PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #1
DIAGNOSIS AND TREATMENT OF TERMINAL DELIRIUM
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Background Some degree of loss of cognitive function occurs in most patients in the week or two before death (1,2). 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 additional discussion of pharmacological treatments of delirium.

Delirium Terminology: The term "confusion" is not an accurate descriptive term—it can mean anything from delirium, dementia, psychosis, obtundation, or encephalopathy. Delirium can be characterized by a *hyperactive/agitated* state, a *hypoactive* state, or a mixture of the two. The hallmark of delirium is an acute change in mentation and attention with either disorganized thinking, easy distractibility, or a fluctuating level of consciousness. It is often accompanied by perception disturbances with illusions, delusions or hallucinations. "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 (3,4).

Delirium Assessment (1-5): Patients need a focused assessment, including orientation to person, place, time, medical situation, and treatment options to better characterize confusion. Clinicians should use one of several validated delirium assessment tools to help quantify and document cognitive function. See *Fast Fact* #160. Prevention and identifying the medical cause of delirium are usually the most effective means of reducing the morbidity from delirium. The cause of delirium is usually multifactorial. In the hospital setting common culprits include infections (urinary, lung, gastrointestinal, etc) and medication, especially anti-cholinergics (e.g. anti-secretion drugs like scopolamine, anti-histamines, and tricyclic anti-depressants), sedative-hypnotics (e.g. benzodiazepines), opioids, and dopamine agonists (e.g. levo-dopa or ropinorole) which may cause hallucinations and delusions. Metabolic derangements (abnormal sodium, elevated calcium, or low glucose or oxygen); CNS pathology, drug/alcohol withdrawal, uncontrolled pain, immobility, dehydration, and lack of sleep are other common contributors. The degree of clinical work-up to identify these causes of delirium is determined by understanding the disease trajectory and the overall *goals of care* (see *Fast Fact* #65).

Non-Pharmacologic Treatments: These are the mainstay in delirium management and should be utilized regardless of the type of delirium (1-6).

- Alter the sensory stimulation in the environment as needed: for example, it may be best to turn off the television if the sounds are distracting or confusing to the patient.
- Ask relatives/friends/familiar people to visit and reorient the patient to the medical situation.
- Perform frequent reminders of time/place/medical setting.
- The ABCDE (Awakening/Breathing Coordination, Delirium monitoring and Early exercise/mobility) bundle has been used to prevent and manage delirium in ICU settings (6).

Pharmacologic Treatments: There is no clear consensus about the role of medications to treat delirium. Antipsychotic medications have long been used to treat delirium. An early, low-quality study in HIV patients with delirium suggested haloperidol, but not lorazepam was superior than placebo at managing delirium symptoms (7). However, subsequent research has not clearly shown that antipsychotics shorten the duration of delirium or reduce the agitation and morbidity associated with it (8-11). Interpreting the research is challenging, given that there are multiple different antipsychotic agents available, a wide range of doses, various patient populations, different outcomes of interest, and unresolved questions about whether pharmacologic treatment should differ based on a hyperactive vs hypoactive delirium type. The following bullet points encapsulate the challenges in interpreting the evidence with regards to the pharmacologic treatment of delirium.

- A placebo-controlled trial (9) of inpatients in hospice or palliative care unit settings and another placebo-controlled study (10) of patients in an intensive care unit, found no significant difference with

either ziprasidone or risperidone (second generation antipsychotics) or haloperidol (a first-generation antipsychotic) in alleviating delirium symptoms, duration, or severity.

- A randomized controlled trial evaluating the effect of lorazepam with scheduled haloperidol vs scheduled haloperidol alone for agitated delirium at the end of life (11) found that the addition of lorazepam significantly *reduced agitation* at 8 hours compared to haloperidol alone.
- Despite this, two areas of consensus seem to remain.
  a. Hyperactive patients who are a danger to themselves or others (pulling out lines or tubes, striking caregivers, etc) despite behavioral and environmental modification, should be treated pharmacologically. Notably, there is no evidence-based drug approach to this, and reasonable treatment options could include antipsychotics (especially if symptomatology includes hallucinations or delusions), or sedatives such as benzodiazepines or dexmedetomidine if prognosis is felt to be short.
  b. Patients with terminal delirium should be treated pharmacologically if it is the judgment of their caregivers that the delirium is a source of suffering. In these circumstances, it is important to consider the therapeutic goal in the context of the patient's prognosis. If sedation is acceptable, or even the goal in a dying patient, a sedating dose of a benzodiazepine or a sedating antipsychotic such as chlorpromazine is probably a prudent approach even though such medications are known to cloud cognitive clarity.

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Version History: Originally edited by David E Weissman MD. 2nd Edition published July 2005; 3rd Edition May 2015. 4th edition edited by Elizabeth Bukowy DO to reflect changes in the evidence.
Conflicts of Interest: None reported