bed. It has sedating, antiemetic, and anxiolytic properties with few drug interactions. Its side effect of weight gain may be beneficial for seriously ill patients; it is available in orally disintegrating tablets.

For patients with a prognosis of several months or longer, SSRIs, including fluoxetine, sertraline, paroxetine, citalopram, escitalopram, and fluvoxamine, and serotonin-noradrenaline reuptake inhibitors such as venlafaxine, are the preferred treatment because of their efficacy and comparatively few side effects. Because low doses of these medications may be effective for seriously ill patients, one should use half the usual starting dose for healthy adults. The starting dose for fluoxetine is 10 mg once a day. In most cases, once-a-day dosing is possible. The choice of which SSRI to use should be driven by (1) the patient's past success or failure with the specific medication, (2) the most favorable side effect profile for that specific agent, and (3) the time it takes to reach steady-state drug levels. For instance, for a patient in whom fatigue is a major symptom, a more activating SSRI (fluoxetine) would be appropriate. For a patient in whom anxiety and sleeplessness are major symptoms, a more sedating SSRI (paroxetine) would be appropriate.

Atypical antidepressants are recommended only in selected circumstances, usually with the assistance of a specialty consultation. Trazodone can be an effective antidepressant but is sedating and can cause orthostatic hypotension and, rarely, priapism. Therefore, it should be used only when a sedating effect is desired and is often used for patients with insomnia, at a dose starting at 25 mg. In addition to its antidepressant effects, bupropion is energizing, making it useful for depressed patients who experience fatigue. However, it can cause seizures, preventing its use for patients with a risk of CNS neoplasms or terminal delirium. Finally, alprazolam, a benzodiazepine, starting at 0.25–1.0 mg tid, can be effective in seriously ill patients who have a combination of anxiety and depression. Although it is potent and works quickly, it has many drug interactions and may cause delirium, especially among very ill patients, because of its strong binding to the benzodiazepine–γ-aminobutyric acid (GABA) receptor complex.

Unless used as adjuvants for the treatment of pain, tricyclic antidepressants are not recommended. Similarly, monoamine oxidase (MAO) inhibitors are not recommended because of their side effects and dangerous drug interactions.

Delirium **(See Chap. 34)** • ***FREQUENCY*** In the weeks or months before death, delirium is uncommon, although it may be significantly underdiagnosed. However, delirium becomes relatively common in the hours and days immediately before death. Up to 85% of patients dying from cancer may experience terminal delirium.

ETIOLOGY Delirium is a global cerebral dysfunction characterized by alterations in cognition and consciousness. It frequently is preceded by anxiety, changes in sleep patterns (especially reversal of day and night), and decreased attention. In contrast to dementia, delirium has an acute onset, is characterized by fluctuating consciousness and inattention, and is reversible, although reversibility may be more theoretical than real for patients near death. Delirium may occur in a patient with dementia; indeed, patients with dementia are more vulnerable to delirium.

Causes of delirium include metabolic encephalopathy arising from liver or renal failure, hypoxemia, or infection; electrolyte imbalances such as hypercalcemia; paraneoplastic syndromes; dehydration; and primary brain tumors, brain metastases, or leptomeningeal spread of tumor. Commonly, among dying patients, delirium can be caused by side effects of treatments, including radiation for brain metastases, and medications, including opioids, glucocorticoids, anticholinergic drugs, antihistamines, antiemetics, benzodiazepines, and chemotherapeutic agents. The etiology may be multifactorial; e.g., dehydration may exacerbate opioid-induced delirium.

ASSESSMENT Delirium should be recognized in any terminally ill patient with new onset of disorientation, impaired cognition, somnolence, fluctuating levels of consciousness, or delusions with or without agitation. Delirium must be distinguished from acute anxiety and depression as well as dementia. The central distinguishing feature is altered consciousness, which usually is not noted in anxiety, depression, and dementia. Although "hyperactive" delirium characterized by overt confusion and agitation is probably more common, patients also should be assessed for "hypoactive" delirium characterized by sleep-wake reversal and decreased alertness.

In some cases, use of formal assessment tools such as the Mini-Mental Status Examination (which does not distinguish delirium from dementia) and the Delirium Rating Scale (which does distinguish delirium from dementia) may be helpful in distinguishing delirium from other processes. The patient's list of medications must be evaluated carefully. Nonetheless, a reversible etiologic factor for delirium is found in fewer than half of terminally ill patients. Because most terminally ill patients experiencing delirium will be very close to death and may be at home, extensive diagnostic evaluations such as lumbar punctures and neuroradiologic examinations are usually inappropriate.

INTERVENTIONS One of the most important objectives of terminal care is to provide terminally ill patients the lucidity to say goodbye to the people they love. Delirium, especially with agitation during the final days, is distressing to family and caregivers. A strong determinant of bereavement difficulties is witnessing a difficult death. Thus, terminal delirium should be treated aggressively.

At the first sign of delirium, such as day-night reversal with slight changes in mentation, the physician should let the family members know that it is time to be sure that everything they want to say has been said. The family should be informed that delirium is common just before death.

If medications are suspected of being a cause of the delirium, unnecessary agents should be discontinued. Other potentially reversible causes, such as constipation, urinary retention, and metabolic abnormalities, should be treated. Supportive measures aimed at providing a familiar environment should be instituted, including restricting visits only to individuals with whom the patient is familiar and eliminating new experiences; orienting the patient, if possible, by providing a clock and calendar; and gently correcting the patient's hallucinations or cognitive mistakes.

Pharmacologic management focuses on the use of neuroleptics and, in the extreme, anesthetics **(Table 10-7)**. Haloperidol remains first-line therapy. Usually, patients can be controlled with a low dose (1–3 mg/d), usually given every 6 h, although some may require as much as 20 mg/d. It can be administered PO, SC, or IV. IM injections should not be used, except when this is the only way to get a patient under control. Newer atypical neuroleptics, such as olanzapine, risperidone, and quetiapine, have shown significant effectiveness in completely resolving delirium in cancer patients. These drugs also have fewer side effects than haloperidol, along with other beneficial effects for terminally ill patients, including antinausea, antianxiety, and weight gain. They are useful for patients with longer anticipated life expectancy because they are less likely to cause dysphoria and have a lower risk of dystonic reactions. Also, because they are metabolized through multiple pathways, they can be used in patients with hepatic and renal

TABLE 10-7 MEDICATIONS FOR THE MANAGEMENT OF DELIRIUM

Interventions	Dose
Neuroleptics	
Haloperidol	0.5–5 mg q2–12h, PO/IV/SC/IM
Thioridazine	10–75 mg q4–8h, PO
Chlorpromazine	12.5–50 mg q4–12h, PO/IV/IM
Atypical neuroleptics	
Olanzapine	2.5–5 mg qd or bid, PO
Risperidone	1–3 mg q12h, PO
Quetiapine	50 mg qd, PO
Anxiolytics	
Lorazepam	0.5–2 mg q1–4h, PO/IV/IM
Midazolam	1–5 mg/h continuous infusion, IV/SC
Anesthetics	
Propofol	0.3–2.0 mg/h continuous infusion, IV