

## Diagnosis and Management of Delirium at the End of Life

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Delirium is a common and distressing symptom that constitutes a significant challenge for end-of-life care. However, reliable techniques are available for the diagnosis of delirium, and effective therapies exist as well. This consensus paper uses a case-based format that begins with an overview of the definition and presentation of delirium. Next, strategies for diagnosis are suggested,

with attention to the unique challenges that clinicians face in pursuing a diagnostic work-up for patients near the end of life. The paper concludes with a review of therapeutic options.

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Patients near the end of life may face a variety of distressing symptoms. Of these, perhaps none is as detrimental to quality of life and is as difficult to diagnose and manage as delirium. Delirium is characterized by a disturbance of consciousness, cognition, and perception, with a course that may wax and wane over a period of hours (1).

Delirium occurs in 28% to 83% of patients near the end of life, depending on the population studied and the criteria used (2–6). This syndrome is a challenge for physicians for several reasons. First, it may frighten patients and may cause as much distress as do pain and other symptoms. Second, families may regret the premature separation from a patient who can no longer communicate. Third, delirium may also be a predictor of approaching death for some patients (7). Fourth, delirium robs patients of valuable time and curtails opportunities to make final choices and plans. For all of these reasons, delirium can be a daunting obstacle to good end-of-life care if not addressed appropriately.

The skills required for diagnosing and managing delirium at the end of life can be a part of every clinician's repertoire. Prompt recognition and appropriate treatment of delirium can improve patient comfort, optimize quality of life, and enhance the leave-taking process for the patient and family. In this paper, we present strategies for the diagnosis and management of delirium, beginning with a description of a patient with mental

status changes. We then describe steps for diagnosing delirium and evaluating potential causes, and conclude by discussing strategies for prevention and treatment.

### DIAGNOSIS OF MENTAL STATUS CHANGES

In evaluating mental status changes near the end of life, as with other clinical decisions, the patient's and family's goals for care are of central importance. Some patients may wish to preserve their ability to communicate, while others focus on comfort, perhaps at the expense of alertness. For the former patients, diagnostic evaluation and treatment would be appropriate, but for the latter, any diagnostic or therapeutic interventions will be more circumscribed.

*Mrs. Ghoduy is a 42-year-old woman with ovarian cancer metastatic to the peritoneum, liver, and lung. She has become increasingly agitated over the past week, and her husband, daughter, and nurse believe that these changes are due to pain. However, increases in her opioid dose have produced unacceptable sedation, and she is admitted for evaluation. Her physician, Dr. Marks, finds her to be somnolent and unresponsive to direct questioning. He is unable to assess her pain or other symptoms.*

Often delirium is obvious, but up to half of delirium episodes are not noted by clinicians (8, 9). Delirium may be missed because the constellation of features that define it—acute onset, inattention, altered level of consciousness, and cognitive impairment—are not al-

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ways readily apparent. Indeed, their detection often requires a careful history and bedside evaluation.

To diagnose delirium, clinicians must first have an accurate picture of the patient's baseline status. Therefore, Dr. Marks can first inquire about Mrs. Ghoduay's mental status at several points in the past. This may require tenacious detective work and questioning of several family members. For instance, Dr. Marks could ask for specific examples of Mrs. Ghoduay's interactions with friends and family a day ago, or a week ago. He might also assess her ability to participate in conversations, or to recognize family. This line of questioning can be valuable in identifying the typical fluctuating course of mental status changes that is seen in delirium.

*Further questioning confirms that Mrs. Ghoduay's decline in mental status began approximately 1 week before admission. Since then, her mental status has fluctuated dramatically, with periods of lucidity punctuated by episodes of somnolence and agitation. During that period, her morphine dosage was increased from 100 mg/24 hours to approximately 400 mg/24 hours, including rescue doses. Her oral intake has been limited. On the basis of this information, Dr. Marks believes that delirium is a possible cause of her somnolence.*

### EVALUATING POSSIBLE DELIRIUM

Delirium is a clinical diagnosis made at the bedside. To determine whether Mrs. Ghoduay's mental status changes are due to delirium, Dr. Marks will need to rely almost entirely on clinical skills to identify the two features of delirium: cognitive impairment and deficits in attention. Of the tests to assess cognitive function, the Mini-Mental State Examination (MMSE) (10) has the advantage of general availability and familiarity to most clinicians and, in most settings, is recommended as the test of choice. To assess attention, the MMSE's immediate repetition of three objects and a backwards-spelled word ("d-l-r-o-w") items can be very useful. Corroboration can be sought in the digit span test, in which inability to repeat at least five numbers forward without errors indicates inattention (11).

These tests of cognition and attention support a diagnosis of delirium, but they are not themselves diagnostic. In addition, Dr. Marks can also use one of several instruments that have been developed to distinguish delirium from other causes of altered mental status (Table 1). The most widely used include the Confusion

Assessment Method (Table 2) (12), which systematizes bedside observations; the Memorial Delirium Assessment Scale (13); the Delirium Rating Scale (DRS) (14, 15); and the Delirium Symptom Interview (DSI) (16). Each has its own strengths and limitations, and the choice among them depends on the goals of use (Table 1).

*Mrs. Ghoduay's mental status seems to improve shortly after admission. Her MMSE score is 16, but she cannot perform the serial sevens task or spell "world" backwards. She is able to repeat only two digits in the digit span test on several occasions. Throughout the interview, Mrs. Ghoduay is easily distracted and often appears to drift off to sleep. Later the same day, she can be aroused only with difficulty, and attempts to repeat the same tests are unsuccessful.*

### CHARACTERIZING DELIRIUM AND IDENTIFYING CAUSES

On the basis of the results of formal testing and Mrs. Ghoduay's fluctuating clinical course, Dr. Marks believes that Mrs. Ghoduay's mental changes are most likely due to delirium. Delirium may present as one of three major types: hyperactive, hypoactive, or mixed. Hyperactive or "agitated" delirium is characterized by agitation and hallucinations and is often readily apparent. In contrast, hypoactive or "quiet" delirium presents as a decreased level of consciousness with somnolence and can be mistaken for sedation due to opioids or obtundation in the last days of life. Finally, delirium of mixed type, alternating between agitated and quiet forms, may also be difficult to recognize. Of these, Mrs. Ghoduay's presentation is most consistent with quiet delirium.

Even when delirium is recognized, a cause is often elusive. Although delirium can be due to a single cause, a multifactorial etiology is most common in the palliative care setting (4). Therefore, once delirium is diagnosed, possible causes should be sought in the medication history, physical examination, and laboratory tests. The clinician's task is to identify potential causes that are easily treatable and offer the best chance of improved quality of life (4, 17) (Table 3).

### Medication History

Available data suggest that medication effects are the most common cause of delirium both in the general patient population (8) and in patients near the end of life (4). Several medications commonly used in the pal-

**Table 1. Available Instruments Used To Evaluate Delirium\***

Description	Domains	Validation	Reference Standard	Reliability	Feasibility
<p>C</p> <p>A (12)</p> <p>B</p> <p>CA</p> <p>B</p> <p>(14, 15)</p> <p>10-</p> <p>0-32,</p> <p>C</p> <p>(16)</p> <p>32.8( )-332.8( )</p> <p>76 3</p>	<p>1. A</p> <p>2. A</p> <p>3. A</p> <p>4. A</p> <p>5. A</p> <p>6. A</p> <p>7. A</p> <p>8. A</p> <p>9. A</p> <p>1. C</p> <p>2. C</p> <p>3. C</p> <p>4. C</p> <p>5. C</p> <p>6. C</p> <p>7. C</p> <p>8. C</p>	<p>= 0.94 - 1.0</p> <p>(26)</p> <p>= 0.90 -</p> <p>0.95 (30</p> <p>)</p> <p>C</p> <p>A</p> <p>B</p> <p>(n = 20)</p> <p>3</p> <p>(n = 9),</p> <p>(n = 9),</p> <p>(n = 9)</p> <p>C</p> <p>A</p> <p>857</p> <p>8</p>	<p>A</p> <p>C</p>	<p>: κ = 1.0</p> <p>= 0.97</p>	<p>0-15</p>

liative care setting deserve attention (Table 3). Opioids can cause both substantial alterations in mental status (18) and more subtle, temporary changes in cognition and attention (19, 20). These changes may become pronounced in the setting of renal failure, particularly with opioids, such as morphine, that have active metabolites

(21, 22). Meperidine is associated with a higher risk for delirium because its active metabolite, normeperidine, is cleared slowly (23). Other than meperidine, few data suggest that one opioid is associated a higher incidence of delirium than others.

A variety of other medications might also contribute



may be a common cause of delirium near the end of life (4). However, the treatment of volume depletion need not be automatic. Fluid replacement using a nasogastric tube or intravenous catheter may impose additional burdens on the patient and his or her family. Other, less invasive interventions, such as hypodermoclysis (30), pose fewer burdens. Nevertheless, all of these may prolong the patient's life, which may not be consistent with his or her goals.

restraints, or continuous intravenous infusions. All of these factors are potentially modifiable and can be considered not only for prevention but also as potential targets for the nonpharmacologic treatment of delirium (Table 4). These interventions will need to be adapted to the needs of patients near the end of life to make them consistent with patients' goals for care; they will not be appropriate for all patients. However, because these interventions can be initiated by family members in the home, they may have a particularly valuable place in end-of-life care by allowing families to take an active role in maintaining the patient's comfort.

#### Pharmacologic Treatment

*Several nonpharmacologic interventions are initiated, including careful attention to the lighting in Mrs. Ghoduay's room and orientation cues. In addition, Dr. Marks recommends initiating a trial of intravenous haloperidol, and he explains the efficacy of this drug as a neuroleptic agent. However, Mrs. Ghoduay's family is reluctant to agree to this plan, arguing that she is not "crazy." The housestaff caring for her also object. They are concerned that haloperidol is not effective for a quiet delirium such as Mrs. Ghoduay's and that, if anything, it will only make her more sedated.*

In most cases, the goal of pharmacologic treatment of delirium should be to bring patients closer to their baseline mental state, not to sedate them or to suppress agitation. Several agents are available (

#### Prevention and Nonpharmacologic Treatment

All patients near the end of life can be considered at high risk for delirium, and clinicians should consider preventive strategies that have been proven effective in other settings (32). For instance, protocols designed to encourage cognitive activity and to help patients orient to place, time, and environment can be useful. Sleep can be improved by a combination of nonpharmacologic interventions, such as relaxation and breathing techniques; quiet music at bedtime; and reductions in environmental light, noise, and other factors that may awaken the patient at night. These strategies also minimize the need for sedative medications, which are a significant cause of delirium (17, 25).

Immobility can be ameliorated in some patients by encouraging time out of bed and active range-of-motion exercises, as well as by limiting the use of catheters,

lirium in patients with AIDS (33). Haloperidol also has the advantages of a fairly wide therapeutic window, availability in both parenteral and oral preparations, and

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