treatment options; nothing inhibits normal anticipatory grief more than ambiguity from the physician. Listen; open the door to meaningful discussion. Ask, “How are you doing with this recent news?” “Are you scared?” “Tell me what is going through your mind?” Ask for help – you are not the only health professional available to help with grief. Contact a nurse, social worker, chaplain or psychologist/psychiatrist if you need assistance. Assess for and aggressively treat pain and depression.

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Background  Distinguishing between a dying patient’s normal grief and a major depression is a part of routine care for patients near the end-of-life. This Fast Fact will review the definitions and clinical features that distinguish these conditions. See Fast Facts #7, #32, and #254 for further discussions of depression, grief, and complicated grief.

Definitions

- **Preparatory (or anticipatory) grief.** This is the grief, “that the terminally ill patient has to undergo in order to prepare himself for his final separation from this world” (1). Features include rumination about the past, withdrawal from family/friends, and periods of sadness, crying or anxiety. *Preparatory Grief is a normal, not pathological, life cycle event.*

- **Depression.** Clinically significant depression in a population of dying patients is likely somewhat more common (25-77%) than in the general population (2). However, depression is not an inevitable part of the dying experience and is treatable. Somatic symptoms (anorexia, weight changes, constipation, etc.) are often present as a part of the normal dying process and may not help to distinguish between preparatory grief and depression. Feelings of guilt, hopelessness, worthlessness, and suicidal ideation are the key factors that differentiate grief from depression. When in doubt, treat for depression. Utilize mental health professionals when available. The following additional points are offered to help the clinician distinguish between preparatory grief and depression.
Distinguishing preparatory grief from depression

- Temporal Variation. A temporal variation in mood is normal in preparatory grief—a mixture of “good and bad days.” In contrast, persistent flat affect or dysphoria is characteristic of depression. Depression is a pathological state; patients can ‘get stuck’ in this state without treatment. Self-Image. A disturbed self-esteem is not typically seen in grief; however, it is a common feature of depression. Overwhelming and persistent feelings of worthlessness to others and of being a burden are common in depression. Distressing guilt is usually generalized to all facets of life in depression, while in grief, the guilt is focused around specific issues (e.g. not being able to attend a child’s wedding).

- Hope. A grieving patient's hope shifts, but is not lost. (Hope may shift from a hope for cure to hope for life prolongation to hope for dying well). In contrast, the depressed patient will comment on feelings of hopelessness and helplessness.

- Anhedonia. The ability to feel pleasure is not lost in preparatory grief. Note: grieving patients often need social interaction to help them through the grief process. Anhedonia is an important clue to underlying depression.

- Response to Support. Social support helps provide the acceptance and assistance necessary for completion of grief work. While social interaction may be helpful in some depressed patients, it will typically not provide the assistance necessary to resolve depression.

- Active Desire for an Early Death. An active desire for an early death is not typical of preparatory grief. A persistent, active desire for an early death in a patient, whose symptomatic and social needs have been reasonably met, is suggestive of clinical depression.

- Self-Image. A disturbed self-esteem is not typically seen in grief; however, it is a common feature of depression. Overwhelming and persistent feelings of worthlessness to others and of being a burden are common in depression. Distressing guilt is usually generalized to all facets of life in depression, while in grief, the guilt is focused around specific issues (e.g. not being able to attend a child’s wedding).

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FAST FACTS AND CONCEPTS #59
DEALING WITH THE ANGRY DYING PATIENT
Rebekah Wang-Cheng MD, FACP

Background Anger is a common emotion expressed by seriously ill patients and their families. A
typical reaction by the health professional, confronted by the angry patient or family, is to either get angry
back or to physically and psychologically withdraw; neither are particularly helpful coping strategies. A
guide to managing these situations is presented below.

Look for the underlying source of anger. Fear is probably the most common source of anger,
especially in the dying and their families – fear of the unknown, being in pain or suffering, the future well-
being of family members, abandonment, leaving unfinished business, losing control of bodily functions or
cognition, being a burden to the family, and dying alone. Other sources of anger include: 1) a genuine insult – so called “rational anger” (e.g. waiting six hours to
see the doctor); 2) organic pathology: frontal lobe mass, dementia or delirium; and 3) personality style/disorder – the person whose approach to much of life is via anger or mistrust.

Recognize the direction of anger. Recognizing the difference between internal and external anger is
critical to effective management, because internal anger may lead to potentially harmful patient
consequences. When the patient directs anger internally because of fear and guilt (e.g. I didn’t take care
of myself; I’m abandoning my family.), this can lead to withdrawal, self-neglect, anxiety, depression, or a
combination of these. Others direct their anger outward at physicians, hospitals, family members or a
deity. Particularly in the case of an angry parent of a dying child, he or she may feel helpless and guilty
about many things – not bringing the child for medical care soon enough, not being a loving enough or
“great” parent (1). This internal guilt and blame can then be displaced towards health care professionals.

Engage rather than withdraw from the patient. The natural tendency for clinicians is to cut short the
office or hospital visit, find ways to avoid contact with the angry patient or family member, or to try to mask
his/her own anger in order to continue to interact with the patient. Robert Houston MD has written a very
helpful article listing 10 rules for engaging the dying patient which will have a beneficial impact on the
physician/patient relationship and the quality of the patient’s end-of-life experience (2). One of his most
important tips is to refrain from personalizing the anger when the patient accuses you of “missing the
diagnosis” or under treating the pain. Some of his rules which are pertinent to this discussion are:

• Engage the patient, but do not enmesh with and do the emotional work for the patient.
• Maintain adult-adult communication rather than fostering the patient’s dependency.
• Do not personalize the patient's anger.
• Adopt a patient-centered worldview by ascertaining his/her values, priorities, hopes.
• Normalize anger so that the patient can move through this stage.

**Use the "BATHE" approach to create an empathic milieu (3).** As with any difficult patient situation, communication techniques are especially important so that both the patient and physician do not become further embittered and frustrated.

- **Background:** Use active listening to understand the story, the context, the patient's situation.
- **Affect:** Name the emotion; for instance, *You seem very angry....* It is crucial to validate feelings so the angry person feels that you are listening. Attempting to defuse it, counter it with your own anger or ignore it, will be counter-productive. Acknowledging their right to be angry will help start the healing process and solidify the therapeutic relationship.
- **Troubles:** Explore what scares or troubles them the most about their present and future. Just asking the question *Tell me what frightens you?* will help them to focus on circumstances they may not have considered.
- **Handling:** Knowledge and positive action can help mitigate fears and reduce anger. How are they handling the dying – are they making concrete plans about their finances, their things, their family? Have they thought about formal counseling to help deal with the depression, the anger?
- **Empathy:** By displaying empathy and concern you can help the person feel understood, less abandoned and alone. Avoid trite statements such as *I know what you're going through.* Paraphrasing the patient's comments is an effective way to convey that you heard and are seeking to understand: *You feel like it's so unfair that the cancer appeared out of nowhere after all these years.*

**Summary**  The journey from life to death almost always is accompanied by some degree of anger. A caring, patient clinician can assist the patient and the family in recognizing, mobilizing, and modifying the anger into positive emotional energy. Established communication approaches are available such as BATHE which have shown improvements in self-efficacy for communicating with angry patients.

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FAST FACTS AND CONCEPTS #60
PHARMACOLOGIC MANAGEMENT OF DELIRIUM: UPDATE ON NEWER AGENTS
Earl Quijada MD and J Andrew Billings MD

Background  Delirium is common in those with serious medical illness (See Fast Fact #1). Delirium is an acute change in mental status that fluctuates and has underlying physiologic causes and can be categorized as hyperactive, hypoactive, or mixed. Common reversible etiologies include constipation, urinary retention, medications (benzodiazepines, opioids, steroids, and anticholinergic drugs), electrolyte abnormalities, and sleep deprivation. Initial management strategies include identifying and treating the underlying cause, as well as non-pharmacological treatment. However, when these strategies are not effective pharmacological interventions may be necessary. The below pharmacological interventions are for potentially reversible, hyperactive delirium.

1st Generation Antipsychotics
Haloperidol  Although no medication has been approved by the FDA for the treatment of delirium, the best studied antipsychotic, and the agent of choice for most patients, is haloperidol (Haldol), which can be administered safely through oral and parenteral routes. Starting doses are 0.5 – 1 mg PO or IV. Titration can occur by 2 – 5 mg every 1 hour until a total daily requirement is established, which is then administered in daily or twice daily doses. Recommended maximum dose is 100 mg/day. Intravenous haloperidol may cause less extrapyramidal symptoms than oral haloperidol.

Chlorpromazine  Chlorpromazine (Thorazine) has more sedative effects than haloperidol for patients in whom sedation is desired. The starting dose is 25 - 50 mg PO. Titration can occur by 25 - 50 mg every 1 hour until a total daily requirement is established, which is then administered in daily or twice daily doses. Recommended maximum dose is 2000 mg/day.

2nd Generation Antipsychotics
Also known as atypical antipsychotics, no evidence currently exists for improved efficacy with 2nd generation antipsychotics, so they are not considered to be first-line treatment. These agents are associated with fewer extrapyramidal side effects than 1st generation antipsychotics, hence, in Parkinson’s disease and related neuromuscular disorders and in patients with a history of extrapyramidal reactions from 1st generation antipsychotics this class of agents may be preferred. For acutely agitated patients requiring onset of action within minutes, providers should know that these agents do not work as fast as conventional antipsychotics.

Olanzapine  The starting dose for olanzapine (Zyprexa) is 5 mg PO every day; after one week, the dose can be raised to 10 mg a day; then to 20 mg a day. It is available as an orally disintegrating tablet.

Quetiapine  Quetiapine (Seroquel) is initially given 25 mg PO twice a day which can be raised by 25 – 50 mg per dose every 2 – 3 days up to a target of 300 – 400 mg a day, divided into 2 – 3 doses. Compared to the atypical neuroleptics, it is the most sedating and causes the least extrapyramidal side effects. It has more orthostasis than olanzapine and risperidone.

Risperidone  Risperidone (Resperidal) is given 1 – 2 mg PO at night and is gradually raised 1 mg every 2 – 3 days until an effective dose (usually 4 – 6 mg PO hs) is reached. It has minimal anticholinergic effects and does not cause orthostasis. It is the least sedating of this class of antipsychotics.
Newer antipsychotics include ziprasidone (Geodon) and aripiprazole (Abilify); their role in the management of delirium is not firmly established.

**Risks**  The FDA has issued a black-box warning about the increased risk of death when first- or second-generation antipsychotics are used to treat dementia-related psychosis in elderly patients. This warning is based on a number of limited studies which have not been replicated and do not address the short-term use of antipsychotics to manage delirium. Delirium is a poor prognostic marker. Goals of care and values must be discussed in the management of delirium.

**Benzodiazepines**  With the exception of treating delirium due to drug withdrawal or anticholinergic excess, benzodiazepines should be avoided for potentially reversible, hyperactive delirium unless the agitation is severe and uncontrolled by the neuroleptic. Benzodiazepines can make delirium worse and precipitate withdrawal syndromes.

**Melatonin**  This hormone is produced naturally in the pineal gland and can help regulate the sleep-wake rhythm cycle. Randomized placebo-controlled trials have validated the use of both melatonin and a melatonin analog (ramelteon) in the prevention of delirium in at-risk, hospitalized patients.

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FAST FACTS AND CONCEPTS #88
NIGHTMARES
Seema Malhotra MD, Robert Arnold MD, and Kevin Patterson MD

Background  Good, restful sleep is essential to quality of life – providing renewed energy for the next day. Nightmares are vivid, frightening dreams that typically lead to full awakening with detailed recollection of the dream sequence and content. Following a nightmare, heart rate and blood pressure are elevated, and residual anxiety may interfere with the ability to return to sleep. Nightmares occur almost exclusively during REM (Rapid Eye Movement) sleep.

Causes
Psychiatric. Anxiety is a common symptom during a life-threatening illness. Specifically, anxieties related to the illness course and prognosis, procedures and treatments, family issues, and death, can be significant. Nightmares may arise as a complication of anxiety or other psychiatric disturbances (such as post-traumatic stress disorder, delirium, mood disorders, schizophrenia, and adjustment disorders).

Medications/Drugs/Alcohol. Medications causally linked to nightmares include: beta-blockers, sedative/hypnotics, amphetamines and other stimulants, dopamine agonists, and antidepressants. Withdrawal from REM-suppressing drugs, including antidepressants, benzodiazepines, and alcohol, predisposes to the development of nightmares.

Brain disorders. CNS infections, brain tumors and other structural problems of the brain may lead to nightmares.

Metabolic: hypoglycemia.

Psychotherapeutic Interventions can be particularly helpful for people whose nightmares are related to stress/anxiety or an underlying psychiatric condition.

Supportive Psychotherapy. Brief, supportive psychotherapy can address a patient’s anxieties and concerns; the therapist helps the patient with problem solving, seeking information and support, and accepting aspects of their situation which cannot be changed.

Behavioral techniques. Relaxation training, desensitization, and dream imagery rehearsal therapy may help reduce nightmares. In imagery rehearsal therapy, the patient writes down the disturbing dream, changes the content, and practices the new, positive scenario mentally during the day; this new imagery during the day reduces nightmares at night.

Pharmacologic Management  The pharmacologic treatment of nightmares has not been studied in controlled clinical trials. Case studies and anecdotal reports suggest the following drugs or drug classes may be effective:

• Atypical Antipsychotics: risperidone (0.5-2 mg qhs) and olanzapine (5 mg) have both been shown to reduce nightmares in small pilot studies of patients with acute stress and PTSD, including reduction in flashbacks, hyperarousal, and disturbed sleep.
• Alpha-1 Antagonists: prazosin (2-15 mg qhs) has been shown to reduce nightmares and other sleep-related symptoms in PTSD patients in multiple small studies and a single randomized controlled trial involving 13 patients.
• Benzodiazepines and Tricyclic Antidepressants may be of benefit in suppressing REM activity. Note: trazadone does not suppress REM activity.
• Other: Both cyproheptadine and topiramate have been reported to suppress nightmares in small case series.
References


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Background  Sleep disorders are common in the general population, the elderly, and the terminally ill. Sleep deprivation causes reduced tolerance to pain and increased fatigue that prevents patients from participating in meaningful daytime activities and decreasing their quality of life. This Fast Fact focuses on the assessment of insomnia; it is the first of a series of three Fast Facts about insomnia (see #104, 105).

Definitions

* Primary Insomnia: difficulty initiating or maintaining sleep, or non-restorative sleep, for at least 1 month; does not occur exclusively during another mental disorder; is not due to the direct physiological effects of a substance/medication or a general medical condition; and significantly impairs functional/social quality of life. [DSM-IV-TR Diagnostic Criteria 307.42]. The International Classification of Sleep Disorders (ICSD-2) classifies insomnias into various categories:
  i. Acute/Adjustment Insomnia: Usually related to an acute physical/psychosocial stressor, change in environment; is short-term, expected to resolve when stressor disappears, usually lasts less than 3 months.
  ii. Idiopathic Insomnia/Life-Long Insomnia: Begins during infancy or childhood, etiology is unknown; patients may have learning disabilities.
  iii. Psychological Insomnia/Conditioned/Learned Insomnia: Caused by an acute event such as a significant life stress, pain, or illness; the individual no longer associates the bed with sleeping.
  iv. Paradoxical Insomnia/Pseudo-insomnia/Sleep Hypochondriasis: Subjective feeling of insomnia, with no polysomnographic evidence of a sleep disorder.
  v. Inadequate Sleep Hygiene: Related to irregular sleep schedule, consumption of caffeinated beverages, nicotine or alcohol, or exercise before bed-time.
  vi. Circadian Rhythm Sleep Disorders: Jet lag and shift-work.

* Parasomnia: a disruptive physical act that occurs during sleep or during sleep–wake transitions which may cause awakening or other disturbance in sleep. It includes nightmare disorder, sleep terror disorder, sleepwalking disorder and other parasomnias.

* Sleep Apnea: short periods of breathing cessation during sleep; can be obstructive or central in origin.

* Restless Legs Syndrome (RLS): paresthesias and dysesthesias of the legs that typically occur in the evening or at night and may be relieved by movement (see Fast Fact #217).

* Periodic Limb Movement Syndrome (PLMS): involuntary, rhythmic twitches, typically ankle dorsiflexion, occurring every 20–40 seconds, leading to brief arousals and accidental kicking of bedmates. In contrast to RLS, PLMS occurs during sleep and patients often are not aware of it.

* Narcolepsy: a disorder of excessive daytime fatigue associated with abnormalities in rapid-eye-movement sleep.

Sleep History  Obtain a focused sleep history from the patient and bed partner. If needed, the patient should be asked to record their daily sleep patterns in a sleep log for one week; see http://www.webmd.com/sleep-disorders/guide/how-to-use-a-sleep-diary.

* Sleep hygiene. Has the patient altered their bedtime routine (e.g. change in bedtime, use of sleep aids, lying in bed watching TV prior to sleep)?
* Sleep chronology. Evaluate the onset, pattern and duration of sleep and whether the insomnia is transient, intermittent or persistent. A persistent problem usually is a consequence of a medical, neurologic or psychiatric disorder. Ask if the patient has difficulty initiating sleep, staying asleep, or both. Sleep apnea rarely causes disorders in initiating sleep. Nightmares (see Fast Fact #88) cause difficulty staying asleep and may reflect spiritual suffering. Ask about multiple nocturnal or early
morning awakenings. Frequent awakening is often due to medicine and early awakening is classically due to depression.

* Sleep environment. Are any environmental factors (e.g. noise, light, odors) preventing sleep? This may be particularly important in the hospital or a situation where a patient has moved into an unfamiliar setting (e.g. children’s house).

* Physical symptoms. Are there physical symptoms interfering with sleep (e.g. cough, pain, dyspnea)? Symptoms occurring just prior to sleep may reflect primary sleep disorders.

* Medical conditions. Are there co-morbid medical conditions that are associated with insomnia?
  I. Worsening of chronic medical conditions (e.g. CHF, COPD).
  II. New onset or worsening depression and/or anxiety.
  III. Drugs (e.g. steroids, beta blockers, psychostimulants); use of alcohol and caffeine, especially in the evening.
  IV. Restless leg syndrome or periodic limb movements in sleep (see above).

* Spiritual concerns. Fears about dying may cause a patient to be afraid of falling asleep or to not want to turn off the lights; this is especially common in patients with dyspnea. This is in contradistinction to more typical insomnia where the patient is bothered by the lack of sleep.

References

Author Affiliations: University of Pittsburgh Medical Center, Pittsburgh, PA.
**Introduction**  This *Fast Fact* addresses non-pharmacologic therapies for insomnia; *Fast Fact #101* discusses patient assessment and #105 discusses pharmacologic treatment of insomnia.

**Non-Specific Treatments**

**Improving Sleep Hygiene**  Sleep hygiene education should be provided to anyone with insomnia. First, there is no arbitrary rule for how much someone should sleep. Generally, older patients need less sleep. Second, patients should be advised to keep a regular sleep schedule; this means going to bed and getting up at the same time. Third, patients should avoid long daytime naps, alcohol, and caffeine. These principles may be difficult for seriously ill patients, particularly maintaining a regular routine for hospitalized patients and avoiding naps for fatigued, seriously ill patients.

**Behavioral Treatments**

a. **Relaxation therapies:** The patient can be taught to use various relaxation techniques just prior to bedtime such as progressive muscle relaxation, guided imagery, meditation, diaphragmatic breathing or hypnosis (see *Fast Fact #211*).

b. **Stimulus control therapy:** This focuses on establishing a connection between the bed and sleep. It emphasizes not watching TV, reading in bed, or using bedroom for any other activity (except sexual activity).

c. **Sleep restriction therapy:** This therapy requires patient motivation as it involves restricting the time allowed in bed depending upon the actual time spent in bed over the past 2 weeks and then going to bed 15 minutes earlier every night (increased weekly) until the target bedtime is achieved. **Sleep compression therapy** is a variant of sleep restriction but the reduction is sleep is made gradually.

d. **Cognitive behavioral therapy:** This is a multi-component psychotherapy, and includes sleep restriction, stimulus control and cognitive therapy which focuses on identifying unwanted feelings or thoughts and replacing them with more positive thoughts. It is effective in treating chronic insomnia in the general population, in patients with chronic pain, and in women with metastatic breast cancer.

The last two therapies are the only evidence-based psychological treatments for insomnia in older adults.

**Physical Exercises:**  Although the data is limited, studies in elderly patients suggest significantly improved sleep duration and onset latency and minimal enhancement in sleep efficiency with community-based endurance training programs such as low impact aerobics, brisk walking, and Tai Chi Chih.

Choosing which therapy to use first depends mainly on provider experience and patient motivation. It is difficult to know how long non-pharmacologic therapy should be tried before attempting other measures. This depends on the patient, the severity of the insomnia, or the severity of the illness. Many studies which showed cognitive behavioral therapy to be effective used a treatment regimen of 7-8 weeks.

**Specific Treatments**  **Obstructive sleep apnea** is treated with positive airway pressure (e.g., ‘CPAP’) ventilation at night. Although some patients report difficulty becoming accustomed to sleeping with the CPAP mask on, this therapy can dramatically improve symptoms. Surgery is sometimes indicated for obstructive sleep apnea. **Symptoms** from an underlying medical disorder can also contribute to insomnia. Adequately treating a patient’s pain, nausea and vomiting (See *Fast Fact #5*), or dyspnea (See *Fast Fact #27*) should improve sleep.

**Spiritual and existential concerns** can be an important cause of insomnia in palliative care patients. Patients may be able to avoid these concerns during the day through the distraction of daily activities but have difficulty ignoring them at night. Thus, it is important to directly address a patient’s spiritual concerns, worries, and fears about dying during the day. Brief psychotherapy may be helpful.

**References**


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FAST FACTS AND CONCEPTS #105
INSOMNIA: DRUG THERAPIES
Robert Arnold MD, Michael Miller, and Rohtesh Mehta MD MPH

Introduction Fast Facts #101 and #104 reviewed assessment of insomnia and its non-pharmacological therapy. This Fast Fact focuses on the pharmacological treatment of insomnia. Prior to pharmacological treatment, it is important to improve sleep hygiene and treat any contributing underlying medical conditions (e.g. depression, pain, worsening CHF or COPD).

Non-Specific Drug Treatment:
1. Benzodiazepines have been successfully used for short term insomnia as they improve sleep quality, total sleep time and reduce night-time awakenings, although there are no systematic studies on long-term use and rare studies in palliative care. All drugs are dosed orally, at bedtime. Most commonly used (and FDA approved) are temazepam (start 7.5 mg), estazolam (0.5 mg), triazolam (0.125 mg), quazepam (7.5 mg) and flurazepam (15 mg). The first two are medium half-life benzodiazepines (10-24 hours); triazolam has a shorter half-life (< 6 hours), quazepam and flurazepam are longer lasting (half-life up to 3-7 days in elderly). All of these undergo hepatic metabolism via cytochrome P450 system (except temazepam which is cleared renally) and thus
have numerous drug-drug interactions. Flurazepam and triazolam have active metabolites. Benzodiazepines have a high incidence of amnesia and rebound insomnia, particularly in anxious patients, and may cause paradoxical agitation, increased risk of falls, hip fractures and cognitive impairment, especially in the elderly. Other side effects include tolerance and dependence with long-term use and additive CNS and respiratory side effects when used with other drugs.

2. **Benzodiazepine receptor agonists.** These are rapidly absorbed, metabolized by the liver, do not have active metabolites, have low abuse potential and do not cause rebound insomnia upon abrupt discontinuation. Zolpidem (5-10 mg) and Zaleplon (10-20 mg), both dosed at bedtime, are ultra-short acting agents (half-life 1-2 hours) that restore sleep in patients with nocturnal awakenings, while eszopiclone (1-2 mg) has a half-life of 6-9 hours. Zolpidem is available in a controlled-release formulation.

3. **Antidepressants** such as trazodone (25-100 mg), doxepin (10-50 mg), amitriptyline (10 -50 mg), imipramine (10-75 mg), and mirtazapine (5-15 mg) are commonly used for insomnia due to their sedative properties, however the evidence for their use is less convincing.

4. **Atypical antipsychotics.** Most of the atypical antipsychotics (quetiapine, olanzapine and ziprasidone), except for risperidone, improve total sleep time and/or sleep efficiency in healthy subjects and schizophrenic patients. These may be beneficial in patients with insomnia who do not respond to front-line treatment or insomnia in medically ill patients with delirium.

5. **Miscellaneous sedative hypnotics.** Choral Hydrate has moderate short term efficacy but is more toxic than benzodiazepines. Barbiturates are effective in short term treatment, but tolerance develops rapidly. Once commonly used for insomnia, these drugs are no longer used except in rare circumstances.

6. **Antihistamines and over-the-counter drugs.** Diphenhydramine or other classical antihistamines have sedative properties, but they are generally not preferred in the elderly due to anticholinergic properties and drug interactions. Diphenhydramine (25-100 mg) has been shown to increase sleep duration but not quality (as it does not affect sleep architecture). Its half-life is ~5-10 hours, but is much longer in elderly. Most over the counter products contain diphenhydramine or a similar sedating antihistamine, including products such as Unisom, Tylenol PM, and Nyquil.

7. **Melatonin** is used for circadian rhythm sleep disorders and is less effective for chronic insomnia. It has short half-life (45-60 min), has been used in doses ranging from 0.3 to 20 mg, is not FDA approved, and does not have any significant effects on either sleep onset latency or sleep efficiency.

8. **Melatonin receptor agonists** include ramelteon, tasimelteon and agomelatine. Ramelteon (8 mg) is FDA approved, has a half-life of 1–2.6 hours; has been shown to reduce sleep latency and increased total sleep time in patients more than 65 years old with chronic insomnia. Side effects are similar to that of placebo and include headache, somnolence and sore throat. Its primary advantage is that there is no evidence of abuse and dependence, rebound insomnia, or withdrawal effects.

9. **Herbal remedies.** Preliminary and conflicting evidence suggest that valerian (oral extract 400-900 mg QHS) may be as effective as mild hypnotics. The major side effects are hepatotoxicity, cardiotoxicity and delirium. Evidence is lacking for other medications like kava kava, L-tryptophan, chamomile, St. John’s wort and Jamaican dogwood.

Drugs for specific sleep disorders: See *Fast Fact #217* for treatment of Restless leg syndrome. Discussion of therapies for narcolepsy and nocturnal myoclonus or periodic leg movements is beyond the scope of this *Fast Fact.*

**References**


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Background  Anxiety and fear occur commonly in the dying patient. However, disabling anxiety and/or panic is not a normal aspect of the dying process. Separating “normal” death-related anxiety from pathological panic is an important palliative care skill.

Definitions
- A panic attack is defined in the DSM-IV as “a discrete period of intense fear or discomfort, in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: palpitations, pounding heart or accelerated heart rate, sweating, trembling or shaking, sensations of shortness of breath or smothering, feeling of choking, chest pain or discomfort, nausea or abdominal distress, feeling dizzy, unsteady, lightheaded or faint, derealization or depersonalization, fear of losing control or going crazy, fear of dying.
- Derealization describes a sensation of feeling estranged or detached from one’s environment.
- Depersonalization is an altered and unreal perception of self, one’s feelings and/or situation. Described by one patient as “feeling like you are on the outside looking in”.

Diagnosis
• A combination of physical symptoms (feeling dizzy, weak, nauseous, unsteady, lightheaded, breathless) and affective symptoms (fear of loss of control) are used to diagnose a panic disorder.
• Terminally ill patients may often have many of the physical symptoms listed above as a part of their illness process. Thus the presence of derealization, depersonalization and fear of loss of control are more useful in making the diagnosis of panic disorder in the terminally ill.
A contributing feature to the diagnosis of panic disorder is if a patient develops recurrent symptoms, worries about future ‘attacks’ and alters her/his behavior in anticipation of such attacks.

Terminally ill patients with chronic dyspnea may often worry about “suffocating to death.”

Management

- Educate patients about the diagnosis and reassure them that their symptoms can be greatly palliated with appropriate treatment.
- Optimize medical management of symptoms like pain, non-pain symptoms (especially dyspnea) and depression.
- Ideal therapy is a combination of medical therapy with counseling from a trained psychologist.
- Consider complementary treatments: music therapy, massage therapy, guided imagery, biofeedback.
- Medical management is influenced by anticipated lifespan and severity of panic symptoms.
- Selective serotonin reuptake inhibitors (SSRI) either as monotherapy or augmented with low dose benzodiazepines for a period of 3 to 4 weeks (taper off benzodiazepines after 3 weeks) is indicated in patients with an anticipated lifespan of several weeks or more.
- SSRIs can exacerbate anxiety in some patients during the first few days of therapy. Consider adding benzodiazepines as needed for the first few weeks in such cases.
- Benzodiazepine monotherapy should be considered in patients with anticipated lifespan of days to weeks. Consider low dose long acting benzodiazepine therapy on schedule (e.g. diazepam 1 mg every 12 hours) with short acting benzodiazepines (e.g. lorazepam 0.5 mg every 4 to 6 hours as needed) for acute breakthrough symptoms.
- Many terminally ill patients need maintenance therapy for the rest of their life span, as relapse rates are high on treatment discontinuation. In cases where treatment termination is attempted, it is recommended that the medications be tapered gradually over a several week period to allow early detection of a relapse.
- Abrupt termination of benzodiazepine therapy often may result in intense rebound anxiety. This may happen when the patient is actively dying and unable to take oral medications. In such cases, use alternate routes of drug administration (diazepam gel, diazepam rectal suppository or midazolam infusions).

References

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**FAST FACTS AND CONCEPTS #146**
**SCREENING FOR DEPRESSION IN PALLIATIVE CARE**

Robert Arnold MD

**Background**  Depression is a significant symptom for approximately 1 in 4 palliative care patients and is especially common in patients with metastatic cancer (see Fast Fact #21). Up to 80% of the psychological symptoms that occur in cancer patients go unrecognized and untreated. One reason for this is the difficulty in diagnosing depression in palliative care patients (see Fast Fact #7). In the primary care literature, a number of brief screening instruments such as PRIME-MD are used to identify depression. However, the symptoms associated with depression in primary care (weight loss, loss of energy, fatigue, insomnia) also occur in patients without depression who have a life-threatening disease. Thus, there has been interest in developing a brief scale that can accurately identify depression in the palliative care population. This Fast Fact reviews that literature on depression screening tools.

**Single question screening**: A study of palliative care inpatients found that a single question, “Are you feeling down, depressed or hopeless most of the time over the last 2 weeks?” correctly identified patients with 100 percent sensitivity and specificity and a positive predictive value of 1 (Chochinov 1997). Adding a second question about anhedonia (the absence of pleasure from the performance of acts that would normally be pleasurable), “Have you found that little brings you pleasure or joy over the last two weeks?”, reduced the specificity and positive predictive value. Unfortunately, follow-up studies using a single question regarding mood in other palliative care populations have shown a sensitivity of roughly 55 percent and a specificity of 75 percent.

**A four-item algorithm** asks questions about energy level, anhedonism, depressed mood, and psychomotor retardation/agitation. In a study of hospice patients in Australia this tool had a sensitivity between 62 and 72%, specificity of 75 to 89% and positive predictive value of between 68 and 89% (Robinson 2005).

**The four question Brief Case Find for Depression** asks questions about sleep, depressed mood, life satisfaction, and ability to overcome difficulties. In a study of oncology and palliative care patients this tool had fair agreement with longer depression screening instruments (Jefford 2004).
Other studies have examined 10-20 question depression instruments that have been validated in other patient populations. The *Edinburgh Postnatal Depression Scale* (Lloyd-Williams 2000), a self-assessment scale consisting of ten items each rated on a 4-point scale, had a sensitivity of 70% and specificity of 80% in patients with metastatic cancer receiving palliative care. The *Hospital Anxiety and Depression Scale* (Lloyd-Williams 2003) is a 14 item scale with separate sub-scales for anxiety and depression. In a group of patients with metastatic cancer, summing the two subscales gave a sensitivity of 77%, specificity was 89% and a positive predicted value of 0.48. Two more recent articles reported lower sensitivity and specificity in patients with advanced metastatic disease.

**Summary and Recommendations**

- Clinicians should have a high clinical suspicion for depression—especially in patients who exhibit feelings of hopelessness, worthlessness, guilt, anhedonia, sustained periods of feeling sad, and/or those with suicidal ideation and/or suicidal plans.
- The literature does not suggest that any of the above scales are clearly superior for helping to diagnose depression in a population of palliative care patients.
- Depression screening scales may be helpful in individual cases to provide the clinician with additional data in formulating a diagnosis; if used, it is suggested that clinicians be familiar with the sensitivity/specificity data for one scale and consistently use that scale so as to gain clinical familiarity.
- Psychiatric consultation is indicated in cases of diagnostic uncertainty and/or when patients present with profound depression and/or are overtly suicidal.

**Definitions** (Further resources available at: [http://www.musc.edu/dc/icrebm/diagnostictests.html](http://www.musc.edu/dc/icrebm/diagnostictests.html))

- **Sensitivity**: The fraction of those with the disease correctly identified as positive by the test.
- **Specificity**: The fraction of those without the disease correctly identified as negative by the test.
- **Positive predictive value**: The fraction of people with positive tests who actually have the condition.

**References**


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FAST FACTS AND CONCEPTS #156
EVALUATING REQUESTS FOR HASTENED DEATH
Tim Quill MD and Robert Arnold MD

Background A patient’s request to a health care professional to help hasten death is not uncommon. The motivation for this request is usually a combination of relentless physical symptoms, progressive debility, in combination with a loss of sense of self, loss of control, fear of the future, and fear of being a burden on others. Some physicians are frightened by these requests, feeling that they are being asked to cross unacceptable professional boundaries. Others may be tempted to quickly accede, imagining that they would want the same thing in the patient’s shoes. But requests for a hastened death may provide awareness into a patient’s experience of suffering, and may lead to opportunities for more effective treatment if fully evaluated. In general, the clinician should clarify, explore, evaluate, intensify treatment, and support the patient to ensure a full understanding of the request and to ensure that all alternatives have been considered before responding. This Fast Fact provides guidance on how to evaluate and initially respond to a patient who raises the topic of a hastened death. Fast Fact #159 will explore how to respond when the request for a hastened death persists after a full evaluation and search for alternatives.

1. Clarify which question is being asked before responding. Is the patient simply having thoughts about ending his life (very common), or is he exploring the possibility of a hastened death in the future if his condition deteriorates, or is he exploring your willingness to assist right now (1, 2)?

2. Support the patient, and reinforce your commitment to trying to find a mutually acceptable solution for the patient’s problem and to continue to work through the process. This does not mean violating fundamental values, but it does mean searching in earnest with the patient and family to find a way to approach the dilemma (3). Attend to your own support by discussing the patient with trusted colleagues and/or with your multidisciplinary team.

3. Evaluate the patient’s decision-making capacity. Is she seeing her medical condition clearly? Is the request proportionate to the level of unrelieved suffering? Are there dominating aspects of anhedonia, worthlessness and guilt, or is the capacity for pleasure and joy preserved in some small ways? Is this request consistent with the patient’s past values? Get help from an experienced psychiatrist or psychologist if you are unsure (4).

4. Explore the many potential dimensions that may contribute to the patient’s “unbearable” suffering to be sure you (and the patient) fully understand its underlying cause(s). Sometimes in may be an unrelenting physical symptom, other times feelings of depression, or a family or spiritual crisis, or perhaps a combination of many factors (1, 2).
5. **Respond** to the associated emotions, which may be strong and conflicted. Try to empathically imagine what the patient is going through and asking for. Distinguish your own feelings and reactions from those of the patient.

6. **Intensify treatment** of any potentially reversible elements of the patient’s suffering. Depending on the patient’s circumstances, offer to increase treatment of pain or other physical symptoms, consider biological or interpersonal treatment of depression; see if an appropriate and acceptable spiritual counselor is available. Be creative and brainstorm potential solutions with your multidisciplinary team (1, 2).

7. **Respond** directly to the request for hastened death only after this multidimensional evaluation has been completed. If the patient has full decision-making capacity and all alternative approaches to the patient’s unbearable suffering have been fully considered, then re-explore exactly what is being requested, and look for mutually acceptable ways to potentially respond — see Fast Fact #159 (5). Note that many patients may be looking for the potential of an escape they will never use, but a smaller number will be looking for a way to hasten death in the present.

References

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FAST FACTS AND CONCEPTS #159
RESPONDING TO A REQUEST FOR HASTENING DEATH
Timothy Quill MD and Robert M Arnold MD

Background  Requests for hastened death among terminally ill patients occur commonly (see Fast Fact #156). With good symptom management, psychological and spiritual support, most patient requests do not persist. This Fast Fact focuses on ways of responding to patients with persistent wishes for a hastened death despite every effort to find appropriate alternatives. This Fast Fact does not address such requests by surrogate decision makers of patients who have lost decision-making capacity.

1. Reflect on your personal feelings about the request and discuss with other professionals. These cases are emotionally and ethically difficult. Brainstorm options with other members of the care team including physician colleagues, nurses, psychologists, chaplains and others. Allow trusted colleagues to support your emotional reactions.

2. Seek out consultation/2nd Opinion. Make sure you understand the medical, legal and ethical issues involved in responding to a particular request for hastened death. Palliative care and/or ethics consultations are invaluable. Independent second opinions may be helpful in clarifying the prognosis and ensuring that all potentially effective therapeutic alternatives have been considered.

3. Learn the possibilities. Possibilities are listed below from least to most ethically controversial. Considering these possibilities assumes that aggressive measures to control physical, psychological and spiritual suffering have been exhausted and/or rejected by the patient:
   ○ Withdrawal of life-sustaining treatments. While most clinicians consider stopping invasive treatments under these circumstances (e.g. ventilators, ICDs, feeding tubes), simpler therapies such as insulin, antibiotics, oxygen, or steroids might also be voluntarily discontinued if they are prolonging life against the patient’s wishes. (Unlike the other possibilities, there is widespread legal and ethical consensus about the permissibility of this response based on the right to bodily integrity.)
   ○ Voluntary withdrawal of oral intake. Patients may choose to stop eating and drinking to shorten the dying process. Completely stopping oral food and liquids will typically result in death within two weeks.
   ○ Sedation for severe intractable physical symptoms (see Fast Facts #106,107). The intent of sedation is to relieve intolerable suffering by a reduction in patient consciousness. If artificial hydration and feeding are simultaneously stopped, death will come within 1-2 weeks.
   ○ Assisted Suicide. Assisted suicide is defined as someone who provides the means for another person to end their life (e.g. prescribing an overdose amount of medication), but the patient is the one to decide if and when the medicine is actually used, and the patient is responsible for taking
the medicine. Physician-assisted suicide is illegal in the United States except for selected states (e.g. Oregon, Washington, Vermont, and Montana).

4. **Decision making process.** Have a detailed conversation regarding the risk and benefits of the different possibilities that fit the patient’s clinical circumstances, and which the patient, family and you find ethically acceptable. Be as specific as possible, and document your thinking process clearly. Thus, if stopping eating and drinking is being considered, be sure everyone understands the importance of complete cessation of drinking or else the process can take months rather than weeks.

5. **Balance integrity and non-abandonment.** It is not always possible to find common ground between the patient and physician. When asked if one can support a particular act, a physician needs to be as specific as possible about what he/she can and cannot do, and why. While the physician should not violate personal principles to respond to a request he/she finds unacceptable, he/she should search in earnest with the patient and family for alternative options that might be mutually acceptable. Typically, this approach will allow the physician to maintain integrity while not abandoning the patient, even if agreement on the particular act in question is not possible (1-4).

References


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Background  Anxiety is a state of apprehension and fear resulting from the perception of a current or future threat to oneself. The term is used to describe a symptom and a variety of psychiatric disorders in which anxiety is a salient symptom. This Fast Fact will discuss the causes and evaluation of anxiety.

Prevalence  Anxiety is commonly reported in those facing life-threatening illnesses. At least 25% and cancer patients and 50% of CHF and COPD patients experience significant anxiety. At least 3% of patients with advanced cancer and 10% of COPD inpatients meet DSM criteria for Generalized Anxiety Disorder (see below).

Etiologies
- Anxiety may be present as part of one of several psychiatric disorders (see below).
- Anxiety is often a prominent component of acute or chronic pain, dyspnea, nausea, or cardiac arrhythmias.
- Adverse drug effects: corticosteroids, psychostimulants, and some antidepressants.
- Drug withdrawal: alcohol, opioids, benzodiazepines, nicotine, clonidine, antidepressants, and corticosteroids.
- Metabolic causes: hyperthyroidism and syndromes of adrenergic or serotonergic excess.
- Existential and psychosocial concerns about dying, disability, loss, legacy, family, finances, and religion/spirituality.

Psychiatric Disorders with anxiety as a prominent symptom
- Generalized anxiety disorder is a psychiatric disorder characterized by pervasive and excessive anxiety and worry about a number of events or activities (such as work or school performance), occurring more days than not for at least 6 months. The anxiety and worry are associated with at least 3 of the following 6 symptoms: restlessness, easy fatigue, difficulty concentrating, irritability, muscle tension, and sleep disturbance.
- Panic disorder is characterized by recurrent panic attacks. See Fast Fact #145 for its evaluation and management.
- Adjustment disorder occurs within 3 months of a major stressor, and causes marked distress and functional impairment. Usually it is characterized by a depressed mood but anxiety can also be its most prominent affective component.
- Acute- or post-traumatic stress disorders occur after an emotionally traumatic life-event and are characterized by anxiousness and arousal, as well as by numbness, flashbacks, intrusive thoughts, and avoidance of stimuli which remind the patient of the trauma.
- Phobias are marked, persistent fears brought about by specific situations or objects.

Evaluation
• Complete a thorough history and physical exam, in particular ask about:
  o Prior episodes or anxiety, depression, PTSD, alcohol, and drug use.
  o Prior and current treatment by a mental health professional.
  o Presence of specific trigger situations or thoughts leading to anxiety.
  o Presence of apprehension, dread, insomnia, and hypervigilance; as well as physical
    symptoms such as diaphoresis, dyspnea, muscle tension, and tremulousness.
• Seek help from a professional familiar with the psychiatric disorders when anxiety is a prominent and
  functionally impairing part of a patient’s symptoms.
• Symptoms that can be confused with anxiety are agitated delirium (see Fast Facts #1,60) and
  akathisia, an unpleasant sense of motor restlessness from dopamine-blocking medications such as
  antipsychotics and some antiemetics.
• Formal screening tools exist, but there is no consensus on the benefit of their routine use. Commonly
  used tools which evaluate for anxiety as a symptom include the Edmonton Symptom Assessment
  Scale, the Memorial Symptom Assessment Scale, and the Hospital Anxiety and Depression Scale.

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FAST FACTS AND CONCEPTS #210
SUICIDE ATTEMPTS IN THE TERMINALLY ILL
Sean Marks MD and Drew A Rosielle MD

**Background**
Chronic or advanced medical illness is a significant risk factor for suicidality (1). This Fast Fact discusses evaluating and responding to suicidality in patients with life-limiting diseases. Note: this Fast Fact does not address cases of ‘physician assisted suicide’ which have occurred after a deliberative process including psychiatric screening such as in Oregon in the US (2).

**Ethics**

- Core Principles: It is a core obligation of physicians to prevent a patient from initiating suicide and to intervene medically to prevent a patient from dying after a suicide attempt (3). This obligation can include detaining and restraining patients against their will and the use of invasive medical interventions such as mechanical ventilation if needed, although such restrictions to a patient’s liberty should be kept to the minimum necessary. Most suicidal patients are considered impaired by depression or other mental illnesses and their actions are not considered autonomous, thus justifying detaining patients and providing medical interventions against their will (4). Such interventions can create further opportunities to treat the patient’s psychiatric condition, and only 20% of people who are prevented from committing suicide subsequently complete another attempt.

- Exceptions at life’s end: The above logic is less compelling in terminally ill patients who have attempted suicide, particularly with short prognoses (e.g., <1 month). In these patients most medical interventions are unlikely to restore health or significantly alter the dying process in a way that would materially benefit the patient. Clinicians may opt to forgo certain interventions (e.g., mechanical ventilation), particularly if family/proxy decision makers consider such interventions inappropriate in their dying loved ones. In these situations clinicians are advised to 1) verify the certainty of the very short prognosis, utilizing consultants liberally, 2) discuss with proxy decision makers all possible treatment plans including, when feasible, less-invasive supportive care options with treatment limitations (e.g., ICU monitoring, gastric lavage and charcoal administration for an overdose, but establishing a do-not-resuscitate/do-not-intubate order even if the patient deteriorates), and 3) seek ethics consultation.

- Advance Directives: Advance directives such as living wills stating a patient’s wish to not be mechanically ventilated are not binding in the setting of a suicide attempt. However, they should be honored in patients with short prognoses per the discussion above. Advanced directives specifying treatment limitations should be re-evaluated if it is suspected those statements were made during a period of undetected depression (5,6).

**Epidemiology and Risk Factors**
There has been limited research into specifically ‘terminally ill’ populations, hence the rate of suicide in the terminally ill is unknown. What is clear is that advancing age and psychiatric comorbidity are risk factors for suicide along with male sex, AIDS diagnosis, a family history of suicide, and uncontrolled pain (7,8). Cancer patients have nearly twice the incidence of suicide than the general population (rate of 31.4 vs. 16.7/100,000 patient-years) and the first year after diagnosis carries a higher risk (6,9). Lung, prostate, pancreatic, and head and neck cancers have the highest suicide rates among all cancer types (9). Up to 8.5% of terminally ill cancer patients express a sustained and pervasive wish for an early death, and in one survey 10% of terminally ill patients reported “seriously pursuing” physician assisted suicide (10,11). Rates of actual suicide attempts are presumably lower.
Assessment All patients with life-limiting illnesses should be routinely assessed for depression and mood disorders (see Fast Facts #7, 43); depressed patients should be screened for suicidal thoughts. Patients who admit to suicidal thoughts or a desire for hastened death should be asked about specific plans for self-harm, past history of suicide attempts, access to firearms or other lethal means to carry out a suicidal act, and level of support/supervision available in the home (e.g. family caregivers). Although some clinicians may be concerned that exploring suicidal thoughts may make suicide more likely, there is no evidence that this occurs. Many ill patients who express a desire for death are simply communicating unresolved emotional and existential concerns about dying: see Fast Facts #156 & 159.

Responding to Suicidal Intent All patients who are seriously threatening self-harm, or who have pervasive thoughts of ending their life, should be evaluated urgently by a psychiatrist (12). Immediate resources depend on local availability and can include prompt evaluation by an established psychiatrist, medical or psychiatric urgent care clinics or emergency departments, or even voluntary hospital admission. Options include voluntary psychiatric treatment, arranging 24-hour safety monitoring from the patient’s family and friends, introducing home hospice or home nursing support, removing means to carry out a suicidal act, and imposing emergency detention. For disabled patients close to death, removing the means of self-harm (e.g. limit access to pain medications as long as a reliable family member can administer them) and providing close supervision through, for instance, hospice services are often sufficient and minimally restrictive.

References

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Background The majority of individuals experience normal grief after the death of a loved one (see Fast Fact #32). However, about 10-20% of bereaved individuals experience a persistent, debilitating phenomenon referred to as complicated grief (CG) (1). Complicated grief has also been referred to as prolonged or pathologic grief (2); and in the most recent revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM V), CG was relabeled as Persistent Complex Bereavement Disorder (3).

Risk Factors CG is principally considered an attachment disorder (1). Insecure attachment styles (excessive dependency, compulsive care-giving, defensive separation) are correlated with CG. Additionally, supportive marital relationships (characterized as security-enhancing, confiding and emotionally supportive) are correlated with CG after the loss of a spouse suggesting that the loss of a spouse who provides emotional stability and security may lead to an exacerbated grief reaction (4). Other risk factors include weak parental bonding in childhood, childhood abuse and neglect, female gender, low perceived social support, and low preparation for the loss (1,5).

Impact on Health CG is associated with mental and physical health problems including depression, hypertension, work and social impairment and reduced quality of life. Additionally, CG increases an individual's risk of suicide and suicidal behavior (7).

Diagnosis CG shares characteristics with major depressive disorder (suicidal ideation, preoccupation with worthlessness) and post-traumatic stress disorder (re-experiencing intrusive thoughts of the deceased, avoidance of reminders of the deceased and emotional numbness). However, these are separate entities differentiated by precipitating events, risk factors, course of illness and response to intervention (2). The precise diagnostic criteria for CG are currently being debated (5). Commonly agreed upon characteristics include:

- yearning, pining, or longing for the deceased
- trouble accepting the death
- feeling uneasy about moving on with one’s life
- inability to trust others since the death
- excessive bitterness or anger about the death
- persistent feeling of being shocked, stunned, or emotionally numb since the death
- frequent intense feelings of loneliness
- feeling that life is empty or meaningless without the deceased (refraining from doing things/going places that remind one of the loss)
- frequent preoccupying thoughts about the person that died

Symptoms must cause marked dysfunction in social, occupational or other important domains. The duration of symptoms required to meet criteria for CG has not been defined and varies between six to twelve months after the death (1, 5).

Screening The following Brief Grief Questionnaire is a 5-item screening tool scored on a 0-2 Likert scale (‘not at all,’ ‘somewhat,’ ‘a lot’) which has been used to screen for CG (6).

1. How much of the time are you having trouble accepting the death of a loved one?
2. How much does your grief interfere with your life?
3. How much are you having images or thoughts of your loved one when he or she died or other thoughts about the death that really bother you?
4. Are there things that you used to do when your loved one was alive that you don’t feel comfortable doing more, that you avoid? How much are you avoiding these things?
5. How much are you feeling cut off or distant from other people since your loved one died, even people you used to be close to, like family or friends?

Expert recommendation is that individuals with scores of ≥5 should undergo a diagnostic evaluation by a mental health professional (7).
Treatment  A recent meta-analysis on the treatment of CG showed efficacy of interventions including cognitive-behavioral and group therapy in alleviating symptoms with a duration of benefit from 3-6 months. Limitations of the meta-analysis include under-representation of men (average 71% female), small number of studies included (n=5), and small number of participants (n=485, 109 lost to follow up) (8). There have been no randomized controlled trials evaluating the pharmacologic treatment of CG and there is currently no defined role for drug therapy. A randomized trial is currently underway to evaluate the effect of a selective serotonin reuptake inhibitor on CG. Many hospice agencies provide bereavement services, even if the bereaved’s loved one was not a patient of the hospice agency.

Bottom Line  Most bereaved individuals experience normal grief. A minority will experience long-term, persistent, disruptive symptoms that impair functioning and increase the risk for negative mental and physical health states. Individuals suffering from CG benefit from referral to a trained mental health provider who can administer therapy specific to CG.

References

Authors’ Affiliation: University of Pittsburgh Medical Center, Pittsburgh, PA.

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Adults with serious illness have a higher incidence of major depressive disorders than healthy adults, with an estimated incidence of 15% (1). In this Fast Fact, we will provide a clinical framework for selecting pharmacologic agents for seriously ill patients with depression. See Fast Facts #7, 43 and 146 for assistance in diagnosing and screening for depression in palliative care patients.

**Determine the patient’s prognosis**  Because most traditional antidepressants take more than 4 weeks to become effective, they should only be considered in patients expected to live at least that long (2). Use is also limited to patients who are able to swallow oral medications or place them in a feeding tube. For patients with a prognosis < 4 weeks, a psychostimulant such as methylphenidate or dextroamphetamine may act within 1-2 days and be safe in patients without significant cardiovascular disease or delirium. Although the data on psychostimulants are somewhat mixed, controlled trials have shown benefit as both a monotherapy or to augment the effects of another anti-depressant (3-5). See Fast Fact #61.

**Consider co-morbid symptoms**  When choosing an antidepressant, consider the patient's other co-morbid symptoms such as insomnia, neuropathic pain, or poor appetite (6). Other considerations include the patient's past responses to specific agents and possible drug interactions. Common classes of antidepressants include serotonin-selective reuptake inhibitors (SSRIs), serotonin-selective norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and others.

**SSRIs**  Also called “second generation antidepressants”, these are the most commonly prescribed antidepressants. SSRIs should be started at a low dose and then titrated to the minimum effective dose to minimize adverse effects such as QTc prolongation, sexual dysfunction, headaches, nausea and diarrhea. Fluoxetine is associated with emotional activation and may worsen anxiety. Paroxetine can be sedating and lead to withdrawal phenomena with missed doses. Because sertraline, citalopram, and escitalopram have lower side effect profiles and are neither activating nor sedating, they may be better choices for palliative care patients (7). The starting dose of sertraline is 25-50 mg/day with a usual effective dose of 50-200 mg/day; it is available in a concentrated liquid formulation for patients with dysphagia related issues. Both citalopram and escitalopram have been shown to have few drug interactions. The starting dose of citalopram is 20 mg/day with a maximum daily dose of 40 mg. The starting dose of escitalopram is 10 mg/day with a usual effective dose of 10-20 mg/day (8-10).

**SNRIs**  Inhibit serotonin and norepinephrine reuptake, two neurotransmitters important in endogenous pain pathways (11). This class may be helpful for neuropathic pain, vasomotor instability, and anxiety-predominant depression. In particular, venlafaxine has shown effectiveness for the amelioration of hot flushes and the prevention of chemotherapy-induced polyneuropathy (CIPN); duloxetine has shown efficacy for the treatment of CIPN (12). SNRIs may prolong bleeding times and therefore may not be safe in patients with active bleeding or intracranial metastases. The starting dose for venlafaxine is 37.5 mg with a usual effective dose of 75-225 mg/day. It requires close monitoring for missed-dose withdrawal and hypertension. The starting dose for duloxetine is 30 mg with a usual effective dose of 60-120 mg/day. It has been associated with hepatic insufficiency and a worsening of acute-angle glaucoma.

**TCAs**  are an older class of anti-depressants that can be cost-effective when used at lower doses. They also are proven adjuvant analgesics for neuropathic pain and chronic low back pain. Unfortunately, their anticholinergic properties can induce delirium, prolong the QTc interval, and be dangerous in overdose. Therefore, their use is limited to heart-healthy patients under the age of 65 with comorbid neuropathic pain and insomnia. Although the preponderance of supporting data for the analgesic effects is for amitriptyline (usual starting dose 10-25 mg/day; usual effective dose is 150 mg/day), nortriptyline is felt to be less sedating (usual starting dose 25 mg/day; usual effective dose is 50-100 mg/day).

**Other Medications**  Mirtazapine has histaminergic side effects that can be helpful especially for cancer patients who often experience insomnia, poor appetite, and nausea (13). It has few drug interactions but can be associated with orthostatic hypotension. Its usual starting dose is 7.5-15 mg/nightly; usual effective doses are 15-30 mg/day. Bupropion is thought to be less sedating and have a lower incidence of sexual side effects, but it may lower the seizure threshold. The usual starting dose for bupropion is 150 mg/day; the usual effective dose is 150-300 mg/day (14). Single-dose treatment with NMDA antagonist ketamine has shown promise in early investigational studies (15). Aripiprazole may augment the antidepressant effects of SSRIs and SNRIs as early as a week after initiation (16).
Summary Recommendations:
• For patients with prognoses of weeks, consider the use of a psychostimulant like methylphenidate.
• Consider duloxetine or venlafaxine when neuropathic pain is present.
• When polypharmacy is present, consider citalopram, escitalopram or mirtazapine.
• If the patient has insomnia, nausea, or anorexia, consider the use of mirtazapine.
• Closely monitor patients initiated on an antidepressant for adverse effects and dose titration.
• Refer to a mental health clinician for pre-existing major depression, the presence of comorbid psychiatric illness, suicidal ideation, refractory symptoms, or psychiatric polypharmacy.
• Refer to social work and/or spiritual support services if the depression appears to be escalating in relation to social or spiritual factors.

References:

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Schizophrenia is a chronic and debilitating psychotic illness affecting 1% of the population. Patients with schizophrenia are at risk of receiving worse end-of-life care than other patients (1). This Fast Fact reviews relevant medical evidence and offers care suggestions for seriously ill patients with schizophrenia.

Illness Background: Schizophrenia is characterized by:

- **Positive psychiatric symptoms**: these include paranoid delusions and auditory hallucinations which often have a relapsing-remitting pattern and respond to anti-psychotic medications.
- **Chronic negative symptoms**: cognitive changes such as executive dysfunction, amotivation, blunted affect, and social withdrawal. These symptoms are often refractory to pharmacotherapies.
• **10-20 year shortened survival:** Medication side-effects; a reduced access to medical care; an increased rate of substance abuse (particularly tobacco); and an increased prevalence of comorbid illnesses such as cardiovascular disease, cancer, and emphysema are all contributing factors (2-4).

**Access to Palliative Care:** In the last six months of life, patients with schizophrenia are about half as likely to access palliative care specialists (1). Additionally, they receive less opioid analgesia, have a higher likelihood of spending extended time in a nursing home, and are less likely to engage in advance care planning despite evidence that many schizophrenic patients are capable of doing so (1,5).

**Determining Capacity:** Many patients with schizophrenia retain capacity for medical decision-making especially when the support of trusted providers, friends, or family is sought out (6-8). Some patients who lack capacity to make complex medical decisions, such as determining code status, may nonetheless retain capacity to make less complex decisions such as designating a surrogate decision-maker (9). Because symptoms of schizophrenia can make the determination of capacity challenging, psychiatric consultation is often essential (10). Some patients with schizophrenia will have legal guardians who may be a family member or a non-family member appointed by the legal system. Depending on state laws, guardians may be limited in their capacity to withdraw life-extending treatment such as artificial feedings (11,12). In such cases, involvement of social work and bioethics may be necessary.

**Advance Care Planning:** Even when patients with schizophrenia are medical candidates for life-extending treatments like dialysis or chemotherapy, psychotic symptoms such as paranoia may make them unwilling to cooperate with treatment, requiring ethically problematic interventions such as the use of restraints or sedation to deliver treatment. This can generate conflict about the best treatment course and necessitate the involvement of psychiatry and clinical ethics consultants.
- Outpatient discussions regarding potential conflicts with the patient and/or surrogate should occur prior to an acute medical or psychiatric crisis (11).
- Psychiatric-specific advance directives exist which detail not only medical contingencies, but psychiatric treatment preferences and outpatient mental health providers (e.g. case managers and group home staff) in the event of a psychiatric decompensation (13). Although supporting data on these tools are inchoate, they may reduce violent episodes and need for crisis management (14,15).

**Pain Management:** Schizophrenic patients often struggle to recognize and report pain (16,17), especially in inpatient settings when cared for by clinicians unfamiliar to them. The Pain Assessment in Advanced Dementia Scale (PAINAD) has been utilized even though it was not designed nor validated for this patient population (17). Otherwise, engaging longstanding caregivers in symptom assessment may foster trust and empower patients to share their symptoms more openly.

**Psychiatric Care:** Antipsychotic dosing may be much greater for schizophrenia (haloperidol doses of 20-30 mg/day are not uncommon) than for treatment of delirium, agitation, or nausea. Antipsychotics exhibit dose-dependent QT prolongation and resultant risk of torsade de points, which can be worsened when combined with other QT-prolonging medications such as anti-emetics, methadone, and antibiotics. In patients with estimated survivals longer than a few months, recurrent ECG monitoring may be necessary. Clinicians should be cautious about deprescribing antipsychotics, however, in patients who are not imminently dying, as the stress of medical illness may worsen positive psychiatric symptoms. If a medical issue arises in a schizophrenic patient who is not imminently dying preventing intake of the oral psychopharmacologic regimen, psychiatric consultation should be considered.

**Psychosocial Support:** Schizophrenic patients are at risk for poverty, homelessness, hunger, and violence (18-20). Such concerns can be primary drivers in medical decision making. Unfortunately, finding safe and appropriate care settings can be challenging for terminally ill patients with schizophrenia. Psychiatric group homes and inpatient psychiatric care settings may be poorly equipped to offer a sufficient end of life care plan and environment; conversely, hospices or nursing homes may be poorly equipped to address uncontrolled psychiatric symptoms. Thus, patients with schizophrenia may be at heightened risk for prolonged hospitalizations at the end of life. Social workers, chaplains, psychiatrists, and/or community case managers may be able to clarify unmet psychosocial and spiritual needs (20).

**Summary of Key Points:**
- Schizophrenic patients are at risk for suboptimal symptom control and unmet psychosocial needs.
• Schizophrenic patients do not inherently lack capacity, but may require medical explanations and advance care planning for medical and psychiatric contingencies “early and often”.

• Involvement of multiple disciplines including psychiatry, social work, trusted outpatient providers and clinical ethicists may be necessary.

References:
Background: Transference and countertransference influence any human interaction, including the patient-clinician relationship. Transference is the unconscious redirection of a patient’s feelings, attitudes, desires, often regarding a close personal relationship in their earlier life, onto the clinician (1). Countertransference is the unconscious redirection of a clinician’s feelings, attitudes, and desires about a close personal relationship onto the patient (1). This Fast Fact illustrates the impact of unrecognized transference and countertransference and offers strategies to mitigate their consequences.

Importance: Transference phenomena is common in clinical care. It is not inherently pathologic, nor does it reflect failure on the part of the clinician or patient. Yet, if unrecognized, it can potentially lead to harmful consequences for patients and clinicians. For example, transference phenomena can contribute to implicit biases toward certain ethnic or socio-economic groups (2,3); avoidance behaviors which may contribute to the inappropriate use of life-sustaining medical technologies via the failure to identify patient-centered goals; and mistrust of the health care system (4). Unlike psychiatrists, psychologists and social workers, most clinicians lack the training to recognize and understand this phenomenon (4). Hence, transference feelings go unrecognized by many clinicians and may contribute to professional loneliness, cynicism, burnout, and depression (4). This topic is particularly relevant for hospice and palliative care clinicians who often care for dying patients who may evoke intense, often unexamined emotions. The following cases illustrate how transference phenomena can impact palliative care encounters.

FAST FACTS AND CONCEPTS #371
TRANSFERENCE AND COUNTERTRANSFERENCE IN PALLIATIVE CARE
Ashwini C. Bapat MD1, Emeric F. Bojarski MD2

Background: Transference and countertransference influence any human interaction, including the patient-clinician relationship. Transference is the unconscious redirection of a patient’s feelings, attitudes, desires, often regarding a close personal relationship in their earlier life, onto the clinician (1). Countertransference is the unconscious redirection of a clinician’s feelings, attitudes, and desires about a close personal relationship onto the patient (1). This Fast Fact illustrates the impact of unrecognized transference and countertransference and offers strategies to mitigate their consequences.

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**Case 1:** A 54-year-old male with an opioid use disorder and lung cancer presents for opioid management of cancer-related chest pain which has stabilized since his tumors have regressed in response to cancer treatment. The clinician introduces titrating down his opioids, but the patient responds in anger.

**Transference:** The patient feels stigmatized within the healthcare system (5). He interprets tapering of opioids as a sign the clinician no longer believes his pain reports (5), leading to feelings of helplessness and clinician abandonment. The patient is unconsciously reminded of prior experiences of abandonment within the healthcare system or from family members from whom he was hoping to obtain support. This impacts his willingness to discuss non-opioid analgesic approaches.

**Countertransference:** The clinician is influenced by prior patients with substance use disorder who diverted or misused opioids and left the clinician feeling betrayed and helpless. This reactivates childhood experiences of feeling powerless within his family. To avoid these feelings, the clinician desires to taper the opioids quickly. He severely enforces the terms of the taper and spends less time with the patient, which compromises the clinician’s pain assessment and care.

**Reflection:** Both the patient and clinician act out transferred feelings of alienation and helplessness. A clinician unable to recognize these reactions likely will not engage in a constructive pain assessment and discussion of analgesic management.

**Case 2:** A 32-year-old female who is an internal medicine chief resident is seen in a palliative care clinic to discuss her goals of care regarding progressive glioblastoma. After two months of treatment, she now spends more time in bed, has a poor appetite, and is withdrawn from her family.

**Transference:** As a young physician, she does not want to burden her colleagues nor be perceived as a “needy” patient (6). She minimizes her daily challenges (6) and does not share her feelings regarding her transition from a high-achieving physician to feeling like an “invalid”.

**Countertransference:** The clinician feels that the patient has a high-level of health literacy and would be forthcoming with her concerns (6). The clinician does not want to offend and therefore avoids asking questions the patient will recognize as screening for depression or suicidal ideation.

**Reflection:** Failure to recognize transference phenomena contributes to substandard care by missing opportunities to explore the patient’s feelings of helplessness and to screen for depression.

**Conclusions and next steps:** Whenever a clinician experiences intense emotion during a clinical encounter, be it pleasant or unpleasant, this may signify the presence of transference and/or countertransference (6). A methodical approach to self-reflection, self-monitoring, and coping can help clinicians recognize these feelings more consciously and thereby prevent harmful consequences (4).

1. **Name the feeling:** Transference and countertransference are unconscious processes. Naming the associated feeling(s) enables conscious awareness and thereby more control over behaviors.
2. **Normalize the feeling:** Anger, guilt, helplessness, and betrayal, though distressing, are common in clinical care. Acknowledging and normalizing these feelings can prevent clinicians from over-catastrophizing unwanted emotions triggered during the clinical encounter.
3. **Name the behaviors triggered by the feeling:** After bringing their feelings to conscious awareness, clinicians should reflect on how that emotion impacted their behavior. Doing so could lead to more adaptive responses should the unwanted feelings reemerge. For example, if a clinician notices inner helplessness, he or she could utilize those feelings to screen the patient for emotional distress.
4. **Incorporate routine consultation with trusted colleagues.** Sharing an intense patient interaction with colleagues can decrease isolation and build social support (4). Interdisciplinary teams should create intentional venues where clinicians feel safe to discuss the lived experience of caring for seriously ill patients. Such forums should be distinct from Morbidity and Mortality rounds since they are not intended to act as quality-improvement-themed “fix-it” rounds (7,8). Rather, they should help clinicians safely examine the social, emotional, and personal aspects of care, ideally in the presence of a mental-health professional.

**References:**


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