UNIT NO. 6

AGITATION

Dr Tan Yew Seng

ABSTRACT

Agitation and delirium are commonly encountered symptoms in palliative care. Based on the clinical features, delirium may present in the hypoactive, hyperactive and mixed forms. By reason of the prevalence, the significant distress and symptom burden, as well as the possibility of reversibility, it is vital that the clinician be vigilant in identifying and treating delirium and its symptoms. This article describes how delirium may present, the clinical features, aetiologies and the methods to screen and diagnose delirium. When managing a delirious patient in the palliative care setting, it is necessary to contextualise any investigation and intervention in terms of the disease condition and trajectory, the level of distress and the care preferences and goals of the patient and family. Non-pharmacological management should always be in place though pharmacological treatments also have a definite role in the relief of distressing symptoms of agitation and delirium. Support and education for the patient, family and care providers are integral and continuous aspects of care for the agitated or delirious terminally ill patient.

Keywords:
Agitation; Delirium; Terminal Illness; Palliative Care; Non-Pharmacological Treatment; Pharmacological Treatment

SFP2016; 42(3): 45-52

AGITATION, RESTLESSNESS, CONFUSION AND DELIRIUM

Agitation is a commonly encountered symptom in the palliative care setting. As a result of significant overlap in aetiologies and symptomatology, some have used the term "agitation" synonymously with other descriptors such as restlessness, confusion and delirium. Some clarification of these terms is needed as they have somewhat different meanings and clinical connotations.

Agitation and restlessness generally represent states of psychomotor hyperarousal which are characterised by the inability to relax or be still. Often, they may be accompanied by a compelling need to move or keep doing some activity or task.

Confusion, on the other hand, describes states of impaired cognitive or psychological functions. It is evident that agitation and restlessness can occur without changes in cognition or consciousness. Examples would include patients with anxiety, psychosocial or spiritual distress, and sometimes those with pain and early bladder distension or breathlessness. These patients would not be typically described as having delirium, which tends to be a more specific and better-defined term. Notably, the diagnostic label of delirium also applies to patients with mental impairment from similar pathological processes but do not overtly display the psychomotor hyperactivity that is usually associated with agitation or restlessness.

Therefore, while agitation is the more conspicuous condition that often brings the patient to medical attention, framing the clinical approach as delirium would include those that are particularly precipitated by medical aetiologies, as well as those who suffer from similar processes which, though clinically more subdued, are no less distressed and deserving of medical attention and intervention.

THE SCOPE AND IMPACT OF DELIRIUM

Delirium is probably the most common neuropsychiatric disorder among terminally ill patients. In one review, the prevalence among patients with advanced cancer range from 20 to 88 percent.[1] A significant number of patients are also admitted to palliative care institutions primarily because of delirium. And in the days prior to death, about a third to half of patients with advanced cancer are known to develop delirium.[2–4]

Based on the observed disturbances in psychomotor activity, perception and consciousness levels, delirium may be classified as hypoactive, hyperactive, and mixed. In the palliative care setting, the hypoactive subtype is the most common one, with a prevalence as high as half to over 80 percent in the palliative care setting.[4-6] This form is characterised by psychomotor retardation, lethargy, sedation, and reduced awareness of the surroundings — features which are often mistaken for depression or sedation due to opioids or obtundation in the last days of life.

The hyperactive subtype, which describes the prototypical delirious patient that many are familiar with, actually forms the minority in the palliative care setting (13-46%). Patients with hyperactive delirium present with restlessness, agitation, hypervigilance, hallucinations, and delusions. They are therefore occasionally mistaken as having schizophrenia or dementia. Some studies have suggested that the subtypes may have different causes and responses to treatments. The hypoactive subtype may be associated with hypoxia, metabolic disturbances, and anticholinergic medications, while the hyperactive subtype has been correlated with alcohol and drug withdrawal, drug intoxication, and medication adverse effects. The hypoactive subtype may also have a higher mortality than the hyperactive subtype; the worst prognosis was found in the mixed group.[6,7]

TAN YEW SENG
Senior Consultant,
Palliative Medicine,
Bright Vision Hospital

Despite its prevalence, delirium should not be construed as normative in the dying process. Studies on the experience of delirium have highlighted the distress delirium causes patients, family members, and care staff. Breitbart et al found that 54 percent of patients actually recalled the delirium episode after they had recovered from it, especially if it was less than severe, or when there were hallucinations and delusions.[8] Patients were found to relate to these episodes with significant distress, regardless of whether they had been hyperactive or hypoactive. Some were also afflicted by posttraumatic stress disorder as a result of the hallucinations and delusions experienced during the delirious episode.[9] In one study, two-thirds of family members of delirious patients were reported to be highly distressed, particularly when the patient had agitation or cognitive impairment. Many spouses also mistook that the patient had developed a psychiatric illness, instead of appreciating the medical nature of delirium. Caring for the delirious patient has also been found to be distressing for care providers to similar degrees. In a study of hospice nurses by Johnson et al, the symptom that nurses most frequently considered as difficult to manage was delirium.[10]

Recognising Delirium

As mentioned earlier, cases of delirium have often been missed when changes in the patient are attributed to functional impairment, and behavioral or psychological disturbances. In a study on nurses' recognition of delirium and its symptoms, Inoyue et al found that only about a third of delirious patients and a fifth of observations were identified.[11] The risk factors associated with under-recognition included hypoactive delirium, age 80 years and older, vision impairment, and dementia. Under-recognition increased with the number of risk factors, and patients with 3 or 4 risk factors had a 20-fold risk of under-recognition. Another study indicated that 61 percent of patients with a diagnosis of delirium by a palliative care specialist were missed by the primary referring team.[12]

Table 1: Symptoms and signs of delirium

Altered level of consciousness (wakefulness or arousal)
- Hypervigilant (as in hyperactive delirium) — overly sensitive to environmental stimuli, startled very easily
- Hypovigilant (as in hypoactive delirium) — lethargic (i.e. drowsy, easily aroused); stupor (i.e. difficult to arouse); coma (unarousable)
- Mixed hyper-hypoactive delirium — transitions from one state to another on a continuum from awake and hypervigilant to somnolent or drowsy with fluctuations also in the short time period

Impaired attention
- E.g. difficulty focusing attention — being easily distractible, or having difficulty keeping track of what was being said

Altered sleep-wakefulness cycle regulation
- E.g. excessive daytime sleepiness with insomnia at night

Motor changes (hyperactivity or hypoactivity)
- Unusually increased level of motor activity such as restlessness, picking at bedclothes, tapping fingers or making frequent sudden changes of position
- Unusually decreased level of motor activity such as sluggishness, staring into space, staying in one position for a long time or moving very slowly

Affective changes

Perceptual disturbances
- Hallucinations
- Illusions

Delusions

Cognitive performance failure at formal testing
- Orientation
- Memory
- Visual spatial abilities
- Calculation
- Writing
- Reading

Involuntary movements
- Asterixis
- Myoclonus

The clinical features of delirium are varied and may often be confused with other conditions. The main signs and symptoms are listed in Table 1. Identifying and eliciting them is the first step to diagnosing delirium. Delirium is essentially a clinical diagnosis; laboratory tests are not required for one to diagnose delirium. The DSM-5 lists the diagnostic criteria as follows:[13]

A. A disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness and tends to fluctuate in severity during the course of a day.
C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability or perception).
D. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. because of a drug of abuse or to a medication), or exposure to a toxin, or is because of multiple aetiologies.

Several screening tools have also been found to be useful in identifying delirious patients. A useful screening tool at the bedside is the Confusion Assessment Method,[14] which makes use of 4 key clinical aspects of delirium. Concurrent validation with psychiatric diagnosis revealed sensitivity of 94–100 percent and specificity of 90–95 percent.

Delirium is present if the following are present:
Feature 1-Acute Change or Fluctuation (any symptom) + Feature 2-Inattention
AND
EITHER Feature 3-Disorganised Thinking OR Feature 4-Altered Level of Consciousness

The clinical subtype of hypoactive is frequently misdiagnosed as depression. Table 3 shows some points of differentiation of hypoactive delirium from depression.

Table 2: Confusion Assessment Method (Short)

	Feature	Clinical question
1	Acute onset and fluctuating course	This feature is usually confirmed by comments of a family member or healthcare professional and is shown by positive responses to the following questions: a. Is there evidence of an acute change in mental status from the patient's baseline? b. Does the (abnormal) behaviour fluctuate during the day, tending to come and go, or increase and decrease in severity?
2	Inattention	This feature is shown by a positive response to the following question: • Does the patient have difficulty focusing attention? For example, is the patient easily distracted or having difficulty keeping track of what is being said?
3	Disorganised thinking	This feature is demonstrated by a positive response to the following question: • Is the patient's thinking disorganised or incoherent, as evidenced by rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
4	Altered level of consciousness	This feature is shown by one answer other than "alert" to the following question: • Overall, how would you rate the patient's level of consciousness? o Alert (normal) o Vigilant (hyperalert) o Lethargic (drowsy, easily aroused) o Stuperous (drowsy, difficult to arouse) o Comatose (unarousable)

Table 3: Differentiating hypoactive delirium from depression		
Features	**Hypoactive Delirium**	**Depression**
Disturbance of arousal	Hypoaroused, hypoalert, drowsy	Normal level of arousal, awake, and alert
Cognitive changes	Short-term memory loss, dysnomia, impaired attention, decreased concentration, disorientation, agnosia, aphasia	Mild cognitive deficits may be present, primarily slowing of cognition, subjective problems with concentration
Temporal onset	Abrupt onset	Slow onset
Perceptual disturbances	Present in up to 75% of patients Visual hallucinations most common Misperceptions and illusions are common	Rarely present Only seen in depression with psychotic features Usually auditory hallucinations
Disturbance of thought content	Paranoid delusions often present Usually vague and not systematised	Guilt, worthlessness, hopelessness are common in depression Delusions are rare, but sometimes present in severe depression with psychotic features
Mood symptoms	Patients may appear sad, depressed, irritable Mood is often labile Disinhibition, due to delirium, can lead to expressions of desire for death or suicidal ideation	Patients frequently verbalise sad, depressed mood Suicidal ideation is common and related to thoughts of hopelessness, worthlessness, and guilt or burden
Psychomotor activity	Hypoactive, quiet, withdrawn Slowed	Usually hypoactive, withdrawn, or slowed Occasionally hyperactive and agitated
Family history	Not applicable	Family history of depression common
Past psychiatric history	Previous episodes of delirium may be present	Past episodes of depression not uncommon
Neurological examination	Asterixis, frontal release signs may be elicited	Usually normal examination

From Breitbart W, Alici Y. Agitation and delirium at the end of life. JAMA. 2008;300:2898–910.

Aetiologies of Delirium

The underlying aetiologies of delirium are multiple and some may be difficult to identify without onerous investigations. Nevertheless, there is demonstrable benefit in discovering the aetiology and providing treatment even to patients with poor prognosis. Indeed, among patients with advanced cancer admitted to a palliative care unit, the reversibility rate of delirium can be as high as 49–52 percent when the aetiologic precipitant was explored.[2,7] A careful history and simple investigations may reveal precipitants which are also easily reversible at the bedside, such as constipation and urine retention. A list of potential precipitants of delirium is shown in Table 4. The ones that are particularly notable in this group of patients include fluid and electrolyte imbalances; medications (benzodiazepines, opioids, steroids, and anticholinergics); infections; hepatic or renal failure; hypoxia; and haematological disturbances.[15]

However, in the palliative care setting, it is important to contextualise the identification of delirium in terms of the following:

- Underlying diagnoses and comorbidities as well as their expected trajectories;
- Functional status;
- Past responses to treatments or reversibility;
- Prognosis;
- Goals of care of the patient and family; and
- Level of distress in the patient, family, and care staff.

Any intervention to investigate and treat should only be made when they are consistent with these contextual factors. For example, investigating and treating a suspected metabolic disturbance in a patient who is actively dying from organ failure is not only futile (unlikely to be reversible and therefore produce benefit), it can also add to the patient's suffering and

Table 4: Potential precipitants of delirium	

Drugs
• Opioids
• Hypnotics
• Anticholinergic drugs
  ○ Neuroleptics
  ○ Antihistamines
  ○ Antidepressants
  ○ Antiparkinsonian agents
• NSAIDs
• Corticosteroids
• Psychotropic drugs
• Levodopa
• Substance withdrawal
  ○ Alcohol
  ○ Nicotine
  ○ Corticosteroid
  ○ Anticonvulsants
  ○ Benzodiazepines
	Medical conditions
	• Dehydration
	• Hypoxia
	• Hypercapnia
	• Anaemia
	• Sepsis
	• Increased intracranial pressure (tumour, haemorrhage)
	• Stroke
	• Uncontrolled pain
	• Urinary retention
	• Faecal impaction
	• Chemotherapy
	• Radiotherapy
	• Metabolic disturbances
	  ○ Hypercalcaemia
	  ○ Renal failure
	  ○ Liver failure
	  ○ Hypoglycaemia
	  ○ Hyponatraemia

therefore is unlikely to be in keeping with the care goals at the end-of-life. On the other hand, stopping potentially delirogenic medications or looking out for faecal loading in a moaning and confused patient even when imminently dying, may lead to appropriate and effective interventions. Generally, when it comes to the nature of the aetiologic agent, delirium that is precipitated by medications, electrolyte abnormalities, and infection may be more likely to be reversible. Patients are less likely to improve if they have had previous episodes of delirium or have a delirium related to hypoxic or global metabolic encephalopathy.[7] Clearly, when there is obvious end-stage primary organ failure or when death is imminent, the physiological changes are usually not reversible. In such a setting, the resulting delirium should also be considered irreversible and efforts should be made to maximally focus on reducing symptoms and distress instead of pursuing any attempts to alter the putative causes. Knowing the likelihood that untreated terminal delirium may inevitably end in death, it is therefore not sensible to dally otherwise at the expense of the patient and family's distress.

An approach to management

Understanding the impact of delirium on the patient and family (as well as the members of the care team), the task that needs to be maintained continuously is support and education. Many family members (and some care staff) may not understand the nature of the behavioural changes and may misattribute it to the patient being in physical discomfort,

Table 5: Non-pharmacological management

Non-pharmacological measures for orientation	Non-pharmacological measures in care provision
• Identify yourself each time; don't "test" patient with "who am I?" • Limited staff changes • Ensure patient has the necessary sensory aides (e.g. hearing aids, glasses) • A visible clock or calendar; or family objects (such as family photo); orientation board stating where the patient is • Well-lit (soft lighting) room with familiar objects • Reduced noise stimulation • Avoid over stimulation • Practice sleep hygiene measures • Allow presence of family; use sitters if available	• Minimise the use of catheters, feeding tubes, intravenous lines • Avoid use of physical restraints, unless necessary to prevent self-harm or physical aggression directed at caregivers • Avoid immobility, mobilise where possible • Padding bed rails; lowering the bed • Monitor nutrition • Monitor dehydration and fluid-electrolyte balance • Monitor bowel and bladder functioning • Control pain and other symptoms • Review medication burden • Reschedule medication times to permit patient to rest, especially at night

upset, depressed, fighting or struggling, going mad, just being difficult or being afflicted by supernatural causes. Even when they know, it is difficult to face the "loss" of the personality that they knew — almost as if the person had already "died" even before the impending physical death — or to accept that the last memory of the loved one will be one of disorder and chaos.

In engaging the family, one should also establish the expectations and goals of care, given the context of the patient's illness, the likelihood of reversibility and the current location along the disease trajectory.

Sensible application of the non-pharmacological interventions listed in Table 5 should always be part of the management for all delirious patients.

The next step would be to assess for potential reversible causes by taking a careful history and performing a thorough physical examination. As mentioned earlier, investigations should be considered in the context of the disease condition and goals of care.

Some of the more commonly practiced interventions that may be relevant for terminally ill patients include:

Cause	Treatment
Opioid toxicity →	Switch to another opioid
Sepsis →	Start antibiotics if appropriate
Drugs →	Discontinue drugs that would be aggravating the delirium, eg. tricyclic antidepressants, corticosteriods, benzodiazepines
Dehydration →	If a patient is unable to take in enough oral fluids, then consider hypodermoclysis with normal saline
Hypercalcaemia →	Hydration; bisphosphonates
Hypoxia →	Treat underlying cause and administer O2
Brain metastases →	Cognitive impairment induced by brain metastases may respond, at least temporarily, to corticosteroid therapy.

When deciding on investigations and interventions to reverse the causes of delirium with the patient and family, it is important to be explicit about the duration and extent of the investigation and treatment, the expected outcomes and how all these fit in with the goals of care. This would help frame the boundaries of this line of management so that such measures do not distract from the critical tasks of relieving the patient from distress and discomfort.

Regardless of the intention to proceed with a time-limited trial to find or reverse the cause, when the symptoms are inadequately addressed by non-pharmacological measures, pharmacological interventions should be considered.

First-line pharmacological treatment/when delirium is reversible

In the setting where delirium may be reversible, or where sedation is not consistent with the goals of care, the treatment should be focussed on relief of the symptoms of delirium, especially agitation, without undue sedation.

There is generally limited data from double-blind, randomised control trials to guide the pharmacological treatment of delirium. But based on the available evidence and current practice, it is widely recognised that "typical" antipsychotic medications such as haloperidol, have a definite role in controlling the symptoms of delirium.[1,6,15–17]

Haloperidol is the usual first-line medication for delirium. It is known to be efficacious in reducing agitation, relatively less sedative, can be given in different routes, and lack active metabolites. As such, it is useful for patients with potentially reversible delirium, for whom we expect improvement in cognitive and conscious statuses.

Initial dosing may start at 1-2mg (0.5mg for the elderly), and be titrated to relieve distressing symptoms. One method of rapidly titrating to effectiveness is based on the administration of breakthrough doses by the time the plasma concentration is maximum (tCmax).[18] For haloperidol, this would be every 60 minutes by the oral route, 30 minutes by subcutaneous and 15 minutes via intravenous route. The maintenance dose range is typically 0.5–2mg 2 to 12 hourly. When the patient refuses oral medications, bolus subcutaneous haloperidol 1–2mg may be administered. When the delirium is controlled or reversed, there should be a deliberate attempt to reduce and discontinue the treatment.

Caution should however be taken in prescribing antipsychotic medications, especially in the elderly. The risk of extrapyramidal side effects should be assessed, and titrations should take into account the findings of such side effects. Keeping with the lowest possible dose to get a positive effect is important as extrapyramidal side effects tend to occur at doses >4.5mg/day.[15] In addition, screening for prolonged QTc interval and electrolyte imbalance should also be considered in those with longer prognosis or those at risk for such disturbances, although the data on the impact of short-term use in this patient population.

Presently, the role of "atypical" antipsychotic medications (olanzapine, risperidone and quetiapine) as alternatives to haloperidol in this particular setting has not been well established as they have not been shown to offer increased efficacy and they tend also to be more sedating.

Second-line pharmacological treatment/when delirium is irreversible

In the event that agitation is still not controlled with first-line treatment with haloperidol, or when a more sedating approach is consistent with the care goals (e.g. for patients who are agitated and close to the end of life), benzodiazepines may be considered. The titration may involve lorazepam 0.5mg–1mg sublingually or orally, and repeated at the tCmax (60 minutes PO; 30 minutes SC; 15 minutes IV), subsequently

maintaining at twice-daily dosing.[18] In patients who refuse oral medication, bolus subcutaneous midazolam 1–2mg may be administered Q30mins.

The common side-effects of benzodiazepines include sedation, lethargy, ataxia, falls, weakness, impaired concentration and motor coordination and anterograde amnesia. Prolonged use may also result in withdrawal seizures and physical and psychological dependence. As such, benzodiazepines may not be appropriate when the clinical intent is to find the cause or to reverse delirium. It is also known in practice that benzodiazepines may paradoxically result in more agitation especially when used alone and in sub-sedative doses. As such, a commonly employed strategy for the acute management of very severe agitation is to combine an antipsychotic with a short-acting benzodiazepine.

An alternative to benzodiazepines is to use antipsychotics that are more sedative. For example, the "typical" antipsychotic that has some evidence in palliative care is chlorpromazine. Atypical antipsychotics may also be considered. Table 6 lists the various antipsychotic medications and their doses.

When a more sedating approach is needed to relieve agitation

The need to support and educate the family and staff becomes even more critical when a more sedating approach is

Table 6: Pharmacological management

Medication	Dose range	Route	Adverse effect	Comments
Typical antipsychotics				
Haloperidol	0.5–2 mg every 2 to 12 h	• Oral • Subcutaneous • Intravenous	• Extrapyramidal effects can occur with doses 4.5 mg/d • Monitor QTc interval on ECG	• Remains first-line therapy for terminal delirium • May add lorazepam (0.5–1 mg every 2 to 4 h) for agitated patients
Chlorpromazine	12.5–50 mg every 4–6 h	• Oral • Per rectal	• More sedating and anticholinergic compared with haloperidol • Monitor blood pressure for hypotension	• Preferred in agitated patients due to its sedative effect
Atypical antipsychotics				
Olanzapine	2.5–5 mg every 12–24 h	• PO	• Sedation is the main dose-limiting effect in short-term use	Older age, preexisting dementia, and hypoactive subtype of delirium are associated with poor response
Risperidone	0.25–1 mg every 12–24 h	• PO	• Extrapyramidal adverse effects can occur with doses 6 mg/d • Orthostatic hypotension	Clinical experience suggests better results in patients with hypoactive delirium
Quetiapine	12.5–100 mg every 12–24 h	• PO	• Sedation • orthostatic hypotension	Preferred in patients with Parkinson disease or Lewy body dementia due to its lower risk of extrapyramidal adverse effects

Modified from Breitbart W, Alici Y. Agitation and delirium at the end of life. JAMA. 2008;300:2898–910.

administered. In some patients, severe agitation may occur as a terminal event and the symptoms directly precede death. Sedation may therefore appear to be the intervening event that resulted in death. This highlights the need to carefully explain about the patient's condition, treatment goals as well as the patient's location in the dying trajectory. It is similarly vital to clarify that unless there is a situation where the patient may be a danger to himself or herself, or to others, the primary aim of the treatment is NOT to sedate the patient. Rather, the goal is still to bring about the relief of delirium symptoms, such as agitation, hallucinations, and confusion, although in this clinical situation, some sedation may be unavoidable in the treatment to bring relief to the patient. It is important to dispel the notion that such treatments constitute palliative sedation (which should be done with specialist input when the symptoms become intractable), or worse, euthanasia.

REFERENCES

1. Centeno C, Sanz A, Bruera E. Delirium in advanced cancer patients. Palliat Med. 2004;18:184–94.
2. Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. Arch Intern Med. 2000;160:786–94.
3. Gagnon P, Charbonneau C, Allard P, DeSerres M. Delirium in terminal cancer: a prospective study using daily screening, early diagnosis, and continuous monitoring. J Pain Symptom Manage. 2000;19:412–26.
4. Spiller JA, Keen JC. Hypoactive delirium: assessing the extent of the problem for inpatient specialist palliative care. Palliat Med. 2006;20:17–23.
5. Leonard M, Donnelly S, Conroy M, Trzepacz P, Meagher DJ. Phenomenological and neuropsychological profile across motor variants of delirium in a palliative care unit. J Neuropsychiatry Clin Neurosci. 2011; 23:180–8.
6. Stagno D, Gibson C, Breitbart W. The delirium subtypes: a review of prevalence, phenomenology, pathophysiology, and treatment response. Palliat Support Care. 2004; 2:171–9.
7. Morita T, Tsunoda J, Inoue S, Chihara S. Underlying pathologies and their associations with clinical features in terminal delirium of cancer patients. J Pain Symptom Management. 2001; 22:997–1006.
8. Breitbart W, Gibson C, Tremblay A. The delirium experience: delirium recall and delirium related distress in hospitalized patients with cancer, their spouses /caregivers, and their nurses. Psychosomatics. 2002;43:183–94.
9. DiMartini A, Dew MA, Kormos R, McCurry K, Fontes P. Posttraumatic stress disorder caused by hallucinations and delusions experienced in delirium. Psychosomatics. 2007;48:436–9.
10. Johnson DC, Kassner CT, Houser J, Kutner JS. Barriers to effective symptom management in hospice. J Pain Symptom Manage. 2005;29:69–79.
11. Inouye SK, Foreman MD, Mion LC, Katz KH, Cooney LM, Jr. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. Arch Intern Med. 2001;161:2467–73.
12. De la Cruz M, Fan J, Yennu R, Tanco K, Shin SH et al. The frequency of missed delirium in patients referred to palliative care in a comprehensive cancer center. Support Care Cancer. 2015:23:2427–33.
13. Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5). Arlington County, VA: American Psychiatric Association; 2013.
14. Inouye S, van Dyck CH, Alessi CA, Balkin S, Siegal A, Horwitz RI. Clarifying confusion: the confusion assessment method. Ann Intern Med. 1990;113:941–8.
15. Brietbart W, Alici Y. Agitation and delirium at the end of life. JAMA. 2008;300:2898–910.
16. Moyer DD. Terminal delirium in geriatric patients with cancer at end of life. Am J Hosp Palliat Med. 2011;28:44–51.
17. Bush SH, Leonard MM, Agar M, Spiller JA, Hosie A, Wright DK, et al. End of life delirium: issues regarding recognition, optimal management and the role of sedation in the dying phase. J Pain Symptom Manage. 2014;48:215–30.
18. Irwin SA, Pirrello RD, Hirst JM, Buckholz GT, Ferris FD. Clarifying delirium management: practical, evidence-based, expert recommendations for clinical practice. J Palliat Med. 2013:16:423–35.

LEARNING POINTS

- **Delirium is commonly encountered in palliative care and contributes significantly to the burden of the patient, family and the care team.**
- **Delirium may be missed, especially the common hypoactive subtype. There is a need to actively screen and diagnose delirium.**
- **The attempt to find and treat the causes of delirium should be considered in the context of the underlying diagnoses and comorbidities as well as their expected trajectories, functional status, past responses to treatments or reversibility, prognosis, goals of care of the patient and family, and the levels of distress in the patient, family and care staff.**
- **Non-pharmacological management is relevant in all stages of care for the delirious patient.**
- **Haloperidol can be safely and rapidly titrated to achieve symptom relief; use only the smallest dose to bring relief.**
- **Supporting and educating the patient, family and care team should be ongoing aspects of care in the management of the agitated or delirious patient in the palliative care setting.**