Delirium in Older Adults With Cancer: Implications for Practice and Research

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This article has been chosen as being particularly suitable for reading and discussion in a Journal Club format. The following questions are posed to stimulate thoughtful critique and exchange of opinions, possibly leading to changes on your unit. Formulate your answers as you read the article.

1. Is this article research-based? Can we assess the level of evidence being presented?
2. What percentage of our patients are older adults? Do we see delirium or confusion in our patients more or less frequently than the literature suggests? Why or why not?
3. How often is confusion or delirium in our patients unanticipated?
4. What are the most common etiologies in our patient population?
5. Is a standing protocol in place to treat a patient who is or becomes confused?
6. What measures can we institute to orient and protect patients at risk for confusion?

At the end of the session, take time to recap the discussion and make plans to follow through with suggested strategies.

Purpose/Objectives: To provide a comprehensive review of the literature and existing evidence-based findings on delirium in older adults with cancer.

Data Sources: Published articles, guidelines, and textbooks.

Data Synthesis: Although delirium generally is recognized as a common geriatric syndrome, a paucity of empirical evidence exists to guide early recognition and treatment of this sequelae of cancer and its treatment in older adults. Delirium probably is more prevalent than citations note because the phenomenon is under-recognized in clinical practice across varied settings of cancer care.

Conclusions: Extensive research is needed to formulate clinical guidelines to manage delirium. A focus on delirium in acute care and at the end of life precludes identification of this symptom in ambulatory care, where most cancer therapies are used. Particular emphasis should address the early recognition of prodromal signs of delirium to reduce symptom severity.

Implications for Nursing: Ongoing assessment opportunities and close proximity to patients' treatment experiences foster oncology nurses' mastery of this common exemplar of altered cognition in older adults with cancer. Increasing awareness of and knowledge delineating characteristics of delirium in older patients with cancer can promote early recognition, optimum treatment, and minimization of untoward consequences associated with the historically ignored example of symptom distress.

Key Points . . .

- Delirium is a common symptom yet is under-recognized in older adults with cancer.
- It is correlated with numerous preventable adverse effects.
- Early recognition and reduction of symptom intensity are highly amenable to nursing management.

Of all the symptoms my mother experienced during cancer therapy, her confusion was by far the worst. Maybe that was because no one seemed to know what to do about it. She had drugs for her pain and nausea and to keep up her blood counts, but everyone seemed clueless about how to manage her confusion. It really hit me when my daughter came home from college to see my mother. My mother got all mixed up and thought my daughter was my older sister. My daughter was crushed and frightened. She had never seen her grandmother like this. At that point, we all worried, would we ever get my quick-witted, articulate, and loving mother back again?

—Personal communication

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Change in mental status resulting in delirium is a common yet ill-defined and frequently unrecognized symptom in cancer care. Although not accorded equal prominence with other symptoms such as pain, immunosuppression, and gastrointestinal disturbance, delirium is an important problem that requires sound nursing assessment and proficient intervention. Of note is that in the field of psychiatry, delirium is considered a medical emergency (Antai-Otong, 2003; Lawlor & Bruera, 2002).

Oncology nurses must become experts in recognizing and minimizing delirium for many reasons. Delirium is associated with physiologic sequelae such as falls, fractures, skin breakdown, and unanticipated catheter and tube withdrawal; it also may interfere with hydration, nutrition, medication administration, and completion of courses of radiotherapy. It may lengthen hospital stays and subsequently increase costs of care (including admission to the intensive care unit) and risks of problems associated with prolonged hospitalization such as infections and thromboemboli. Delirium often is the impetus for the use of restraints. It influences patients' ability to recognize and articulate symptoms, which ultimately affects their quality of survival. It has an impact on patients' understanding of their cancer and influences their ability to make decisions on their own behalf. Delirium causes emotional distress because it may frighten patients or cause embarrassment and frustration in patients partially aware of their impaired cognition. It affects family coping and grief as patients' uncustomary behavior is observed and endured. Delirium creates a communication barrier between patients and families; it adds strain to a family dynamic already marked by stress and anticipatory loss and may preclude a family's ability to provide care at home. Finally, delirium is a clinical phenomenon associated with increased mortality. Death occurs more frequently in acutely confused patients than in patients without the symptom; additionally, at the end of life, confusion may herald approaching death and interferes with meaningful exchanges and opportunities to say good-bye at the end of life (Boyle, Abernathy, Baker, & Wall, 1998; Brown & Degner, 2001; Caraceni et al., 2000; Ely et al., 2004; Kakuma et al., 2003; Lawlor & Bruera, 2002; Lawlor, Fainsinger, & Bruera, 2000; Leipzig, Cumming, & Tinetti, 1999; Leslie et al., 2005; Marcantonio et al., 2005; McCusker, Cole, Dendukuri, & Belzile, 2003; Milisen, Foreman, Godderis, Abraham, & Broos, 1998; Ravdin, Mattis, & Lachs, 2004; Sandberg, Gustafson, Brannstrom, & Bucht, 1999; Sullivan-Marx, 1994; Tamblyn, Abrahamowicz, du Berger, McLeod, & Bartlett, 2005; Tuma & DeAngelis, 2000; Wise, Hilty, Cerda, & Trzepacz, 2002).

Despite these considerable implications, delirium remains a clinical quandary (Roth-Roemer, Fann, & Syrjala, 1997; Sandberg et al., 1999). In cancer care, it rarely is appreciated as a significant determinant of symptom distress.

Seldom addressed in basic nursing education, confounded by a lack of nomenclature consistency, having no universally accepted assessment methodology, and characterized by the absence of intervention protocols, delirium is a nurse-intensive phenomenon that remains a seriously neglected problem (Cronin-Stubbs, 1996; Ludwick, 1999). This reality is disconcerting because nurses are in unique positions to determine the presence of delirium as a result of their close interactions with patients over time (Antai-Otong, 2003; Baumgartner, 2004; Gaudreau, Gagnon, Harel, Tremblay, & Roy, 2005; Inouye, Foreman, Mion, Katz, & Cooney, 2001). In particular, early recognition of delirium by nurses can facilitate prompt intervention to reduce symptom intensity (Olofsson, Weitzner, Valentine, Baile, & Meyers, 1996).

Incidence

Delirium's true epidemiology is hampered by inconsistencies in diagnosis and assessment. Yet, despite the variability, delirium is a well-recognized barrier to quality of life. Consider the following (Arnold, 2004; Fann & Sullivan, 2003; Foreman, 1991, 1993; Foreman & Zane, 1996; Gleason, 2003; Lipowski, 1987; Ljubisavljevic & Kelly, 2003; Ludwick & O'Toole, 1996; Minden et al., 2005; Morency, Levkoff, & Dick, 1994; Naylor, Stephens, Bowles, & Bixby, 2005; O'Keeffe & Lavan, 1997; Pompei, Foreman, Cassel, Alessi, & Cox, 1995; Tuma & DeAngelis, 2000; Wise et al., 2002).

- Delirium is undiagnosed in 32%–67% of patients.
- Delirium is the cause of admission for 10%–15% of acute care hospitalizations.
- Whether overtly or covertly, 10%–40% of all older people admitted to the hospital are confused at admission.
- Ten percent to thirty percent of hospitalized older adults experience an episode of delirium during their hospital stays.
- As many as 80% of all older people admitted to the hospital for acute physical illness develop new cognitive impairment during the course of their stays.
- Within 24 hours of surgery, 15% of older people become confused.
- Medical surgical nurses often care for three confused patients per week.

Although delirium may occur in any adult patient with cancer, it is most frequent in older patients with cancer (Boyle, 2003b; Lawlor, 2002; Ljubisavljevic & Kelly, 2003; Weinrich & Sarna, 1994; Welch-McCaffrey & Dodge, 1988).

Delirium is the second most common psychiatric diagnosis in patients with cancer (Massie & Holland, 1992; Roth & Breitbart, 1996). Overall, 25%–40% of patients with cancer experience delirium (Olofsson et al., 1996; Weinrich & Sarna, 1994; Zimberg & Berenson, 1990). In hospitalized patients with cancer, 14%–40% have an abnormality in cognitive function (Fann & Sullivan, 2003; Tuma & DeAngelis, 2000). During the last weeks of life, as many as 85% of patients with advanced cancer experience some problem with altered mental status (Breitbart, Bruera, Chochinov, & Lynch, 1995; Bruera & Beattie-Palmer, 2001; Casarett & Inouye, 2001; Fainsinger, De Moissac, Mancini, & Oneschuk, 2000; Foreman & Zane, 1996; Morita, Tei, Tsunoda, Inoue, & Chihara, 2001; Morita, Tsunoda, Inoue, Chihara, & Oka, 2001; Sarhill, Walsh, Nelson, LeGrand, & Davis, 2001; Sheehan & Foreman, 1997; Weinrich & Sarna, 1994). Hence, all patients near the end of life should be considered to be at high risk for delirium (Cassarett & Inouye, 2001). Preventive strategies and astute assessment are required. Of note is the absence of data on the incidence of delirium in the ambulatory population of patients with cancer.

Definition and Defining Characteristics

The varied manifestations of delirium among individuals and its fluctuating nature over time increase the complexity of symptom recognition (Foreman, 1993; Morrison, 2003). Nurses and physicians fail to identify delirium in two-thirds of patients

with the symptom (Bruera & Beattie-Palmer, 2001; Foreman, 1990, 1991; Ljubisavljevic & Kelly, 2003; Morency et al., 1994). Under-recognition of delirium in assisted-living facilities is particularly problematic (Magsi & Malloy, 2005). Older patients with cancer residing in such settings require special scrutiny. Inouye (1994) proposed that a number of factors impede the recognition of delirium in the medically ill, including failure to understand the significance of delirium, ambiguity of delirium's diagnostic terminology, absence of objective screening, prominence of a hypoactive subtype of delirium, fluctuation of severity and lucid intervals, multifactorial causes, and the possibility that delirium is superimposed on dementia.

To identify delirium, oncology nurses must be cognizant of all the potential impediments and, in particular, recognize the physiologic, behavioral, and cognitive parameters of delirium that provide important data for timely diagnosis.

Delirium is an altered mental state somewhere on the continuum between coma at one extreme and normal alertness at the other (Trzepacz, 1994a). It is a condition of acute cerebral insufficiency resulting from widespread disruption of brain metabolism caused by multiple factors (Adams, 1988). A reversible encephalopathy, delirium frequently is the first indication of serious medical illness in older adults (Cronin-Stubbs, 1997). Delirium is to older patients what fever is to children.

Delirium (or acute confusion) involves a disturbance of consciousness and a change in cognition that develop over a short period of time (American Psychiatric Association [APA], 2000). Delirium often is linked to internally derived conditions (e.g., metabolic changes associated with an illness state) or externally imposed challenges (e.g., medications that have central anticholinergic effects). Frequently, multiple causative factors are present. Four hallmark features of delirium relate to the nature of its presentation, disturbances in consciousness, cognitive changes, and alterations in the sleep-wake cycle (see Figure 1).

Delirium has a sudden onset with a fluctuating pattern of symptoms. It evolves over hours or days rather than weeks or months (Chan & Brennan, 1999). Symptoms are not consistent over a 24-hour period (Breitbart, 1994). Patients may exhibit significant disorientation in the evening and appear lucid and clear the following morning. Symptoms usually are diurnal in nature, being worse at night and upon awakening.

Disturbances in consciousness are characterized by impaired clarity of environmental awareness. Varied states of alertness compromise a patient's ability to "keep things straight." Additional cueing and clarification are required to maintain accurate perception of events. Another component of disturbance in consciousness is impaired attention span. This often is characterized as "wandering thoughts." Delirious patients have difficulty focusing, sustaining, and shifting their attention. Easily distracted by stimuli in their immediate environments, patients lose track of a question being asked or repeatedly return to an earlier question they can remember. Therefore, they often are unable to sustain meaningful conversations.

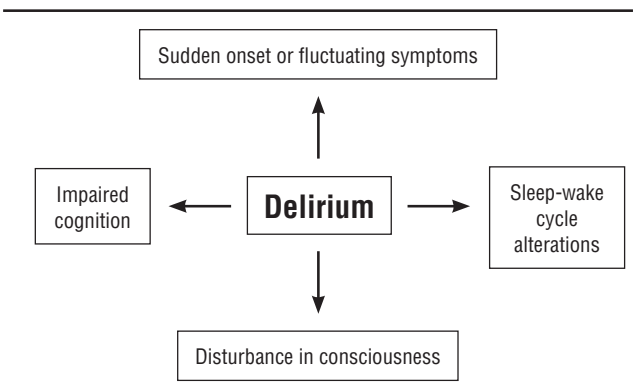

Figure 1. Hallmark Features of Delirium

The third important feature of delirium relates to impaired cognition. The phenomenon is exemplified best by alterations in memory function, which is highly vulnerable to a variety of pathologic processes (Budson & Price, 2005). Memory impairment usually relates to recent events. Disorientation, often an early prodromal sign of delirium, is manifested by problems recognizing place and time. It may be obscured by humor or attributed to a benign slip or mistake. Because the components of altered cognition are common and easily measurable, they frequently are tested using the Mini-Mental State Examination, a test that screens for memory impairment and disorientation (Folstein, Folstein, & McHugh, 1975).

The final essential feature of delirium is disturbance in the sleep-wake cycle. A varied state of alertness may result in periodic daytime sleepiness, nighttime agitation, or complete reversal of the normal sleep-wake cycle (i.e., sundowning syndrome). Disturbed psychomotor behavior may culminate in hyperactivity. Attempts to get out of bed, get dressed, and pick at bedclothes are some examples of the feature. The hyperactive variant is diagnosed prototypically most often, yet it only represents less than one-third of all cases (Ljubisavljevic & Kelly, 2003). Less common is a hypoactive state exemplified by lethargy, sluggishness, somnolence, or stuporous behavior. The presentation is especially under-recognized and often is mistaken for depression (Breitbart, Gibson, & Tremblay, 2002; Fann & Sullivan, 2003; Valentine & Meyers, 2001). The two variants may evolve during the same day. A patient may appear sleepy and only mildly confused in the morning but at night becomes hypervigilant, very disoriented, and periodically combative. All four of the essential clinical features must be present to make a diagnosis of delirium (APA, 2000).

The numerous manifestations of delirium, coupled with misperceptions and a lack of knowledge about altered mental status in older people, often result in misdiagnosis or under-recognition of the symptom (Gaudreau, Gagnon, Harel, et al., 2005; Gleason, 2003; Inouye et al., 2001). Additionally, multiple abnormal processes may evolve concurrently in older adults (e.g., delirium superimposed on dementia), which confounds early and accurate identification (Fick, Agostini, & Inouye, 2002; Fick & Foreman, 2000). Dementia and depression commonly are confused with delirium (Arnold, 2004). Table 1 summarizes the clinical features of delirium and compares them with those of dementia and depression. Awareness of the distinguishing characteristics can promote the accurate and timely assessment of delirium in older adults with cancer.

Pathophysiologic Considerations

Historically, aging has been considered synonymous with cognitive decline. The occurrence of delirium was thought to be inevitable and beyond the influence of professional intervention (Foreman, 1993). Enhanced awareness of the multifaceted characteristics of delirium, however, offers

Table 1. Clinical Features of Delirium, Dementia, and Depression

Feature	Delirium	Dementia	Depression
Onset	Acute (over hours to days); often at twilight; often a corollary of acute illness	Chronic, generally insidious (over months to years)	Episodic, coinciding with life changes; often abrupt, progressing from weeks to months
Course	Short, diurnal fluctuation in symptoms; worse at night, in the dark, and on awakening; symptoms can fluctuate hourly.	Long, no diurnal effects, symptoms progressive yet relatively stable over time	Diurnal effects, typically worse in the morning; situational fluctuations but less than delirium
Progression	Abrupt	Slow but even	Variable and uneven
Duration	Hours to weeks, seldom longer than a month; resolves with treatment	Months to years; progressive and irreversible	At least two weeks, but can be several months to years; resolves with treatment
Awareness	Reduced	Unaffected	Clear but selective
Alertness	Lethargic or hypervigilant; fluctuates	Generally normal	Normal
Attention	Impaired, fluctuates, easily distracted	Generally unaffected	Minimal impairment but may have difficulty concentrating
Orientation	Generally impaired; early disorientation to time and place; fluctuates in severity	Impaired as disease progresses	Selective disorientation
Memory	Recent and acute impairment	Generally impaired; unable to learn new information; unconcerned about memory deficits	Selective or patchy (i.e., slow recall) impairment; "islands" of intact memory; concerned about memory deficits
Thinking	Disorganized, distorted, fragmented, slowed, or accelerated; speech is incoherent.	Difficulty with abstraction; judgment impaired; words difficult to find	Intact but laden with negative thoughts of hopelessness, helplessness, or self-deprecation
Perception	Gross distortions; illusions, delusions, and hallucinations; difficulty distinguishing between reality and misperceptions	Misperceptions often absent; may experience hallucinations	Intact but characterized by depressive themes; delusions and hallucinations absent except in severe cases
Psychomotor behavior	Variable, hypokinetic, hyperkinetic, or mixed	Normal, may have apraxia	Variable, psychomotor retardation or agitation
Sleep-wake cycle	Disturbed; cycle may change hourly or be reversed.	Disturbed; day/night reversal	Disturbed; often early-morning awakening; hypersomnia during the day
Associated features	Variable affective changes; symptoms of autonomic hyperarousal; exaggeration of personality type; associated with physical illness	Affect superficial, inappropriate, and labile; attempts to conceal deficits in intellect; personality changes; aphasia; lack of insight	Affect depressed; exaggerated and detailed complaints; preoccupation with personal thoughts (usually negative); associated with recent or cumulative loss
Mental status testing	Distracted from task; family describes abrupt change in patient norm; in early phase, patient aware of, yet attempts to hide, abnormality.	Failings highlighted by family; frequent "near miss" answers; struggles with test; great effort to find an appropriate reply	Failings highlighted by the patient; frequent "don't know" answers; little effort; frequently gives up; indifferent; does not care or attempt to find answer

Note. Based on information from Arnold, 2004; Casey et al., 1996; Foreman & Grabowski, 1992.

oncology nurses numerous opportunities to identify, minimize, manage, and, at times, prevent the untoward effects associated with the symptom.

In older patients with cancer, delirium occurs in hosts already compromised by functional, age-related decline. Some examples of impairments include general reduced physiologic capacity, which diminishes the ability to respond to stress and illness; reduced sensory function (especially vision and hearing), which influences acuity and perception; decline of cognitive performance, which results in people being more easily distracted and in impairment in the ability to think clearly; malnutrition (quantified by low serum albumin levels), which has implications for protracted recovery and adverse effects on responses to treatment and medication; and decreased metabolic and excretory function, which compromises drug clearance (Foreman & Zane, 1996).

Of special note are pharmacokinetic changes in older people that influence drug disposition (Baker & Grochow, 1997; Lichtman, 1998).

- Reduced gastric secretion of acid, gastric emptying time, gastrointestinal motility, splanchic blood flow, and absorptive surface area, which can influence drug absorption of oral antineoplastics
- Doubling of fat content and decreasing of intracellular water, which may increase the volume of lipid-soluble drugs
- Reduced albumin concentrations, resulting in higher amounts of select unbound drug in the plasma with accompanying drug toxicity
- Impaired hepatic metabolism (e.g., reduced size of the liver and circulation, decline in P450 microsomal function with ultimate decreased hepatic drug clearance)

- Sequential, moderately progressive decline in renal glomerular and tubular function with age (i.e., 10% reduction in renal function per decade of life after age 30), with consequent delayed clearance of drugs excreted by the kidneys

All of the factors are highly individualized, and their manifestations are dependent on a number of host variables, such as lifestyle, use of health-promoting behaviors over time, genetics, and the presence of comorbid illness.

Neurologic changes are particularly important in the consideration of the genesis of delirium in older people. Generally reflective of diminished capacity, the changes include brain atrophy with loss of brain volume and weight; ventricle enlargement; reduced enzymes, proteins, and lipids; and shrinkage of large neurons (Stockton & Burke, 1997). Multiple neurotransmitter modifications (i.e., alterations in neurotransmitter numbers and receptor sites) are common in advanced age and are considered key in the evolution of delirium. The normal components of aging are important considerations because they closely parallel the currently favored pathophysiologic mechanisms for delirium that include cholinergic-dopaminergic imbalance, dopamine and β-endorphin hyperfunction, increased central noradrenergic activity, and intraneuronal damage of enzyme systems (Adams, 1988; Chan & Brennan, 1999). The functional decline of acetylcholine, however, is considered the primary reason for an older person's increased susceptibility to delirium.

The cholinergic hypothesis of delirium is supported by the ability of anticholinergic drugs to induce a state of delirium (Fann & Sullivan, 2003; Sandberg et al., 1999; Trzepacz, 1994a, 1994b). A corollary of the anticholinergic theory involves the proposed excess production of dopamine. Haloperidol, a potent dopamine blocker, causes prompt symptomatic relief in delirium. Hence, dopamine's role in delirium is highly suspect. Age-related central nervous system (CNS) changes that result in widespread dysregulation of neurotransmitter function promote altered cognition, a seminal trademark of acute confusion. Memory is the first area of cognition to be affected, evidenced by deficits primarily in short- but also long-term memory. These normal processes place older patients at heightened risk for delirium because neurologic, functional decline impairs the threshold on which adaptation to cerebral insufficiency occurs. Flacker and Lipsitz (1999, p. B239) wrote

> Age-related changes in the brain predispose older persons to delirium during physiologic disturbances that are tolerated in younger individuals. Changes in the brain with normal aging include a 28% decline in brain blood flow and neuron loss in many areas. Furthermore, norepinephrine, acetycholine, dopamine, and gamma-aminobutyric acid concentrations all decline with advanced age. Although great variability in the decline of these organ systems is the rule among the older population, these structural and functional losses may be reflected in age-related declines in speed of learning, reaction time, verbal fluency, visuoconstructive skills, and logical analysis. Thus, the result of the brain's failure to compensate for the neurologic stress of a drug or illness may then result in the phenomenology called delirium.

Hence, neurotransmission may be rendered defective in older adults with cancer as a result of aberrant metabolic activity in concert with exposure to exogenous pharmacologic agents to treat a malignancy, systemic effects of the malignancy, treatment toxicities, and comorbid conditions (Fann & Sullivan, 2003).

Etiology

Delirium is a direct effect of a general medical condition, substance intoxication, withdrawal, medication use, toxin exposure, or a combination (APA, 2000). Table 2 outlines the myriad of potential physiologic etiologies of delirium. The medical conditions are thought to affect the ascending reticular activating system that is manifested as attention, concentration, sleep-wake cycle deficits, and sensorium (Othmer, Othmer, & Othmer, 1998). Of note is the magnitude of the physiologic causes, many of which are prevalent during the treatment of older people with cancer.

Cranial irradiation for the treatment of primary or secondary malignancies often is associated with cognitive impairment (Brown et al., 2003; Lilja, Portin, Hamalainen, & Salminen, 2001). Morrison (2003) identified a constellation of causes and sequelae of delirium in critically ill patients with cancer. Violation of the CNS by intracranial bleeding, cerebrovascular disease, leptomeningeal carcinomatosis, or infection (particularly meningitis and encephalitis caused by herpes simplex virus) is common. Urinary tract infections, often considered fairly benign in the general population, are frequent causes of cognitive changes (Karch, 2005). Metabolic compromise, the presence of paraneoplastic syndromes, and the use of steroids in older patients undergoing bone marrow transplantation or being systemically treated for leukemia, lymphoma, or multiple myeloma put them at high risk for delirium. Often ignored, alcohol or sedative withdrawal or use of concomitant alcohol with alcohol-interactive drugs (e.g., antidepressants, antihistamines, barbiturates, muscle relaxants, benzodiazepines, opioids) may cause acute delirium (Blondell, Powell, Dodds, Looney, & Lukan, 2004; Glass, Lanctot, Herrmann, Sproule, & Busto, 2005; Pringle, Ahern, Heller, Gold, & Brown, 2005). Sequelae of delirium in the critical care treatment setting may include aspiration pneumonia, decubiti, prolonged hospitalization, increased requirements for intensive nursing care, and agitation resulting in falls, self-extubation, increased systemic oxygen consumption, and myocardial demand (Morrison).

Pharmacologic agents are the most frequent cause of acute confusion. In particular, drugs with central anticholinergic properties and those with CNS effects that are capable of crossing the blood-brain barrier are the primary causes of drug-induced delirium (Milisen et al., 1998; Morrison, 2003). In older adults even without cancer, users of conventional antipsychotic medications (e.g., chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine, trifluprom azine, and atypical antipsychotic medications [e.g., aripirazole, olanzapine, quetiapine, risperidone, and ziprasidone]) are at increased risk of death when the agents are prescribed (Wang et al., 2005). Parenterally administered opioid analgesics and benzodiazepines are the most common offenders (Breitbart, 1994; Bruera & Neumann, 1998; Fann & Sullivan, 2003; Lawlor, 2002; Tamblyn et al., 2005; Tuma & DeAngelis, 2000). Figure 2 lists important prescription medications to consider when identifying drug-related etiologies of delirium in older patients. Many of the drugs are used to improve cancer-treatment sequelae and treat comorbid illnesses in older patients (Boyle, 2003a; Kalash, 1998).

Table 2. Physiologic Etiologies of Delirium

Type of Physiologic Risk Factor	Cancer-Specific Considerations
Nutritional deficiencies B vitamins Vitamin C Hypoproteinemia	• Symptom distress: nausea, emesis, mucositis, diarrhea, pain, and anorexia or cachexia syndrome • Surgical alteration of the head and neck region or gastrointestinal tract • Nonoral feeding routes: gastrostomy feeding tube and use of total parenteral nutrition
Cardiovascular abnormalities Decreased cardiac output states: myocardial infarction, dysrythmias, congestive heart failure, and cardiogenic shock Alterations in peripheral vascular resistance: increased and decreased states Vascular occlusion: emboli and disseminated intravascular coagulopathy	• Septic shock syndrome • Hypercoagulopathy and hyperviscosity • Anthracycline-related cardiomyopathy • Central line occlusion • Thrombi associated with immobility and paraneoplastic syndromes • Disseminated intravascular coagulopathy
Cerebral disease Vascular insufficiency: transient ischemic attacks, cerebral vascular accidents, and thrombosis Central nervous system infection: acute or chronic meningitis, brain abscess, and neurosyphylis Trauma: subdural hematoma, contusion, concussion, and intracranial hemorrhage	• Intracerebral bleed caused by thrombocytopenia • Meningeal carcinomatosis • Central nervous system edema secondary to brain maligancy or whole brain radiation therapy • Fall risk • Malignancy: primary or metastatic involving brain and cranial irradiation
Endocrine disturbance Hypothyroidism Diabetes mellitus Hypercalcemia Hyponatremia Hypopituitarism	• Mantle field radiation therapy • Steroid induced • Related to bone metastases • Syndrome of inappropriate antidiuretic hormone, rigorous hydration, and dehydration • Brain tumor in or adjacent to pituitary gland
Temperature regulation fluctuation Hypothermia Hyperthermia	• Absence of customary warm clothes • Fever
Pulmonary abnormalities Inadequate gas-exchange states: pulmonary disease and alveolar hypoventilation Infection: pneumonia	• Hypoxemia • Anemia • Lung metastases • Bleomycin-induced pulmonary fibrosis • Radiotherapy to chest • Chest tubes • Neutropenia and immobility
Systemic infective process (acute or chronic) Viral Fungal Bacterial: endocarditis, pyelonephritis, and cystitis	• Prominence of neutropenia • Steroids • Hypogammaglobunemia
Metabolic disturbance Electrolyte abnormalities: hypercalcemia, hypo- and hypernatremia, hypo- and hyperkalemia, hypo- and hypercalcemia, and hyperphosphatemia Acidosis and alkalosis Hypo- and hyperglycemia Acute and chronic renal failure Volume depletion: hemorrhage, inadequate fluid intake, diuretics, and diarrhea Hepatic failure	• Syndrome of inappropriate antidiuretic hormone • Bone metastases • Diabetes secondary to steroids • Renal malignancy • Dehydration and diarrhea secondary to pelvic radiotherapy or chemotherapy • Liver primary or metastases with ascites or encephalopathy • Tumor lysis syndrome
Drug intoxication (therapeutic or substance abuse) Misuse of prescribed medications Side effects of therapeutic medications Drug-drug interactions Drug and herb interactions Improper use of over-the-counter medications Alcohol intoxication or withdrawal	• Polypharmacy with drugs having anticholinergic or central nervous system effects • Inadequate knowledge about geriatric-specific pharmacokinetic considerations in dosing • Self-medication with over-the-counter or herbal remedies in the absence of healthcare professional awareness • Alcohol withdrawal perioperatively in patients with head and neck cancer

Drugs to Treat Cancer in Older Patients

Antineoplastic agents: carmustine, chlorambucil, cytarabine, etoposide, fluorouracil, ifosphamide, L. asparaginase, methotrexate, mitomycin, procarbazine, vinblastine, and vincristine

Biologic response modifiers: interferon alfa and interleukin

Glucocorticoids: dexamethasone, hydrocortisone, methylprednisolone, and prednisone

Supportive Care Drugs

Narcotics: belladonna and opium, meperidine, pentazocine, and propoxyphene

Non-narcotics: salicylates and nonsteroidal anti-inflammatory drugs (ibuprofen and ketorolac)

Anticonvulsants: carbamazepine, phenobarbitol, phenytoin, and valproic acid

Antimicrobials: acyclovir, amphotericin, ciprofloxacin, clarithrymycin, erythromycin, ganciclovir, gentamycin, and trimethoprim-sulfamethoxazole

Urinary antispasmodics: flavoxate, oxybutynin, and tolterodine

Gastrointestinal: cimetidine, famotidine, loperamide, metaclopromide, nizatadine, propantheline, ranitidine, and scopolamine

Psychotropics

Antipsychotics: chlorpromazine, perphenazine, and thioridazine

Antianxiety agents: alprazolam, clonazepam, clorazepate, diazepam, lorazepam, and midazolam

Antidepressants: amitriptyline and nortriptyline

Hypnotics or sedatives: chloral hydrate and triazolam

Miscellaneous

Antidiabetics: glipizide, glyburide, and insulin

Cyclosporine

Glucocorticoids: dexamethasone, hydrocortisone, methylprednisone, and prednisone

Drugs to Treat Comorbid Illness

Anti-Parkinsonian: amantadine, benztropine, levodopa, and carbidopa

Muscle relaxants: baclofen, carisoprodol, cyclobenzaprine, and methocarbamol

Antidysrhythmics: lidocaine, procainamide, propranolol, and quinidine

Antihypertensives: clonidine and methyldopa

Cardiac glycosides: digitalis

Coronary vasodilators: isosorbide dinitrate, isosorbide mononitrate, and nitroglycerin

Antihistamines: brompheniramine, chlorpheniramine, cyproheptadine, and diphenhydramine

Bronchodilators: theophylline

Decongestants and expectorants: phenylpropanolamine and pseudoephedrine

Figure 2. A Compendium of Potential Causative Medications of Delirium

Note. Based on information from Anonymous, 1993; Flaherty, 1998; Inouye & Charpentier, 1996; Jenkins & Bruera, 2000; McConnell et al., 1997; Weinrich & Sarna, 1994; Wills, 1995.

Corticosteroid-induced psychosis is a well-described form of delirium evident in clinical practice (Casarett & Inouye, 2001; Morrison). Finally, select chemotherapy agents may have central neurotoxic effects that can cause delirium (Jansen, Miaskowski, Dodd, Dowling, & Kramer, 2005a, 2005b; Verstappen, Heimans, Hoekman, & Postma, 2003; Wefel, Kayl, & Meyers, 2004).

Not listed in Figure 2 are over-the-counter (OTC) medications and complementary approaches that also must be considered. Many of the drugs contain antihistamines that have central anticholinergic effects and are frequent causes of delirium in older people (Armstrong & Cozza, 2003; Casarett & Inouye, 2001; Gunn, Taha, Liebelt, & Serwint, 2001; Hanlon et al., 2004). First-generation antihistamines noted on drug labels of OTC preparations (e.g., azatadine, brompheniramine, chlorpheniramine, cyproheptadine, dexchlopheniramine, diphenhydramine, hydroxyzine, phenindamine) should be considered a cause if delirium occurs (Drug Facts and Comparisons, 2002). Polypharmacy with such nonprescription drugs may promote toxicity, resulting in altered mental state (Bond & Hannaford, 2003; Kalash, 1998; Gunn et al.). Table 3 lists common OTC medications that contain antihistamines. In addition to delirium and disorientation, other anticholinergic effects include dry mouth, constipation, urinary retention, blurred vision, insomnia, and restlessness (Eliopoulos, 1997). Additionally, drug interactions between herbal and prescription medications may cause CNS toxicity (Brown et al., 2003; Lilja et al., 2001; Williamson, 2003). Memorial Sloan-Kettering Cancer Center has an excellent evidence-based Web site that identifies toxicities, contraindications, and special precautions specific to herbal products (www.mskcc.org/mskcc/html/11570.cfm).

Altered pharmacokinetics in older people (i.e., age-related changes in absorption, distribution, metabolism, and excretion of drugs) heighten the risk of adverse events when medications are prescribed in normal dose ranges (Wildiers, Highley, de Bruijn, & van Oosterom, 2003). For example, long-acting benzodiazepines often produce exaggerated CNS effects in older people, resulting in altered mental status (Larson, Kukull, Buchner, & Reifler, 1987). Establishing adequate creatinine clearance as an index of renal function in older adults (Finkel, 2004) is imperative prior to administering drugs that are cleared predominantly through the kidneys. Impaired renal function may delay drug and metabolite excretion, causing concentration-related adverse effects (Flaherty, 1998; Tett, Kirkpatrick, Gross, & McLachlan, 2003). Lastly, the prominence of polypharmacy and the likelihood of drug interactions always warrant consideration.

Secondary precursors of delirium are the psychological and social variables that have an additive effect on physiologic etiologies. The following should be considered when trying to identify causative factors of delirium and plan interventions.

- **Orientation:** relocation to an unfamiliar environment, absence of normative cues, lack of meaningful routines, and reactions to immobilization
- **Social support:** absence of familiar loved ones and friends and accommodation to strangers as roommates and to numerous new healthcare professionals
- **Adaptation:** sensory deprivation or environmental monotony, protective or required isolation, sensory overload, sleep deprivation, emotional responses to anxiety, anticipatory grief, or depression

When the basis of a delirious state is considered, remember that delirium most often is multifactorial and rarely emanates from a single source (Bruera & Beattie-Palmer, 2001; Gaudreau, Gagnon, Roy, Harel, & Tremblay, 2005; Irwin, Murray, Bilinski, Chern, & Stafford, 2005; Kalash, 1998; Lawlor, Fainsinger, et al., 2000; Olofsson et.al., 1996). In the genesis of delirium in older surgical patients, for example, delirium may be precipitated by the combination of intraoperative hypotension, intra- and postoperative hypothermia, hemorrhage, hypoxia, imposed immobilization, sensory overload, sleep deprivation, and the CNS and anticholinergic effects of medications such as anesthetics, analgesics, antiemetics, and benzodiazepines. What is of utmost importance is consideration of

Table 3. A Sampler of Over-the-Counter Medications With Central Anticholinergic Effects

Drug Category	Examples
Allergy remedies	Aller-Chlor Allergy, Chlor-Trimeton Allergy-D tablets, Benadryl Allergy and Sinus tablets, Claritin, Contac Day and Nite Allergy/Sinus Relief tablets, Dayhist-1, Drixoral Allergy Sinus tablets, Tavis®Allergy, Tylenol Severe Allergy caplets
Antidiarrheals	Diar-Aid caplets, Donnagel, Imodium A-D caplets, Kaopectate (II caplets, advanced formula), Maalox antidiarrheal caplets, Pepto Bismol, Pepto diarrhea control
Antiemetic and antivertigo	Bonine, Calm-X, Dramamine, Vergon
Antacids	Alka Seltzer (original effervescent tablets and extra-strength tablets), Bromo seltzer effervescent granules
Cough, cold, and flu preparations	Actifed C; Advil tablets (cold and sinus, flu and body ache); Aleve cold and sinus tablets; Alka Seltzer Plus cold and sinus tablets; Allerest sinus pain formula caplets; Comtrex; Coricidin cold, flu, and sinus tablets; Dimetapp cold and allergy; Dristan; Motrin sinus headache; Robitussin cold, sinus, and congestion tablets; Sine-off sinus medicine tablets; Sinutab; Sudafed; Theraflu flu and cold medicine; Tylenol Flu night-time maximum-strength gelcaps; Vicks 44D cough and head congestion relief liquid; Dayquil; Nyquil
Histamine antagonists	Axis AR, Pepcid (AC, complete), Tagamet, Zantac 75
Sleep aids	Unisom nighttime sleep aid, Nytol, Sominex, Extra Strength Tylenol PM, Excedrin PM, Bayer Select maximum strength nighttime pain relief, Extra Strength Doan's PM, Midol PM, Nighttime Pamprin

Note. Manufacturers may change or substitute ingredients of over-the-counter preparations without notification on drug labels.

Note. Based on information from Armstrong & Cozza, 2003; Drug Facts and Comparisons, 2002; Gunn et al., 2001; Karch & Karch 2001; U.S. Food and Drug Administration, 2002.

what transpired in a patient's clinical situation in the 48 hours prior to the presentation of suspicious symptomatology.

Assessment

As with pain, the ability to minimize the sequelae associated with delirium is proportionate to its accurate assessment. Nurses must be astute in the recognition of the symptom before planning any interventions to ameliorate its intensity (Baumgartner, 2004). Several unique considerations must be addressed that directly influence timely and appropriate assessment of delirium. First, the complex nature of symptom presentation must be acknowledged. Physiologic symptom distress in patients with cancer often is accompanied by emotional and interpersonal sequelae. Pain, nausea, fatigue, bowel obstruction, mucositis, and dyspnea, for example, all have psychosocial correlates such as anxiety and depression. Patients usually have the ability to state their degree of symptom distress and cite the emotional implications of the problem. However, unlike other symptoms with physiologic etiologies, delirium is unique owing to barriers in symptom reporting. As a result of altered mental status, patients may not be able to articulate their symptoms or describe the psychological repercussions associated with delirium (Lawlor, 2002; McDonald, 1999). This puts the burden of diagnosis solely in the hands of others. Whenever people other than patients have the responsibility of identifying symptom distress, problems related to recognition ensue. Nurses' and physicians' perceptions may not reflect patients' experiences accurately (Ganguli et al., 2004). Yeaw and Abbate (1993, p. 193) wrote

> Because confusion is operationalized and conceptualized from an "outsiders perspective" there is some distortion of reality. This "outsider looking in" view seems to focus on how confusion interferes with nurses' and doctors' functions rather than how the confusion interferes with the patient's ability to function.

This perspective may promote negative labeling of patients. For example, in reviewing hospital records of older, confused patients, Foreman (1993) noted that in physicians' notes, terms such as "forgetful," "poor historian," "cannot understand directions," "poor memory," and "incoherent" were used commonly. The words imply that the physicians were compromised in their diagnostic determinations. Nurses routinely used descriptors such as "uncooperative," "hostile," "difficult to manage," and "belligerent." The terms reflect frustration in getting nursing work done in an uninterrupted manner. Although the descriptors portray common clinical correlates of delirium, they often are used in the absence of formal quantitative measures to determine the actual presence and intensity of delirium.

Particularly in the early stages of delirium, patient efforts at symptom concealment often interfere with early diagnosis. The prodromal signs are easily attributable to other causes (see Figure 3). However, the signs in conjunction with the presence of risk factors for delirium should heighten suspicion about an evolving presentation of delirium. Families are critical partners in the quest for timely assessment of the problem (Albert et al., 1992). They must be queried and educated about subtle changes to recognize in their loved ones. The changes may include

- Patient report of
  - Confused thinking
  - Forgetfulness
  - Difficulty concentrating
  - Difficulty judging the passing of time
  - Feeling "mixed up" or "thinking fuzzy"
  - Perceptual distortions
- Behavioral manifestation of
  - Anxiety, unusual restlessness
  - Irritability
  - Withdrawal
  - Mood disturbance
  - Hypersensitivity to light and noise
  - Insomnia with daytime sleepiness and vivid dreams
  - Single nocturnal episode of confusion

Figure 3. Prodromal Signs of Delirium

Note. Based on information from Henry, 2002; Matthiesen et al., 1994; Milisen et al., 1998; Wise et al., 2002.

anxiety, anger, depression, restlessness, and mild insomnia that differs from usual behavior (Langhorne, 1999). Family report of altered behavior helps in evaluating a suspect clinical picture and its evolution over time (Pisani, Inouye, McNicoll, & Redlich, 2003). Collaboration with families also promotes discovery of potential causative factors that preceded the onset of acute confusion (e.g., introduction of new medications).

Efforts to assess and measure acute confusion must be accompanied by critical thinking in the determination of potential etiologies. Delirium often is reversible once offending causes are identified and corrected (Lawlor, 2002; Olofsson et al., 1996; Trzepacz, 1996). In older patients with cancer, causative factors frequently are numerous. Etiologies can be identified through patient history (the family must participate in this process), illness review (including evidence of infection or recent change in the status of cancer, particularly metabolic alterations or recurrence), laboratory findings (especially fluid and electrolyte imbalance and hypoxia), new medications (especially drugs with CNS or anticholinergic effects), and changes in drug dose, route, or schedule.

The reversibility of potential causative factors is of paramount importance in intervention planning. Etiologies that can be corrected (e.g., giving oxygen for hypoxia, treating bone metastases causing hypercalcemia, discontinuing a medication) should become the primary focus of treatment. During end-of-life care, when an etiology may not be amenable to correction, managing the intensity of the delirium, rather than attempting to reverse it, becomes the primary focus of intervention (Breitbart & Strout, 2000; Cobb et al., 2000; de Stoutz, Tapper, & Fainsinger, 1995; Lawlor, 2002; Stewart, 2005). Agitated delirium not responsive to standard symptom-reduction efforts may require pharmacologic intervention to induce sedation (Fainsinger et.al., 2000; Stirling, Kurowska, & Tookman, 1999).

Measurement

Quantifying delirium requires oncology nurses to consider several caveats. First, they must remain aware of the transient nature and variability of the symptom. An evolving clinical picture in one patient over time is the norm. Additionally, a wide variation in symptom presentation must be expected from patient to patient. One patient may exhibit symptoms of mild disorientation with lethargy during the evening hours, whereas another may become hyperactive and try to get dressed and leave the hospital. Second, formal evaluation instruments sensitive to severity rather than mere presence must be used to measure delirium over time. This provides data on the progression of the clinical problem and offers evidence of the efficacy of interventions (Capuron, Ravaud & Dantzer, 2001; Gagnon, Allard, Masse, & DeSerres, 2000). Third, acknowledgment that measurement scores may reflect impaired performance as a result of setting or circumstance is critical (Souder & O'Sullivan, 2000). Pain, sleep deprivation, medications, and anxiety may influence outcomes of testing. Fourth, in establishing the magnitude of the clinical problem, the absence of documentation at the bedside is troubling. Inadequate reporting underestimates prevalence and minimizes the importance of the symptom. The lack of data also compromises nurses' ability to advocate for early pharmacologic intervention. Finally, any realistic hope of nurses integrating the assessment of delirium routinely into nursing care must be tempered by the reality of time constraints, duplicity of documentation, and discomfort related to questioning about mental abilities on the part of nurses.

A variety of tools are available to assess delirium. Regular screening has the potential to reduce symptom severity and morbidity associated with the symptom (Morita, Tei, & Inoue, 2003a, 2003b). Existing tools range from brief instruments that solely determine the presence of cognitive impairment to detailed tools used in clinical research on altered mental status designed to measure impaired cognition over time. A brief review of the more commonly used tools follows.

- The **Mini-Mental State Examination (MMSE)** and its edited version (the Modified Mini-Mental State Examination, or the 3 Ms) have been the most frequently used neuropsychological tests in the clinical evaluation of delirium (Bassuk & Murphy, 2003; Folstein et al., 1975; McDowell, Kristjansson, Hill, & Herbert, 1997). Verbal responses and a minimum of an eighth-grade level of education are required (Fann & Sullivan, 2003). The MMSE includes 11 questions and requires 5–10 minutes to complete. It assesses only gross general cognitive status and has low sensitivity for recognition of mild changes (Meyers & Wefel, 2003; Rapp et al, 2000; Ravdin et al., 2004). Although it can heighten suspicion about cognitive impairment and discriminate between patients with and without suspicious symptoms of such, a single MMSE score does not help to distinguish between acute, potentially reversible cognitive decline caused by delirium and chronic impairment caused by dementia (O'Keeffe, Mulkerrin, Nayeem, Varughese, & Pillay, 2005). Additionally, it may negatively affect patients' personal sense of dignity as they struggle to answer questions they previously considered to be second nature in daily functioning (Grealish, 2000). A short version of the MMSE has been tested using four to six of the original items (Fayers et al., 2005).
- The **Clinical Assessment of Confusion-A** tool was developed to determine the presence, pattern, and severity of confusion as perceived by nurses (Foreman & Vermeersch, 2004). It consists of a checklist of 25 psychomotor behaviors and a visual analog scale that addresses patients' ability to function in their environments (Vermeersch, 1990; Vermeersch & Henley, 1997). An objective list of observable patient behaviors is used but is highly influenced by the time spent by the rater with the patient.
- The **Confusion Assessment Method (CAM)** allows nonpsychiatrically trained clinicians to identify delirium quickly (usually within five minutes) and accurately (Inouye et al., 1990; Ljubisavljevic & Kelly, 2003). It consists of nine open-ended questions and requires subjective clinical judgment by the rater. The CAM addresses the APA diagnostic criteria and has convergent agreement with the MMSE. However, it does not provide information on severity and, therefore, is not useful in repeated measurement. An attempt to develop a chart-based assessment instrument using the CAM criteria resulted in 74% sensitivity and 83% specificity (Inouye et al., 2005). Hence, the researchers did not recommend the instrument for diagnostic purposes or for use in individual patient care but rather for measuring broad-based effects of clinical programs or quality-improvement initiatives. It has been used successfully with terminally ill patients with cancer (Gagnon et al., 2000). A version of the CAM for intensive care units (CAM-ICU) has been developed (Ely et al., 2001; McNicoll et al., 2003; Truman & Ely, 2003). A recent comparison of the CAM and CAM-ICU identified

that although the CAM-ICU is recommended for critical care patients, the standard CAM may determine more subtle cases of delirium in nonintubated, verbal patients in the intensive care unit because of its brevity and ease of use (McNicoll, Pisani, Ely, Gifford, & Inouye, 2005).

- The **Delirium Index** was adapted from the CAM for use with medical inpatients (McCusker, Cole, Bellavance, & Primeau, 1998). It was intended to measure delirium severity by a nonpsychiatrist based on patient observation, without additional information from family members, nursing staff, or medical charts. It includes 7 of the 10 symptom domains of the CAM (i.e., disorders of attention, thought, consciousness, orientation, memory, perception, and psychomotor activity). Based on operational criteria, the tool uses individual item scoring of 0 (absent) to 3 (present and severe), resulting in a potential cumulative score of 0–21 (higher scores indicate greater severity). It is a reliable, valid, and responsive measurement of the severity of delirium with or without dementia (McCusker, Cole, Dendukuri, & Belzile, 2004).
- The **NEECHAM Confusion Scale** was developed to raise suspicion for impending delirium and for nurses to rapidly document cognitive functioning (Csokasy, 1999; Neelon, Champagne, Carlson, & Funk, 1996; Neelon, Champagne, McConnell, Carlson, & Funk, 1992). Psychometrically sound, the scale uses primarily observational data, allows for retesting, and is sensitive to signs of worsening confusion (Wakefield & Johnson, 2001). Data can be obtained during 10 minutes of routine clinical assessment by staff nurses (Miller et al., 1997).
- The **Delirium Rating Scale (DRS)** is a 10-item tool requiring a psychiatrist's rating based on objective and subjective data retrieved over a 24-hour period (Trzepacz, 1999a, 1999b; Trzepacz, Baker, & Greenhouse, 1988). Using the Diagnositc and Statistical Manual of Mental Disorders (fourth edition, text revisions) (DSM-IV-TR) criteria for delirium, the DRS includes items measuring the temporal onset of symptoms, perceptual disturbances, hallucinations, delusions, psychomotor behavior, cognitive status during formal testing, sleep-wake cycle disturbances, mood lability, and variability of symptoms (Foreman & Vermeersch, 2004). The DRS represents one of the first tools to measure delirium severity over time. It has been tested in children and adolescents (Turkel, Braslow, Tavare, & Trzepacz, 2003). However, the requirements that it be used by a psychiatrist and that 24 hours of symptom surveillance occur preclude its utility in oncology nursing practice.
- The **Memorial Delirium Assessment Scale (MDAS)** is an instrument originally created for, and tested in, oncology populations (Breitbart et al., 1997). The items reflect the APA diagnostic criteria and integrate observational and objective assessment. The tool is designed for repeated measurement, takes 10 minutes to complete, and is intended specifically for frequent (i.e., hourly) severity ratings (Lawlor, Nekolaichuk, et al., 2000). Its major limitation is its lack of sensitivity to detect mild cases of delirium (Foreman & Vermeersch, 2004).
- The **Clock Drawing Test (CDT)** is an examination of visuospatial abilities considered useful in screening global cognitive impairment (Foreman & Vermeersch, 2004). As a screening tool, it requires patients to draw a clock with all of the numbers on it and to set the hands of the clock at a specific time (Huntzinger, Rosse, Schwartz, Ross, & Deutsch, 1992). It involves clock drawing, clock setting, and clock reading (see Figure 4). Difficulty in drawing a clock reflects neuropsychological disturbance termed constructional apraxia (Richardson & Glass, 2002; Wise et al., 2002). Components of this abnormality relate to memory reconstruction, visuoperceptual analysis, motor execution, attention, language comprehension, and numerical knowledge. Use of the test may predict cognitive frailty and high-risk individuals well served by early intervention (Paganini-Hill, Clark, Henderson, & Birge, 2001; Riegel et al., 2002). Scoring of the CDT is determined by the degree of cognitive impairment noted from the clock drawing performance (Mendez, Ala, & Underwood, 1992). Benefits of the approach include the provision of a quick screen for cognitive impairment not requiring special forms or testing tools (Souder & O'Sullivan, 2000). However, patients with visual impairment, problematic hand and joint dexterity, or extreme infirmity have preexisting confounding variables that compromise task outcome (Huntzinger et al., 1992).
- The **Nursing Delirium Screening Scale (Nu-DESC)** is the most recent tool developed as a quick, observational, and longitudinal instrument for delirium assessment (Gaudreau, Gagnon, Harel, et al., 2005). It is a five-item scale that was psychometrically evaluated by comparing it with the CAM and MDAS instruments and the DSM-IV-TR criteria. The researchers who developed the tool proposed that the Nu-DESC is well suited for varied oncology inpatient settings in clinical and research endeavors (Gaudreau, Gagnon, Harel, et al., 2005).

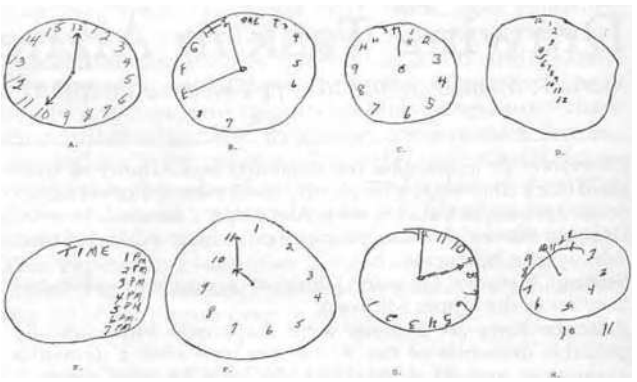

Figure 4. Examples of Clock Drawing Test Performance Identify Cognitive Impairment

For more detailed information about measurement tools, six excellent reviews of delirium assessment instruments have been published (Abrahm, 2000; Foreman & Vermeersch, 2004; Musselman, Hawthorne, & Stoudemire, 1997; Rapp et.al., 2000; Smith, Breitbart, & Platt, 1995; Trzepacz, 1994b).

Three instruments have been created to evaluate confusion in terminally ill patients. The **Communication Capacity Scale** and the **Agitation Distress Scale** were created to quantify confusion severity at the end of life (Morita, Tsunoda, et al., 2001). Their reliability and validity were established, as were their internal consistency and correlation with existing scales to measure confusion. The **Bedside Confusion Scale** is a validated

two-item instrument originally designed and tested in a palliative care setting (Naughton & Homsi, 2002; Sarhill et al., 2001). It evaluates two parameters, the level of alertness and attention, and has the advantage of being brief and easy to use.

Interventions

Historically, professional indifference best characterizes the clinical problem of delirium. A lack of scientific inquiry has resulted in a preponderance of anecdotal commentaries concerning management strategies (Cronin-Stubbs, 1996; Foreman, 1990). However, recent evidence of innovative, nurse-led intervention programs and consultation services that stress education of nursing staff, systematic cognitive screening, and nurse specialist consultation have proven beneficial in reducing the severity of delirium in hospitalized older patients (Marcantonio, Flacker, Wright, & Resnick, 2001; Milisen et al., 2001). Of interest are two reports of innovations by nurses. Balas, Gale, and Kagan (2004) proposed the use of "delirium doulas," trained lay people who offer physiologic, emotional, and informational support to critically ill older people. Rapp et al. (2001) proposed that specialized training as an acute confusion resource nurse could influence staff nurses' knowledge and confidence in the management of delirium. Elements of a novel, nurse-led, multifunctional delirium-abatement program to manage delirium in older patients admitted to postacute skilled nursing facilities have been reviewed (Marcantonio et al., 2005). St. Pierre (2005) delineated the process of facilitating changes in prescribing practices in a community teaching hospital by an advanced practice nurse. Milisen et al. (2004) described details and psychometrics of a new tool, the Strain of Care Delirium Index, to measure the strain nurses experience in caring for patients with delirium.

The primary goals for recognizing and treating delirium are reversing the clinical presentation of the symptom and preventing complications resulting from its presence (Wakefield & Johnson, 2001). Interventions that commonly are used target patient safety, identification of underlying etiologies, symptom control, and psychological support. Table 4 provides a comprehensive list of nursing interventions with their rationales. Although they are termed nursing interventions, a multidisciplinary plan of care is paramount to implement them successfully. The measures should be considered across the confusion continuum, from the identification of early suspicious symptoms to situations where acute confusion is blatant and potentially harmful as evidenced by agitation and incoherence. Use of instruments to measure pain in the cognitively impaired must be considered (Stolee et al., 2005). In particular, early recognition and intervention of underlying pathologies has significant potential (Morita et al., 2003b).

Drug therapy for delirium is challenging. The medications used to treat the condition also may cause or exacerbate its intensity. Which drug to use, which dose, how often, when to start, and adverse drug effects remain pharmacologic concerns (Carnes et al., 2003).

Haloperidol is the preferred neuroleptic for the management of delirium (Abrahm, 2000; APA, 1999; Boyle et al., 1998; Breitbart, 1994; Bruera & Beattie-Palmer, 2001; Bruera & Neumann, 1998; Currier & Trenton, 2002; Fann & Sullivan, 2003; Lawlor & Bruera, 2002; Lawlor, Fainsinger, et al., 2000; Mazzocato, Stiefel, Buclin, & Berney, 2000; Morrison, 2003; Raines, 1998). It is the drug of choice because it

- Is a high-potency dopamine-blocking agent
- Exhibits catecholamine receptors and exerts a diffuse depressive effect at several levels: subcortical, midbrain, and brain stem
- Has no active metabolites
- Can be administered orally, via IV, or intramuscularly
- Has infrequent cardiovascular (hypotensive) side effects
- Causes minimal sedation as compared to phenothiazine-type neuroleptics.

For mild symptoms, patients may be started on doses of 0.5 mg twice a day, whereas, for moderate symptoms, patients may require 2 mg twice a day. Patients may receive as much as 5 mg per dose twice daily depending on the degree of agitation exhibited. Prophylactic use of haloperidol has been described in surgical settings (Kalisvaart et al., 2005). Other pharmacologic options to manage delirium include newer psychoactive drugs, olanzapine and risperidone (Breitbart, Tremblay, & Gibson, 2002; Schwartz & Masand, 2002). However, the lack of historical experience using these atypical neuroleptics mandates continued scrutiny. Estfan, Yavuzsen, and Davis (2005) described two case studies in which patients treated with olanzapine for nausea secondary to bowel obstruction developed severe opioid-induced delirium. Lorazepam also is used; however, it is heavily sedating and has little effect on improving cognitive function (Casarett & Inouye, 2001; Walsh, Doona, Molnar, & Lipnickey, 2000). Yet it has efficacy as an adjuvant drug to treat agitated delirium, particularly in critical care patients (Morrison, 2003). Paradoxical reactions to this and other benzodiazepines (e.g., alprazolam, midazolam, temazepam) also is a concern (Gutierrez, Roper, & Hahn, 2001).

Evaluation of the efficacy of various methods of delirium management in acute care is needed (Carnes et al., 2003). Foreman (1993) proposed that outcomes to measure effective interventions for delirium could include length of hospitalization, mortality, discharge disposition, and evidence of iatrogenic events (e.g., falls, fractures, infection). Additionally, the use of chemical and physical restraints to manage behavior that compromises patient safety should be considered, as well as the cost of sitters. The prevalence of agitation as a nurse-sensitive outcome measurement can help quantify the efficacy of nurse-directed therapies (Gordon, 1999). The result of reduced episodes of agitation and the translation into reductions in length of stay also could be quantified in terms of cost savings (Foreman, 1990, 1991; McCusker et al., 2003).

Research Implications

Naylor et al. (2005) noted that little evidence exists to guide best practice in the management of older adults with cognitive impairment who are hospitalized for acute conditions. Furthermore, research on delirium in older patients with cancer is nonexistent. In the field of cancer care, what exists is a limited and generic focus on terminal delirium.

More than a decade ago, Weinrich and Sarna (1994) outlined elements of a delirium-specific research agenda for older patients with cancer. They emphasized the need to validate the methodology for delirium testing, including identification of a comprehensive test battery suitable for diagnostic screening in clinical practice. Also, in considering the uniform assessment of delirium, the identification of explicit criteria and validation by multiple raters must be established (Kroenke, 2001). Additionally, issues of informed consent with cognitively

Table 4. Nursing Interventions to Manage Delirium

Intervention	Rationale
Provide comfort measures.	• Symptom relief promotes sleep and rest. • Toileting contributes to the promotion of comfort.
Assess causes of delirium; monitor laboratory findings, vital signs, and intake and output; consider new medications.	• Altered pharmacokinetics and pharmacodynamics in older patients may contribute to delirium. • Identification of etiologies is necessary for intervention planning and influences reversibility of delirium.
Monitor the pattern of delirium.	• Note frequency and time of occurrence, which may give clues regarding contributing factors.
Consult a pharmacist for drug evaluation.	• Consider medication offenders or drug interactions. • If opioids are contributing to delirium, consider opioid rotation, dose reduction, or hydration. • Request assistance with drug protocol for agitated delirium.
Facilitate the use of neurosensory aids.	• Visual and auditory impairment in absence of eyeglasses or hearing aids contributes to delirium.
Consider environmental variables.	• Decrease stress, clutter, and excess stimuli. • Identify factors that enhance safety and minimize injury. • Consider room temperature and appropriate lighting.
Implement frequent orienting measures.	• Provide clocks, calendars, and television as tolerated. • Use methods that orient patients to time and current events (e.g., orientation board in a room where patients easily can read details).
Organize treatments, especially in consideration of sleep requirements.	• Alterations in the sleep-wake cycle with resultant sleep deprivation contribute to delirium; lobby for changes in test scheduling to allow for sleep.
Promote continuity.	• Consistent routines and personnel reduce reliance on memory recall and provide a sense of order and security.
Pace activities.	• Fatigue and stress can contribute to delirium.
Use simple, clear, brief instructions.	• Facilitates understanding
Allow patients time to adapt to unfamiliar situations.	• Response time to novel situations is protracted; anxiety and confusion are minimized with ample time to accommodate.
Encourage family visits and participation in care.	• Increases sense of familiarity, security, and trust
Support and teach families.	• Role model appropriate interaction with delirious patients; encourage family not to constantly correct patients; offer assurance of the temporary nature of the problem and the reversibility of the symptom when appropriate. • Provide emotional support for concern over changes in patients' cognitive status.
Monitor hydration and nutritional status.	• These physiologic factors may contribute to delirium; cognitive impairment may interfere with cues to eat and drink.
Administer drug therapy in a timely manner.	• Consider identification of early signs of delirium that prompt initiation of drug therapy to reduce symptom intensity.
Monitor for temperature fluctuation.	• Query patients about temperature sensations; awareness of changes may be the result of cognitive impairment.
Question patients about toileting needs.	• Anticipate problems with bowel and bladder cues. • Develop a regular toileting schedule.
Institute checks every 15 minutes when patients are profoundly delirious.	• Frequent checks support ongoing safety assessment and efficacy of drug therapy. • Reiterate identification with staff whom patients know. • Consider the use of sedating agents to enhance comfort and safety.

Note. Based on information from Boyle et al., 1998; Fann & Sullivan, 2003.

impaired patients pose ethical questions (Fann & Sullivan, 2003; Davis & Walsh, 2001).

Results of interventions that collaborate with family caregivers in the early recognition of symptoms are crucial (Gagnon et al., 2002). Similarly, the impact of intensive nurse and physician education about delirium symptom presentation to foster early recognition is needed (Inouye et al., 2001; Lacko et al., 2000; Ribby & Cox, 1996; Rockwood et.al., 1994). Descriptions of the varying chronologies of the delirium experience over time would help prepare families for the unknown. The determination of the relationship between cognitive impairment and medication regimen adherence is of utmost importance. Finally, family and caregiver distress indices related to confusion also warrant investigation. Examples of topics deserving research attention include family anxiety and grief related to poor communication, dilemmas of proxy decision making in advanced cancer, intrafamilial conflict over analgesia requirements, and delineation of the "destructive triangle," when a patient's agitation causes emotional distress in relatives, who, in turn, pressure nursing and physician staff

to increase sedation or medication (Lawlor & Bruera, 2002). Interventions to support families, similar to those mobilized for families caring for patients with Alzheimer disease, also require study. Finally, the relationship between metabolic markers and neurobehavioral test scores suggesting cognitive impairment deserves scrutiny (Schafer et al., 2005).

In general, patients with the highest risk for delirium are hospitalized older people with advanced cancer (Morrison, 2003; Raines, 1998). In-depth investigation of risk factors for delirium (including symptom clusters) can foster prevention and early intervention. Additionally, longitudinal protocols that initiate management from the emergency room through the remainder of hospitalization should be evaluated (Naughton et al., 2005). Research to date has identified numerous risk factors for delirium in older patients (see Figure 5). It remains unclear, however, in what manner clinical risk factors interface to cause delirium (Eden, Foreman, & Sisk, 1998). Yet five factors have been associated with the risk of delirium in patients with cancer: age older than 62 years, low serum albumin, cognitive impairment on admission, presence of bone metastases, and diagnosis of a hematologic malignancy (Ljubisavljevic & Kelly, 2003). Confirmation and validation of the findings require further study.

- Absence of a clock, watch, or family member at the bedside
- Age older than 80 years
- Alcoholism or alcohol withdrawal
- Blood urea nitrogen or creatinine ratio abnormality
- Dehydration
- Depression
- Fractures
- General anesthesia
- High comorbidity burden
- History of stroke, epilepsy, or congestive heart failure
- Hypoxia
- Admission to the intensive care unit
- Immobility
- IV catheter complications
- Male gender
- New pressure ulcer
- Higher number of room changes
- Polypharmacy
- Preexisting cognitive impairment
- Prolonged hospital stay
- Psychoactive medication use
- Recent fall
- Restraint use
- Sepsis
- Sleep deprivation
- Social isolation
- Temperature alterations (hypo- or hyperthermia)
- Transfusion reaction
- Tube feedings
- Urinary tract infection following instrumentation
- Visual or hearing impairment

Figure 5. Risk Factors for Delirium in Hospitalized Older Patients With Cancer

Note. Based on information from Chan & Brennan, 1999; Cricco et al., 2001; Eden et al., 1998; Fann & Sullivan, 2003; Francis et al., 1990; Inouye et al., 1990, 1999; Lawlor & Bruera, 2002; Lawlor, Gagnon, et al., 2000; McCusker et al., 2001; McNicoll et al., 2003; Mentes et al., 1999; Minden et al., 2005; Morrison, 2003; Olofsson et al., 1996; Pompei et al., 1994; Truman & Ely, 2003; Trzepacz, 1996.

Investigation in the palliative care setting has identified preliminary findings that require further study.

- The number of precipitating factors (i.e., more than five) may influence the development of confusion (Sarhill et al., 2001).
- Specific underlying pathologies may be associated with different variants of confusion (e.g., hyperactive confusion may be triggered by hepatic failure, opioids, and steroids, whereas hypoactive confusion may be associated with the metabolic sequelae of dehydration) (Morita, Tei, et al., 2001; Morita et al., 2003b).
- The prominence of delirium may be affected by the type of opioid used, the dose, and the rotation with other opioids (Bruera, Franco, Maltoni, Watanabe, & Suarez-Almazor, 1995; Maddocks, Somogyi, Abbott, Hayball, & Parker, 1996; Morita et al., 2005).
- The presentation of delirium may be influenced by the stage of cancer when delirium is diagnosed (Lawlor, 2002) (e.g., opioid-related cognitive dysfunction with mild symptoms frequently is subtle when it occurs in early-stage cancer, whereas opioid-related, later-stage delirium, with its blatant behavioral manifestations, occurs predominantly in patients with advanced cancer).
- The degree of hydration during terminal conditions may influence delirium's prominence and intensity (Bruera et al., 1995).
- The circadian distribution of analgesia during times of clinical cognitive impairment has not been investigated (Gagnon et al., 2001).
- The phenomenon of delirium-event recall (a patient's ability to remember the distressing characteristics of his or her altered cognition) as a measure of patient distress warrants study (Breitbart, Gibson, et al., 2002).
- An attempt should be made to quantify costs related to mis- or undermanaged delirium in acute care (Leslie et al., 2005; Naughton et al., 2005).

Also of importance is the investigation of families' coping experiences during episodes of delirium (Zhukovsky, Abdullah, Richardson, & Walsh, 2000). Their responses to refractory delirium and the association with complicated bereavement as well as elucidation of the components of caregiver burden require investigative inquiry.

Conclusion

Delirium frequently is unrecognized, misdiagnosed, and undertreated. It generates major symptomatic distress for patients and formidable anxiety in families, as well as poses management challenges for healthcare teams (Lawlor & Bruera, 2002). It is a prevalent and toxic condition among ill, older patients and is particularly problematic for older adults with cancer.

Oncology nurses play a major role in reducing symptom distress in cancer care. The frequency and consistency of interactions with patients over time make nurses critical in recognizing and ameliorating the neglected symptom. Nursing opportunities prevail in educating, intervening, and researching the problem of delirium (Boyle et al., 1992). In doing so, oncology nurses can help champion the need for addressing symptom management in this frequently ignored cohort of patients with cancer.

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